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Medical Devices
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AI & Software

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Intellectual Property Showcase | Therapeutics

EDITION Th1

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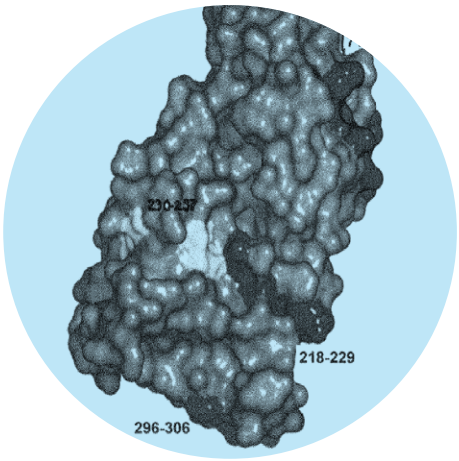
Allergy Antibodies

PATENT TITLE

Antibody-Mediated Modulation of Allergy

PATENT # US 8,883,154

INVENTORS | Randall M. Goldblum, Terumi Midoro-Horiuti, Bo Ning, Ruby Tiwari



PROBLEM

Hypersensitivity to aeroallergens is a major cause of allergic diseases including bronchial asthma, allergic rhinitis, and allergic conjunctivitis. This group of diseases affects up to 30% of the population. Symptoms cause extensive morbidity, lost productivity, and increased health care costs.

Altered regulation of IgE antibody formation is the hallmark of the allergic diathesis. Normal individuals exposed to inhaled aeroallergens produce small amounts of IgG1 and IgG4 antibodies in association with proliferation of T helper 1 (Th1) cells. Patients with an allergic diathesis tend to have exaggerated responses of their T helper 2 (Th2) cells and produce large amount of allergen specific IgE. The process of allergic sensitization also depends on the amount, duration, and group of allergen exposures. Allergic or atopic individuals typically have elevated serum IgE concentrations and IgE antibodies to multiple epitopes of several environmental allergens. When the IgE near the mucosal surface reaches a threshold concentration and is directed against an adequate number of epitopes on the allergen, an allergic reaction can ensue.

Since avoidance of allergens is usually not a practical approach for managing hypersensitivity to outdoor plants, pharmacological therapy with antihistamines, leukotriene antagonists, and topical steroids are the mainstays of current therapy. These modalities have their limitations and adverse effects. Preventive or therapeutic immunization holds the greatest promise of preventing and treating acute hypersensitivity diseases. However, current allergy immunotherapy requires frequent injection of increasing amounts of crude extracts of the offending allergen and takes months to years to become effective. There is a critical need for the identification of effective therapeutic agents that can prevent allergens from inducing allergic reactions.

SOLUTION

This novel technology provides monoclonal antibodies to allergens for use in the prevention of allergic symptoms.

POTENTIAL IMPACT

This technology overcomes the limitations of current pharmacological and immuno-therapies. The technology can greatly reduce the time associated with developed immunity and reduce both health care costs and lost productivity costs.

PATENT DETAILS

ADHD & HPA Treatment

PATENT TITLE

Methods and Compositions for the Treatment of Attention Deficit Hyperactivity Disorder and Hyperphenylalanemia

PATENT # US 8,124,653

INVENTORS | Reuben Matalon, Ofer Matalon

PROBLEM

Attention deficit hyperactivity disorder (ADHD) is a condition characterized by a decreased attention span, hyperactivity, and/or impulsiveness inappropriate for a certain age. Typically, young children have what are known as subtle neurological signs of immaturity. These are involuntary movements of one part of the body that occur while the child is making a voluntary movement of another part of the body.

Despite a complete understanding of the cause of ADHD, current pharmacological options have been found to be ineffective in controlling the condition. Specifically, ADHD has been treated with pharmacological agents that mimic catecholamine or serotonin.

Hyperphenylalaninemia (HPA) is the presence of elevated levels of phenylalanine in the blood, which may result in brain damage and other pathologies. HPA is typically caused by defect(s) in either the BH4 synthetic pathway or the phenylalanine metabolic pathway. Although progress in the neurosciences has been both rapid and broadly based, it has offered little to the practicing pediatrician regarding treatment of HPA.

None of the current methods for the treatment of ADHD and HPA are entirely satisfactory. Therefore, there is a critical need for new and more effective methods and compositions for treating these diseases.

SOLUTION

This novel technology provides methods and compositions for treating attention deficit hyperactivity disorder and hyperphenylalanemia with oftetrahydrobiopterins, an enzymatic co-factor, using a controlled, sustained, or time-release formulation.

POTENTIAL IMPACT

The technology overcomes many of the limitations and complications associated with simulant and amphetamine treatments currently in use.

PATENT DETAILS

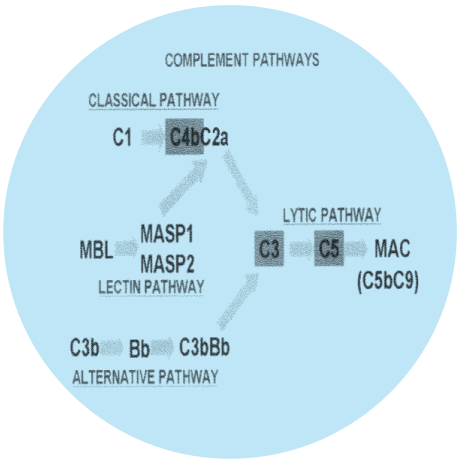
Autoimmune Treatment

PATENT TITLE

Methods and Materials for Treating Autoimmune and/or Complement Mediated Diseases and Conditions

PATENT # US 8,501,705

INVENTORS | Premkumar Christadoss, Erdem Tuzun



PROBLEM

Myasthenia gravis (MG), an autoimmune neuromuscular disease, afflicts about 60,000 individuals in the United States and about 1,250,000 individuals worldwide. Neuromuscular transmission fails in MG because of decreased sensitivity of the postsynaptic membrane to the neurotransmitter acetylcholine (ACh), which results from a loss of acetylcholine receptors (AChRs) due to a T-cell and B-cell mediated autoimmune attack against the AChR. Pemphigus, a group of autoimmune blistering diseases of the skin and/or mucous membranes, afflicts about 12,000 individuals in the United States and about 250,000 individuals worldwide. Autoimmune hemolytic anemia, a condition in which the immune system attacks the red blood cells, resulting in fewer of these oxygen-transporting cells, afflicts about 12,000 individuals in the United States and about 280,000 individuals worldwide. Idiopathic thrombocytopenic purpura, a bleeding disorder characterized by the destruction of platelets by the immune system, resulting in too few platelets in the blood, afflicts about 12,000 individuals in the United States and about 250,000 individuals worldwide. Autoimmune glomerulonephritis, a nephritis which is accompanied by inflammation of the capillary loops in the glomeruli of the kidney, afflicts about 60,000 individuals in the United States and over a million individuals worldwide.

Many autoimmune diseases are treated using non-specific immunosuppressive drugs, such as steroids. However, steroids can have long-term side-effects and can suppress desirable immune responses. There is a critical need for methods and compositions to expand treatment options.

SOLUTION

This novel technology provides methods and compositions for treating autoimmune and/or complement-mediated diseases including myasthenia gravis. The technology provides a composition which inhibits a subject's classical complement pathway and can also be used to suppress transplant rejection.

POTENTIAL IMPACT

The technology provides for expanded treatment option of autoimmune disease and expands access to care. The technology overcomes the side-effects of current drug standards such as steroids. The technology will lead to a reduction in costs related to autoimmune disease treatments and maintenance, while providing better health outcomes.

PATENT DETAILS

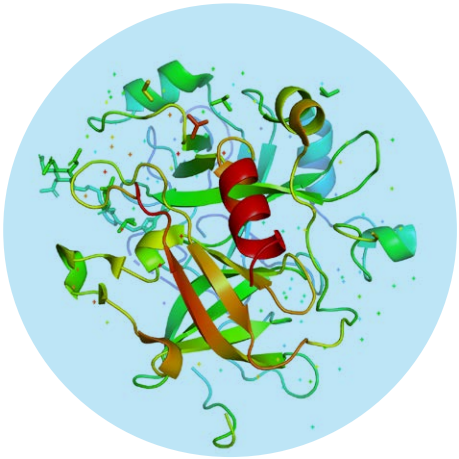
Acetylcholine Receptor Conjugates

PATENT TITLE

Methods and Compositions Related to Acetylcholine Receptor Conjugates

PATENT # US 8,530,245

INVENTORS | Premkumar Christadoss, Windy R. Allman



PROBLEM

Myasthenia Gravis is a chronic autoimmune condition characterized by fluctuating voluntary muscle weakness. Antibodies to acetylcholine receptors (AChR) destroy AChR in the neuromuscular junctions leading to MG. Symptoms of MG include fatigue, muscle weakness, double vision, drooping eyelids, and difficulty chewing or swallowing and in severe disease paralysis and respiratory distress. Currently, diagnosis of MG involves a combination of clinical history, nerve stimulation tests, and blood test for serum antibodies against AChR. Although serum antibodies to AChR are diagnostic for MG, the antibody titer does not correlate with disease severity and around 15% of patients with MG do not have serum antibodies to AChR. There is a critical need for new methods and compositions that are both reliable and convenient for diagnostic testing.

SOLUTION

This novel technology provides enhanced methods and compositions for the detection of autoreactive immune cells (B cells) that recognize the acetylcholine receptor.

POTENTIAL IMPACT

The technology provides a better marker to evaluate the clinical effectiveness of specific MG drug candidates. The technology also greatly reduces the time for diagnostic testing from two days to about an hour. These methods and compositions enable any hospital or institution having a Fluorescence-activated cell sorting machine to perform the testing. These technology aspects will provide greater access to care, reduce costs, and provide better health outcomes.

PATENT DETAILS

Amyloid Oligomer Antibodies

PATENT TITLE

Antibodies that Bind Amyloid Oligomers

PATENT # US 9,895,429

INVENTORS | Rakez Kayed

PROBLEM

Certain protein sequences can form aberrant, misfolded, insoluble aggregates known as amyloid fibrils. These amyloid fibrils are amyloid diseases of genetic, infectious and/or spontaneous origin, including spongiform encephalopathies, Alzheimer's disease (AD), Parkinson's disease (PD), type II diabetes, Huntington's disease, and various prion diseases. Amyloid fibrils lead to the development of amyloid plaques.

Amyloid peptides are the principal constituent of amyloid plaques. In the case of AD, the peptides are termed A or -amyloid peptide. A peptide is an internal fragment of amyloid precursor protein (APP). Several mutations within the APP protein have been correlated with the presence of AD. Such mutations are thought to cause AD by producing an increased or altered processing of APP to A. The processing of APP resulting in accumulation of the longer forms of A is thought to be important in the cause of AD. Mutations in other genes are thought to indirectly affect processing of APP.

It is believed that cytotoxic amyloid-beta peptide aggregates disrupt the integrity of cell membranes and elaborate reactive oxygen intermediates, thereby giving rise to elevations in cytosolic calcium and eventual cell death. Cell surface receptors for amyloid-beta peptide may also activate signal transduction mechanisms.

Prefibrillar aggregates may be more pathologically significant than other forms of the amyloid peptides and therefore may be a more desirable target for detection and treatment. There remains a critical need for the development of agents that bind or inhibit toxic forms of amyloid.

SOLUTION

This novel technology provides methods and compositions related to amyloid oligomers and amyloid oligomer specific antibodies. These antibodies can be utilized to analyze amyloid oligomers from patients with, or suspected of having, amyloid related diseases such as Alzheimer's disease (AD) and many other neurodegenerative diseases.

POTENTIAL IMPACT

The antibodies specifically bind conformational epitopes of an oligomer and do not bind soluble amyloid beta or amyloid-beta fibrils. The technology provides new and improved methods of diagnosis for neurodegenerative disease and can act as a platform for disease specific drug discovery.

PATENT DETAILS

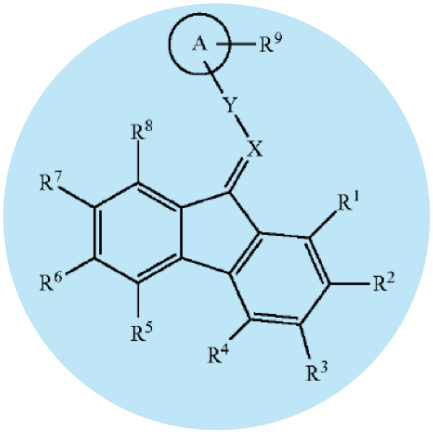
BAX Agonist for Cancer

PATENT TITLE

BAX Agonist, Compositions, and Methods Related Thereto

PATENT # US 9,040,567
 # US 9,402,850 (ASSOC.)

INVENTORS | Xingming Deng, Jia Zhou, Chunyong Ding



PROBLEM

BAX, a member of the BCL-2 (B-cell lymphoma-2) family, is a nuclear-encoded protein that pierces the mitochondrial outer membrane to mediate cell death by apoptosis. BAX adopts a globular alpha-helical structure and converts into pore-forming protein by changing conformation and assembling into oligomeric complexes in the mitochondrial outer membrane. Proteins from the mitochondrial intermembrane space then empty into the cytosol to activate proteases that degrade the cell.

The expression of BAX appears to play an important role in suppressing cancer development and decreased BAX levels contribute to chemoresistance in several cancers including, but not limited to, lung cancer, chronic lymphocytic leukemia (CLL), and prostate cancer. Because BAX is extensively expressed in both small cell lung cancer and non-small cell lung cancer cells, BAX agonists could be particularly useful for treating lung cancer. Thus, there is a need to identify compounds that activate BAX.

SOLUTION

Novel BAX agonists have been developed for treating and preventing cancer, such as lung cancer. These BAX agonists include multiple compounds, derivatives, prodrugs, or esters of compounds.

POTENTIAL IMPACT

The development of these novel BAX agonists provides a new frontline treatment option for lung, leukemia, and prostate cancers. These agonists can play critical roles in the development of personalized/precision medicine for cancer patients.

PATENT DETAILS

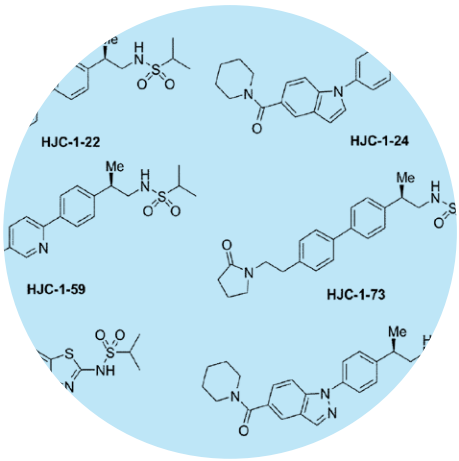
AMPA Receptor Modulators

PATENT TITLE

Bivalent AMPA Receptor Positive Allosteric Modulators

PATENT # US 9,328,125

INVENTORS | Jia Zhou, Haijun Chen, Kenneth M Johnson, Cheng Z Wang



PROBLEM

The positive allosteric modulator of AMPA receptors (AMPARs) are a major class of ionotropic glutamate receptors that mediate the fast excitatory synaptic transmission in the brain. The interdependency between AMPARs and N-methyl-D-aspartate receptors (NMDARs) makes AMPARs a promising target for therapeutic intervention of NMDAR-mediated glutamatergic hypofunction. AMPAR activation is essential for NMDAR neurotransmission. NMDAR activation is crucial for the recruitment of AMPA receptors to the membrane at activated synaptic sites. Direct activation of glutamate receptors by agonists to correct glutamatergic hypofunction increases the risk of excitotoxicity and additional neuronal damage.

AMPAR positive allosteric modulators (PAMs) do not activate the receptor directly but have been shown to increase receptor affinity for agonist, reduce receptor desensitization and deactivation, and enhance the induction of LTP. AMPAR PAMs also improve performance in a radial arm maze task assessing spatial working memory, and robustly ameliorate ketamine-induced impairment of working memory.

Discovery of new AMPAR PAMs aimed at correcting NMDAR-mediated glutamatergic hypofunction is critically needed to moderate or prevent situations associated with diminished NMDAR function. Therefore, bivalent AMPAR PAMs can be used as therapeutics for cognitive abnormalities involving glutamatergic hypofunction including schizophrenia, Alzheimer's disease, Parkinson's disease, addiction, and attention deficit hyperactivity disorder (ADHD).

SOLUTION

This novel technology provides specific bivalent positive allosteric modulators (PAMs) of AMPA receptor (AMPAR) that will enhance glutamatergic neurotransmission, and in turn, prevent the effects of phencyclidine (PCP), a selective NMDA open channel blocker on developmental neuroapoptosis.

POTENTIAL IMPACT

The newly identified AMPAR PAMs will help compensate for diminished excitatory neurotransmission in the treatment of human cognitive deficit diseases, including schizophrenia and Alzheimer's.

PATENT DETAILS

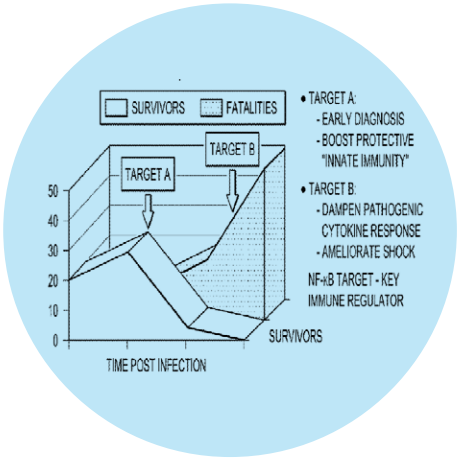
Bioweapon Risk Reduction

PATENT TITLE

Structure Based and Combinatorially Selected Oligonucleoside Phosphorothioate and Phosphorodithioate Aptamer Targeting AP-1 Transcription Factors

PATENT # US 9,567,579

INVENTORS | David G. Gorenstein, Bruce A. Luxon, James Leary, Xianbin Yang



PROBLEM

Virtually all organisms have nuclease enzymes that 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. It has been shown, however, that phosphoromonothioate or phosphorodithioate modifications of the DNA backbone in oligonucleotides can impart both nuclease resistance and enhance the affinity for target molecules.

Recent world events have heightened the awareness of possible bioterrorist threats. Hemorrhagic fever viruses have reportedly been weaponized by the former Soviet Union and the United States. Despite the awareness of the potential of Viral Hemorrhagic Fever viruses, Encephalitic viruses, and other agents both as bioweapons and as emerging viral diseases, few therapeutic options are available to those infected. Apart from supportive therapy, the only drug for treating Arenavirus infections is Ribavirin and it is only partially effective. There is an urgent need to expand the current therapeutic options specifically designed against the mechanisms of viral pathogenesis.

SOLUTION

This novel technology provides methods for the use of Thio-aptamers™ to prevent Arenavirus and Flavivirus induced perturbations of the host response that lead to disease. The technology provides for novel therapeutic interventions for the treatment of hemorrhagic fevers, encephalitic viruses, and other viral infections.

POTENTIAL IMPACT

The technology fills a therapeutic void associated with many dangerous and deadly diseases. These therapeutics can offset the risk of these viruses being used in a nefarious manner or as an emerging epidemic.

PATENT DETAILS

BIAFAC Therapeutics

PATENT TITLE

Compositions and Methods for Detecting and Treating Brain Injury Associated Fatigue and Altered Cognition (BIAFAC)

PATENT # US 10,980,847

INVENTORS | Randall Urban, Melinda Sheffield-Moore, Richard Pyles, Brent Masel

PROBLEM

Following traumatic brain injury (TBI) or other central nervous system (CNS) maladies (e.g., stroke or hemorrhage), patients develop a clinical syndrome characterized by fatigue, altered cognition, chronic inflammation and altered amino acid absorption. Unfortunately, current treatments for these conditions involve daily injections of expensive recombinant human growth hormone that treats the syndrome but does not produce a lasting cure. However, a need remains for tests and treatments for brain injury associated fatigue and altered cognition resulting from diseases or conditions that cause decreased cognition.

SOLUTION

Novel technologies have been developed for detecting and treating brain injury associated fatigue or altered cognition (BIAFAC). This technology identifies patients in need of treatment for brain injury associated fatigue or altered cognition associated with an altered intestinal flora and provides patients with a composition that promotes beneficial bacteria in the intestinal flora.

POTENTIAL IMPACT

This novel technology will provide less expensive and less invasive treatment options for BIAFAC. This is a more natural approach dealing with the intestinal flora, perhaps reducing side effects as compared to the standard, invasive treatment.

PATENT DETAILS

Colon Cancer Treatment

PATENT TITLE

Compositions and Methods for Treating Colon Cancer

PATENT # US 9,308,206

INVENTORS | Satish K Srivastava, Kota V Ramana

PROBLEM

Aldose reductase (AR) is a monomeric protein belonging to the aldo-keto reductase (AKR) superfamily. Aldose reductase is a broad specificity oxidoreductase catalyzing the reduction of a structurally diverse range of aldehydes, including medium to long chain aldehydes, glucose and other aldo-sugars, aldehyde metabolites of neurotransmitters, isocorticosteroid hormones, and a variety of xenobiotic aldehydes to their corresponding alcohols. Reduction of glucose to sorbitol by aldose reductase constitutes the first and rate-limiting step of the polyol pathway that converts glucose to fructose via sorbitol dehydrogenase. Although this pathway usually represents a minor route of glucose metabolism, its activation during diabetes has been linked to the development of several clinically significant secondary complications such as nephropathy, neuropathy, retinopathy, and cardiovascular related complications. Several drugs that inhibit aldose reductase have been shown to prevent hyperglycemia-induced changes.

In addition to glucose, it has been shown that aldose reductase catalyzes the reduction of multiple biologically active aldehydes generated by the peroxidation of membrane lipids and lipoproteins or during glucose and amine metabolism. The aldehyde detoxifying role of aldose reductase is supported by the observation that inhibition of the enzyme increases the

accumulation of lipid peroxidation products that cause cytotoxicity. The most abundant and toxic lipid peroxidation product is 4-hydroxy-trans-2-nonenal which is efficiently reduced by aldose reductase in vitro and in vivo.

SOLUTION

This novel technology provides methods of treating colon cancer using an aldose reductase inhibitor to inhibit colon cancer cell proliferation.

POTENTIAL IMPACT

The technology greatly expands the very limited colon cancer treatment options and gives patients a viable and accessible treatment option other than invasive and life-altering resection surgery.

PATENT DETAILS

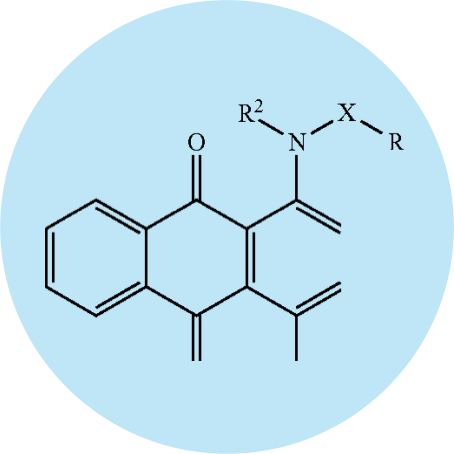
BH4 Antagonist Cancer Therapy

PATENT TITLE

BH4 Antagonists and Methods Related Thereto

PATENT # US 9,980,936

INVENTORS | Xingming Deng, Jia Zhou, Chunyong Ding



PROBLEM

The overall survival for non-small cell lung cancer (NSCLC) is about 16%, whereas for SCLC, overall survival is 6%. Overcoming resistance of lung cancer to either chemo-radiotherapy or epidermal growth factor receptor (EGFR) targeted therapy would prove to be a significant achievement. B-cell lymphoma 2 protein (Bcl-2) is a member of the Bcl-2 family of apoptosis regulator proteins. Bcl-2 is extensively expressed in various types of cancer. One major factor implicated in the resistance of cancer to chemotherapy is the overexpression of Bcl-2 and Bcl-2-like proteins. The BH4 domain of Bcl-2 has been demonstrated to be a required domain for Bcl-2's anti-apoptotic function, which is associated with increased chemo-resistance of cancers. Bcl-2 is extensively expressed in both SCLC and NSCLC cells.

EGFR has been identified as an important therapeutic target for the treatment of NSCLC because more than 60% of NSCLC patients express EGFR. EGFR inhibition by EGFR-tyrosine kinase inhibitors (TKis) (i.e., erlotinib or gefitinib) represents a promising approach for lung cancer therapy. Unfortunately, patients who initially benefited from erlotinib therapy developed acquired resistance to erlotinib after 6-12 months. The mechanisms are not fully understood, but may be associated with activation of EGFR-independent pathways, occurrence of additional EGFR gene mutations, or loss of the target.

In addition to acting as an anti-apoptotic protein, Bcl-2 can also promote tumor angiogenesis. Under hypoxia Bcl-2 promotes hypoxia-inducible factor-I (HIF-1)-mediated vascular endothelial growth factor (VEGF) expression in melanoma and breast carcinoma. Mutations at the BH4 domain abrogate the ability of Bcl-2 to induce VEGF protein expression and transcriptional activity under hypoxia in human melanoma cells and other human tumor histotypes, such as colon, ovarian and lung carcinomas. BH4 peptide is sufficient to increase HIF-la protein half-life impairing HIF-1a protein ubiquitination and enhance VEGF secretion in melanoma cells exposed to hypoxia. HIF-1a is overexpressed in many tumor types.

SOLUTION

This novel technology provides methods and compositions for the treatment of a broad range of cancers. The compositions include mTOR inhibitors in combination with BH4 inhibitors.

POTENTIAL IMPACT

The technology can broaden the treatment options for a variety of deadly cancers and overcome some of the chemo-radiotherapy resistance seen in these types of cancers.

PATENT DETAILS

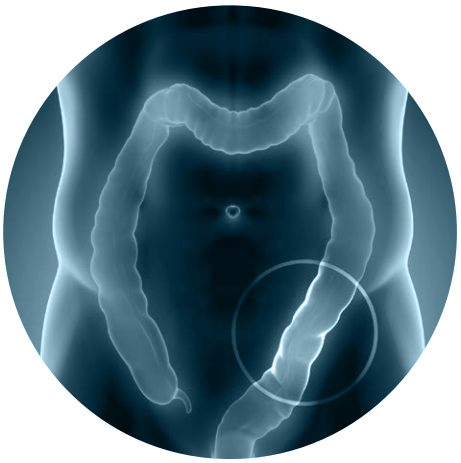
Colorectal Cancer Therapeutic

PATENT TITLE

Use of Hydrogen Sulfide Synthesis Inhibitors for Cancer

PATENT # US 10,335,382

INVENTORS | Mark Hellmich, Jia Zhou, Csaba Szabo



PROBLEM

Colorectal cancer is a common form of cancer, the incidence of which is increasing worldwide. Various methods, including fecal occult blood test and colonoscopy, are currently used for screening colorectal cancer, and have increased the rates of detection for early-stage cancer. Colorectal cancer has proven resistant to chemotherapy, although limited success has been achieved using a combination of 5-fluorouracil and levamisole. Surgery has had the largest impact on survival and, in some patients with limited disease, achieves a cure. However, surgery removes bulk tumor, leaving behind microscopic residual disease, which may ultimately result in recurrence. Thus, there remains a need for additional compositions and methods for treating colorectal cancer.

SOLUTION

A new class of hydrogen sulfide biosynthesis inhibitors has been developed to treat colorectal cancer. Methods for this novel technology include prodrug compositions and prodrug administration.

POTENTIAL IMPACT

Currently, there are limited options for the treatment of colorectal cancer. This technology will offer a new treatment option and provide an added layer of hope to those suffering this very horrible, and increasingly frequent, disease. The combination of this technology with other interventions can provide a longer and better overall survival rate.

PATENT DETAILS

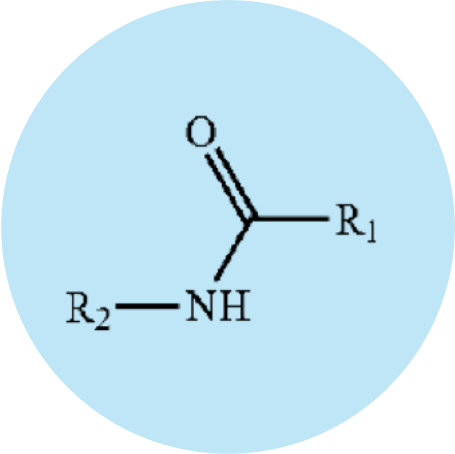
Cancer Reduction by Substituted Amides

PATENT TITLE

Substituted Amides for Treating and Preventing Cancer

PATENT # US 10,457,662

INVENTORS | Nouri Neamati, Jia Zhou, Yuting Kuang, Na Ye



PROBLEM

Cancer is the second most common cause of death in the United States, exceeded only by heart disease. In the United States, cancer accounts for 1 of every 4 deaths. The 5-year relative survival rate for all cancers patients diagnosed in 1996-2003 is 66%, up from 50% in 1975-1977. This improvement in survival reflects progress in early stage diagnosis and improvements in treatment.

QN519 has been identified as a promising anticancer compound through a phenotypic screen of a 20,000 small molecules library representing five million compounds. QN519 represents a novel scaffold with drug-like properties and shows potent in vitro cytotoxicity in a panel of 12 cancer cell lines. Subsequent experiments involved performance of a lead optimization campaign to synthesize a series of novel analogs. Fifty novel analogs were tested in three pancreatic cancer cell lines using MTT assay. Sixteen compounds produced IC50 values <l μM in at least one cell line. One of the optimized compounds, QN523 showed significant in vivo efficacy in a pancreatic cancer xenograft model. No symptoms of gross toxicity such as weakness, weight loss or lethargy were observed in the QN523 treatment group. H&E-stained organ sections of liver, kidney, heart, lung, spleen, and pancreas did not reveal significant histopathological changes, further confirming the safety of the treatment. QN523 treatment was shown to significantly increase the expression of GDF15, ATF3, DDIT3 and HSPA5 genes, indicating activation of the stress response pathway. A significant decrease in the expression of WIPil, GABARAPLI and MAP1LC3B was also observed implicating autophagy as a major mechanism of action.

SOLUTION

This novel technology provides methods and compositions having a quinolin-8-yl-nicotinamide structure that inhibit the growth of cancer cells or supporting cells outright and/or render such cells as a population more susceptible to the cell death-inducing activity of cancer therapeutic drugs or radiation therapies.

POTENTIAL IMPACT

Because of the lack of effective treatments for pancreatic cancer, discovery of novel agents such as QN519 and QN523 will offer new and improved treatment options and will help improve existing treatment options when administered together. The expansion of treatment options and treatment access will provide hope to many patients fighting deadly cancers such as pancreatic cancer.

PATENT DETAILS

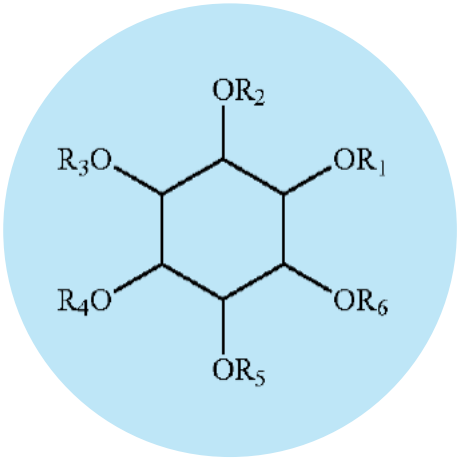
Clostridium difficile Treatment

PATENT TITLE

S-Nitrosylation of Glucosylating Toxins and Uses Therefor

PATENT # US 9,770,500

INVENTORS | Tor C. Savidge, Jonathan Stamler



PROBLEM

Clostridium difficile (C. difficile) infection (CDI) is the most prevalent cause of hospital-acquired infectious diarrhea and life-threatening colitis worldwide. Two large exotoxins, TcdA (308 kDa) and TcdB (270 kDa), are secreted from most C. difficile bacterial strains that cause disease in humans, and there is little ambiguity that these toxins are pathogenic since toxin-deficient strains are avirulent. The clostridial glucosylating toxins and the multifunctional autoprocessing repeats-in-toxins (MARTX) share a common virulence mechanism for cell entry that represents a potential target for therapeutic intervention. Cellular internalization of these exotoxins is dependent on cytosolic inositol hexakisphosphate (InsP6) allosteric cofactor, which activates an autocatalytic cysteine protease domain to facilitate toxin selfcleavage. Intracellular release of the smaller N-terminus glucosyltransferase effector domain results in the mono-O glucosylation of small GTPases of the Rho family, including RhoA, Rad, and Cdc42. Glucosylation of Rho proteins inhibits their molecular switch function, thus blocking Rho GTPase-dependent signaling in intestinal epithelial cells, leading to alterations in the actin cytoskeleton, fluid secretion, acute inflammation, and necrosis of the colonic mucosa.

Host defense mechanisms that might be employed to protect against the clostridial glucosylating toxins are not well defined, although C. difficile toxins are potent inducers of nitric oxide (NO), which is known to be protective against these toxins. However, the precise molecular mechanism for the protective effects of NO remains unknown. Some diverse signaling cascades associated with NO production are attributed to S-nitrosothiol (SNO) species that act via covalent modification of specific cysteine residues in target molecules (S-nitrosylation) and aberrant S-nitrosylation may play a role in disease etiology. There remains a critical need for alternative therapies for infections by toxins such as Clostridium difficile.

SOLUTION

This novel technology provides methods and pharmaceutical compositions which act as allosteric therapeutics for microbial infections and associated glucosylating toxins. The technology provides protection against or ameliorate of the effects of cellular intoxication by pathogenic cysteine proteases.

POTENTIAL IMPACT

The technology provides improved treatment options for treating Clostridium difficile infection. The technology greatly expands access to care and will help reduce both clinical and societal costs associated with this type of infection.

PATENT DETAILS

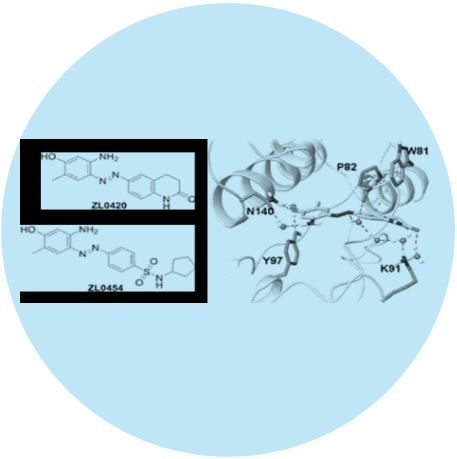
BRD4 Inhibitors

PATENT TITLE

Inhibitors of Bromodomain-Containing Protein 4 (BRD4

PATENT # US 11,117,865

INVENTORS | Jia Zhou, Allan R. Brasier, Bing Tian, Zhiqing Liu, Haiying Chen, Erik Rytting



PROBLEM

The bromodomain, a highly conserved motif of 110 amino acids, is found in proteins that interact with chromatin, such as histone acetylases, transcription factors and nucleosome remodeling complexes. Bromodomain-Containing Protein 4 (BRD4), belonging to bromodomain and extra-terminal proteins (BET) family (BRD2, BRD3, BRD4 and BRDT), contains two bromodomains and functions as a chromatin reader that binds acetylated lysine in histones. It is an epigenetic reader and a critical regulator of transcription in many cell types. BRD4 plays an important role in the regulation of cell cycle control and transcription elongation mediated by interactions with P-TEFb. BRD4 is recently identified as a cancer therapeutic target for Basal-like breast cancer, NUT midline carcinoma (NMC), acute myeloid leukemia, multiple myeloma, and Burkitt's lymphoma.

BRD4 also has an essential role in the induction of inflammatory gene transcription. BRD4 is associated with nuclear factor-KB (NF-KB) signaling pathway via specific binding to acetylated RelA to stimulate NF-KB-dependent inflammatory response. BRD4 is reported as a potential therapeutic target for patients with fibrotic complications.

BRD4 is crucial to neuronal function and mediates the transcriptional regulation underlying learning and memory. The loss of BRD4 function affects critical synaptic proteins, which results in memory deficits. Most recently, BRD4 was validated as an in vivo target for the treatment of pulmonary fibrosis associated with inflammation-coupled remodeling in chronic lung diseases. Therefore, targeting BRD4 represents a novel therapeutic method for a variety of different human diseases.

SOLUTION

This novel technology provides methods and compositions for small molecule selective inhibitors of the BRD4 bromodomain. The technology modulates the bronchiolar NFKB-BRD4 axis, which plays a role in acute neutrophilic response to viral molecular patterns.

POTENTIAL IMPACT

The technology provides more selective inhibitors to facilitate isoform and/or domain specificity to avoid unwanted clinical side effects in treatment. These novel potent and specific BRD4 inhibitors that do not cross the blood-brain barrier (BBB) may hold promise as therapeutics benefiting cancer and inflammation or infectious diseases patients, while displaying less risk of neurological adverse effects.

PATENT DETAILS

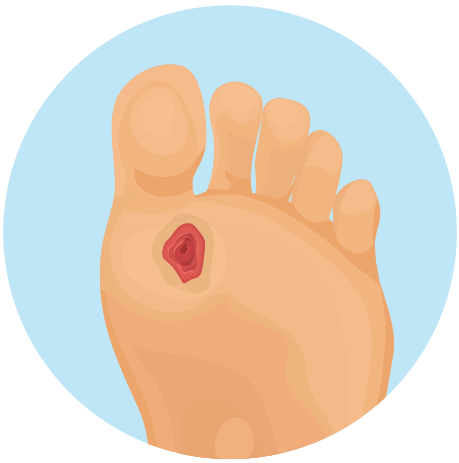
Dermal Ulcer Treatment

PATENT TITLE

Methods of Treating Dermal Ulcers with Thrombin Derived Peptides

PATENT # US 7,833,982

INVENTORS | Darrell H. Carney



PROBLEM

Dermal skin ulcers are an example of wounds that are particularly difficult to treat because they resist healing and consequently often become chronic wounds. Examples of chronic dermal ulcers include those resulting from venous disease (venous stasis ulcers), excessive pressure (decubitus ulcers), arterial ulcers and diabetic ulcers.

Diabetic ulcers are particularly problematic. One in seven individuals with diabetes develops dermal ulcers on their extremities, which are susceptible to infection. Treatment of diabetic ulcers is often prolonged, intensive, and costly with treatment failures common. Current approaches include debridement, frequent changes of wound dressings, specially fitted footwear, oral or intravenous antibiotics, complete bed rest, lengthy hospitalization, and surgical revascularization. Ulcer-related complications can, in some cases, require amputation. Therefore, there is a critical need for treatments which accelerate the rate of the healing of chronic dermal skin ulcers.

SOLUTION

This novel technology provides agonists of the non-proteolytically activated thrombin receptor effective in accelerating the rate of healing of diabetic ulcers. The thrombin peptide derivative TP508, administered topically twice a week at doses of 1.0 µg or 10.0 µg increased the rate at which diabetic ulcers healed and increased the percentage of patients who experienced 100% closure of the ulcer.

POTENTIAL IMPACT

The thrombin peptide derivatives are inexpensive to produce and are effective in accelerating the rate at which chronic dermal skin ulcers heal and in increasing the likelihood of complete closure of the ulcer. The technology overcomes limitations of the current standard of care.

PATENT DETAILS

Delivery to the Brain

PATENT TITLE

Methods and Compositions for Delivering Enzymes and Nucleic Acid Molecules to Brain, Bone and Other Tissues

PATENT # US 7,807,618

INVENTORS | Reuben Matalon

PROBLEM

A wide variety of diseases and other conditions are caused by deficiencies in certain tissue enzymes. A variety of methods have been proposed for treating enzyme deficiency. One such method is enzyme replacement therapy, where exogenous enzyme is delivered to the tissue with the deficiency. Current enzyme replacement therapy methods have not been successful when treating diseases associated with the brain or in bone. Another way of treating enzyme deficiency diseases is by gene therapy where exogenous gene encoding the deficient enzyme is introduced to the tissue. Once delivered to the desired tissue, the enzyme is produced in situ by expression of the exogenous gene. However, delivery of exogenous genes to the brain, and to bone, has proven to be problematic.

Difficulties delivering enzymes and genes, as well as other large biologically active materials, to the brain is the result of the inability of such large biologically active materials to cross the brain capillary wall which forms the blood-brain barrier (BBB). The existence of the BBB frequently necessitates administering the large biologically active materials, such as enzymes and exogenous genes, intracerebrally (e.g., via craniotomy). Intracerebral administration requires specialized skills and renders the brain more susceptible to infection. There remains a critical need for increasing the permeability of the blood-brain barrier and for methods of delivering large biologically active materials, such as enzymes and nucleic acid molecules, to the brain and to bone.

SOLUTION

This novel technology provides systems and methods for delivering an enzyme or nucleic acid to a subject's brain, bone, and/or tissue. The method includes administering a hyaluronidase to the subject, along with the large bioactive material, which increases the permeability of the blood-brain barrier.

POTENTIAL IMPACT

This technology provides a novel solution to the administration of large biologically active compounds across the blood brain barrier. The technology opens new therapeutic opportunities to treat rare and dangerous diseases and conditions. This technology will help reduce costs and improve health outcome for patients.

PATENT DETAILS

Degeneration Regeneration

PATENT TITLE

Method of Treating Degenerative Diseases

PATENT # US 8,952,129

INVENTORS | Darrell H. Carney, Randolph C. Steer

PROBLEM

Many diseases or disorders have chronic and/or progressive effects that can occur over a period of years. Degeneration of function occurs with deterioration of the involved tissue cells. There are many examples of degeneration disease including: Huntington's disease, macular degeneration, diabetic retinopathy, scleroderma, optic neuritis, glaucoma.

With the wide array of degenerative diseases and disorders, treatment options are limited and often non-effective. There is a critical need for treatments to reverse, slow or arrest progression of degenerative conditions.

SOLUTION

This novel technology provides non-proteolytically activated receptor (NPAR) agonists, such as thrombin peptide derivatives, that promote apoptosis inhibition in disease related tissue cells, thereby increasing cell and consequently tissue life.

POTENTIAL IMPACT

The technology greatly expands access to treatment and reduction of health care costs. The technology has the potential to improve quality-of-life and extend life expectancy for patients afflicted by a degenerative disease or disorder.

PATENT DETAILS

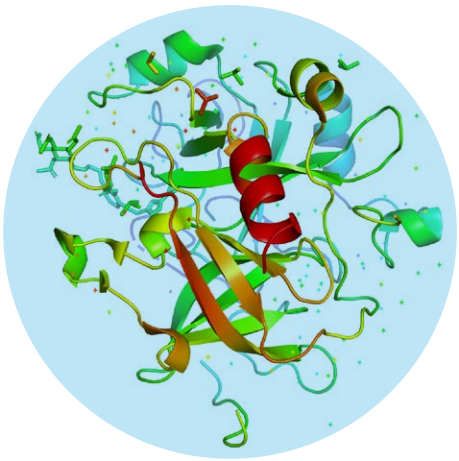
Eating Disorder Therapeutic

PATENT TITLE

Peptide Inhibitors of Serotonin 5-HT2c Receptors: PTEN Interaction

PATENT # US 9,611,292
 # US 10,293,022 (ASSOC.)
 # US 10,544,152 (ASSOC.)

INVENTORS | Kathryn Cunningham, Scott Gilbertson



PROBLEM

Serotonin or 5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter found primarily in the gastrointestinal tract, in platelets, and in the central nervous system. One of its receptors, 5-HT 2C modulate the release of many neurotransmitters and influence various biological and neurological processes such as aggression, anxiety, eating disorders, cognition, learning, memory, mood, nausea, sleep, and thermoregulation.

There is a need for additional therapeutic agents that modulate 5-HT receptors to overcome some of its negative influences on biological and neurological functions.

SOLUTION

New therapeutic agents have been developed to treat addictive disorders and eating disorders. One of the cofactors of the receptor, protein phosphatase and tensin homolog (PTEN), have been shown to be an effective target. These new therapeutics dissociate 5-HT and PTEN or inhibits the association of 5-HT and PTEN, as contrasted with the more traditional approach of inhibiting reuptake of signal molecules. Thus, presenting a novel mechanism, treatment, and therapeutic approach to eating disorders.

POTENTIAL IMPACT

The introduction of the new group of 5-HT therapeutics will provide new avenues for treatment of various eating disorders including anorexia nervosa, bulimia nervosa, weight-gain after smoking cessation, snacking, or binge eating. This treatment will provide life changing improvements to patients dealing with these conditions.

PATENT DETAILS

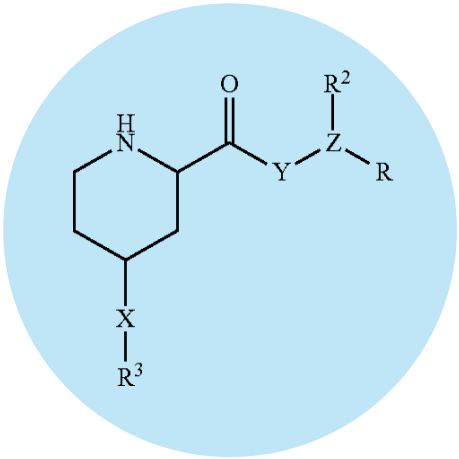
5-HT2CR Allosteric Modulators

PATENT TITLE

Allosteric Modulators of 5-Hydroxytryptamine 2C Receptor (5-HT2CR)

PATENT # US 9,533,973

INVENTORS | Jia Zhou, Chunyong Ding, Kathryn A. Cunningham



PROBLEM

The 5-hydroxytryptamine 2C receptor (5-HT2CR) is involved in a diversity of physiological functions, such as nociception, motor behavior, endocrine secretion, thermoregulation, appetite modulation, and the control of exchanges between the central nervous system and the cerebrospinal fluid. This receptor has also been implicated in numerous pathologies, and the modulation of 5-HT2CR function holds a tremendous amount of therapeutic promise for the treatment of diseases such as addiction, anxiety, depression, obesity/eating disorders, Parkinson's disease, and schizophrenia. Successful development of 5-HT2CR ligands requires selectivity over the highly homologous 5-HT2AR and 5-HT2BR because activity at these receptors can result in significant adverse CNS and cardiovascular events.

Traditional screening for ligands has been optimized to detect standard orthosteric agonists and antagonists. Allosteric modulators of the 5-HT2CR present a novel drug design strategy to augment the response to endogenous 5-HT in a site- and event-specific manner. In addition, there are theoretical reasons that allosteric ligands may be preferred therapeutic chemical targets including the prospects for increased selectivity, better control of physiological systems, and separate control of affinity and efficacy. To date, PNU-69176E, identified via a chemical library screen is the only synthetic compound that has been reported as a selective allosteric modulator of 5-HT2CR; however, the relevant structure-activity relationship (SAR) studies are sparse. There remains a critical need for additional specific allosteric modulators of 5-HT2CR.

SOLUTION

This novel technology provides methods and compositions for the identification and use of allosteric modulators of 5-HT2CR. These compounds include, but are not limited to, a series of piperidine-, piperazine-, and benzazepine-based small molecule 5-HT2CR allosteric modulators.

POTENTIAL IMPACT

Optimization and development of these allosteric 5-HT2CR modulators that bind sites other than the primary ligand binding site generate novel, highly selective, and potent ligands of 5-HT2CR. Such molecules can be used as small molecule probes for the nervous system and as effective therapeutics for a variety of diseases. The technology provides new and effect treatment options that will expand access to care.

PATENT DETAILS

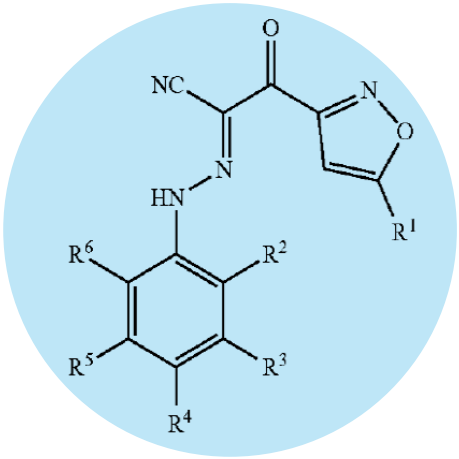
EPAC Antagonists

PATENT TITLE

EPAC Antagonists

PATENT # US 11,124,489

INVENTORS | Jia Zhou, Zhiqing Liu, Na Ye, Fang Mei, Xiaodong Cheng



PROBLEM

Exchange proteins directly activated by cAMP (EPACs) are novel intracellular effector proteins of cyclic adenosine monophosphate (cAMP). Between two ubiquitously expressed intracellular cAMP receptor families, EPAC proteins, unlike PKA, have no kinase activity but act as guanine nucleotide exchange factors to catalyze the exchange of GDP with GTP for the down-stream small GTPases, Rap1 and Rap2, in response to intracellular cAMP. Two structurally homologous but functionally nonredundant isoforms of mammalian EPAC proteins have been identified, EPAC1 and EPAC2.

EPAC1 is more ubiquitously expressed, whereas the expression of EPAC2 is relatively restricted, mainly found in brain, pancreatic islets, and adrenal gland. From nearly two decades of research on EPAC, accumulating studies, including those with the aid of small-molecule EPAC modulators such as various cAMP analogues and newly discovered EPAC-specific antagonists have demonstrated that EPAC proteins play important roles in insulin secretion, energy homeostasis, cardiovascular response, pain sensing, osteoclast differentiation, neurotransmitter release, Treg-mediated immune suppression, integrin-mediated cell adhesion, cell migration and proliferation, cell exocytosis, and apoptosis as well as gene transcription and chromosomal integrity. These EPAC proteins represent potential therapeutic targets for various human diseases such as cancer, bacterial and viral infections, chronic pain, diabetes, obesity, and heart failure.

SOLUTION

This novel technology provides methods and compositions for selectively modulating EPAC, both antagonistically and agonistically.

POTENTIAL IMPACT

The technology provides promising new and effective treatment options for a series of diseases including diabetes, chronic pain, neuropathic pain, peripheral neuropathy, chemotherapy induced peripheral neuropathy heart failure, cancer, atherosclerosis, pathologic inflammation, or neointima formation. The technology will expand access to care and better health outcomes for patients.

PATENT DETAILS

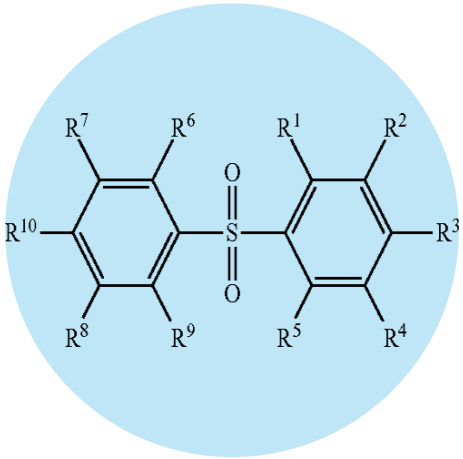
EPAC Modulators

PATENT TITLE

Modulators of Exchange Proteins Directly Activated by cAMP (EPACs)

PATENT # US 9,539,256

INVENTORS | Xiaodong Cheng, Jia Zhou, Tamara Tsalkova, Fang Mei, Haijun Chen



PROBLEM

Identification and development of compounds capable of selectively targeting components of complex cell-signaling networks is a major effort of modern pharmacology. Cyclic adenosine monophosphate (cAMP), a prototypic second messenger, is an important component of cell-signaling networks that control numerous biological processes. In addition to its regulatory functions under physiological conditions, cAMP has been implicated in playing a major role in multiple human diseases, including cancer, diabetes, heart failure, and neurological disorders, such as Alzheimer's disease (AD). Therefore, it is not surprising that current pharmacological therapeutics target the cAMP signaling pathway more than any other pathway.

The major physiological effects of cAMP in mammalian cells are transduced by two ubiquitously expressed intracellular cAMP receptor families: the classic protein kinase A/cAMP-dependent protein kinases (PKAs/cAPKs) and the more recently discovered, exchange proteins directly activated by cAMP/cAMP regulated guanine nucleotide exchange factors (EPACs/cAMP-GEFs). While several pharmacological inhibitors of PKA are available, only a few EPAC specific antagonists/inhibitors have been proposed. There remains a critical need for additional compositions and methods for selectively modulating EPAC1 and/or EPAC2.

SOLUTION

This novel technology provides methods for a sensitive and robust high throughput screening (HTS) assay for the purpose of identifying Exchange Protein Activated by cAMP (EPAC) specific inhibitors to be used as drug candidates.

POTENTIAL IMPACT

These EPAC specific inhibitors will not only provide a powerful pharmacological tool for dissecting the physiological functions of EPAC and for further elucidating the molecular mechanism of cAMP signaling, but also have important impacts on designing potential therapeutics targeting EPAC in diseases where cAMP signaling and EPAC proteins have been implicated.

PATENT DETAILS

Flavivirus Therapeutics

PATENT TITLE

Small-Molecule Inhibitors of Dengue and West Nile Virus Proteases

PATENT # US 8,778,876
 # US 9,408,813 (ASSOC.)

INVENTORS | Stanley Watowich, Suzanne Tomlinson, Scott Gilbertson

PROBLEM

Flavivirus is a genus of the family Flaviviridae. This genus includes West Nile virus, Dengue virus, Tick-borne Encephalitis Virus, Yellow Fever Virus, and several other viruses that may cause encephalitis. West Nile virus emerged in the USA and has successfully spread across the entire country and into Canada, Mexico, and Central and South America.

Dengue virus (DENV) is a mosquito-borne virus that causes significant disease worldwide. DENV infections can result in serious disease including Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Dengue Shock Syndrome (DSS) and even death.

There are no approved antiviral drugs for diseases caused by Dengue or West Nile viruses. Currently, patients are treated with supportive care to relieve fever, pain, and dehydration. Therefore, there exists a need for additional vaccines or antiviral therapies to treat flavivirus infections.

SOLUTION

Therapeutic compositions have been developed for the treatment of various Flaviviruses. These therapeutics are comprised of NS2B-NS3 protease inhibitors. The NS2B-NS3 protease inhibitors do not significantly inhibit other serine proteases such as trypsin.

POTENTIAL IMPACT

Reported cases of Flaviviruses are increasing annually. Approximately 40% of the world's population is at risk of infection from living in regions endemic with the virus. The development of these novel therapeutics will help treat and reduce transmission of Flaviviruses that are estimated to lead to 50-100 million annual infections.

PATENT DETAILS

Ehrlichia Detection and Treatment

PATENT TITLE

Ehrlichia Disulfide Bond Formation Proteins and Uses

PATENT # US 7,824,692

INVENTORS | David H. Walker, Jere W. McBride

PROBLEM

The gram-negative bacterial cell envelope consists of proteins, lipoproteins, carbohydrates, and peptidoglycan, all of which interact to form a complex supramolecular structure. While organisms in the genus Ehrlichia have typical gram-negative cell envelope structures, limited ultrastructural studies suggest that peptidoglycan is not present. In the absence of peptidoglycan, the structure of gram-negative bacterial outer membranes may be more dependent on covalent and noncovalent associations between outer membrane proteins. Covalent disulfide bonds between major surface proteins (MSPs) have been observed, indicating that disulfide linkages are important in the outer membrane structure.

Two ultrastructural forms of Ehrlichia chaffeensis, termed reticulate and dense-cored cells, correspond to ultrastructurally similar reticulate and elementary body forms observed in Chlamydiae. Little is known regarding the mechanism(s) of the outer membrane supramolecular rearrangements leading to these ultrastructurally defined forms, but an increase in disulfide crosslinked proteins has been described. The similarity in ultrastructural forms between these two organisms indicates that disulfide bonds may be involved in cell envelope changes leading to the formation of dense-cored cells.

SOLUTION

This novel technology encompasses the identification and functional characterization of genes encoding homologous thio-disulfide oxidoreductases of E. chaffeensis and E. canis. These proteins may be involved in the development of outer membrane supramolecular structures leading to ultrastructural changes in the cell envelope and folding and assembly of proteins involved in virulence. These changes may play a role in pathogenesis by Ehrlichia

POTENTIAL IMPACT

This technology provides antibodies against specific Ehrlichia disulfide bond formation proteins. The technology also provides enhanced screening methods in combination with the development of vaccines against Ehrlichia chaffeensis to prevent or treat human monocytotropic ehrlichiosis (HME) and against Ehrlichia canis to prevent or treat canine monocytic ehrlichiosis (CME). The technology greatly expands screening and treatment options for patients.

PATENT DETAILS

Enhanced Thrombin Derivatives

PATENT TITLE

Thrombin Peptide Derivatives

PATENT # US 7,713,934

INVENTORS | Darrell H. Carney

PROBLEM

Thrombin, a multi-functional enzyme known for blood-clotting activity, has been reported to be an important cell-growth factor. Thrombin has been shown to promote angiogenesis, the development of new blood vessels, and to stimulate endothelial cell proliferation. These processes are a pivotal part of healing wounds.

Thrombin peptide derivatives are molecules having an amino acid sequence derived, at least in part, from that of thrombin and which are active toward certain thrombin receptors. Thrombin peptide derivatives of human pro-thrombin have been shown to promote thrombin receptor-mediated cell stimulation and for their use in the treatment of wounds, and stimulation of angiogenesis. Because of their biological activity, these thrombin peptide derivatives show great potential as pharmaceuticals.

Strict regulations by the Food and Drug Administration (FDA) require a high degree of purity for biologically active agents when used as pharmaceuticals. It's therefore necessary to obtain active thrombin peptide derivatives that maintain their purity over extended time periods. Unfortunately, the purity of thrombin peptide derivatives diminishes over time because of dimerization resulting from disulfide bond formation.

Therefore, there is a need for new peptides with the activity of thrombin peptide derivatives, but which do not form dimers.

SOLUTION

It has now been found that thrombin peptide derivatives in which cysteine is replaced with non-reactive amino acids of similar size are free of dimers in solution and retain their activity toward thrombin receptors.

This novel technology provides peptides, pharmaceutical compositions comprising these peptides, and methods useful for treating a subject in need of treatment with a thrombin receptor agonist.

POTENTIAL IMPACT

This technology provides thrombin peptide derivatives with longer shelf-life, less susceptibility to oxidation, and are cheaper to manufacture. It is possible to deliver precise and reproducible dosages, even after storage for prolonged periods of time. The technology provides new and improved treatment options for restenosis in patients after angioplasty and to regenerate blood vessels in cardiac tissue.

PATENT DETAILS

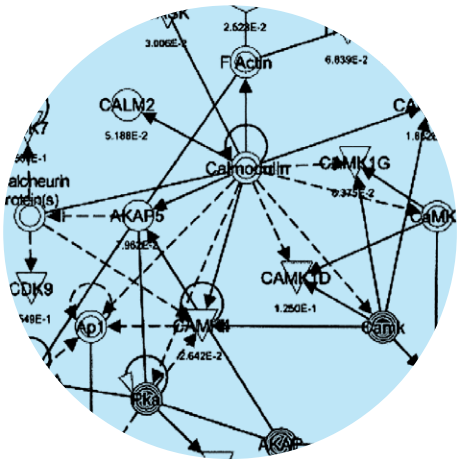
Front Line Ebola Treatment

PATENT TITLE

Inhibition of Filovirus Entry into Cells and Uses Thereof

PATENT # US 8,889,743

INVENTORS | Robert A. Davey,Andrey A. Kolokoltsov, Mohammad F. Saeed



PROBLEM

The Ebola virus is a member of the family Filoviridae and causes severe hemorrhagic fevers. It is an NIH category A agent and is one of the most widely publicized human viruses. Most outbreaks have occurred in isolated communities in Africa and have been effectively contained. Release into a large city would have severe consequences, cause mass panic, and initiate major economic disruption. For these reasons Ebola virus remains one of the most highly effective terrorist bioweapon threats. In the wild, infections initiate from contact of people with dead or dying virus-infected animals. However, these are dead-end hosts and the primary animal reservoir remains unknown.

Apart from palliative treatment, there is no effective treatment for an Ebola. Some success has been found using monoclonal antibodies against envelope proteins and nucleoproteins or using passive transfer of immune serum from convalescent patients, but this is not practical for a virus outbreak. The pantropic nature of Ebola virus infection suggests a role for monocytes in disseminating the virus to distant sites. It has been hypothesized that cytokines released from infected mononuclear cells contribute highly to the hypotensive shock and cell damage seen during the later course of infection. Apoptosis is also seen in endothelial cells from fatally infected patients. There are probably numerous factors involved in the effects seen during Ebola virus infections including virus induced cytokine production that alters vascular permeability, as well as other yet to be identified factors. Identification of these factors is important for the discovery of effective drugs.

SOLUTION

This novel technology provides methods and compositions for treating infection by members of the filovirus family of viruses (Marburg, Ebola, and Zika) by directly inhibiting viral entry into the cells or by preventing envelope protein induced toxicity. The technology utilizes blockage of the PI3 kinase and/or the calcium-associated signaling pathway.

POTENTIAL IMPACT

The technology provides a promising new approach to the treatment of Ebola and other filovirus members. This is a huge step, as it represents treatment options other than palliative care for viruses with mortality rates >80%. The technology will greatly expand access to treatment while reducing the nefarious threat.

PATENT DETAILS

Inflamed Aldose Reductase Inhibitors

PATENT TITLE

Methods Involving Aldose Reductase Inhibitors

PATENT # US 9,198,915

INVENTORS | Satish K. Srivastava, Kota V. Ramana

PROBLEM

Aldose reductase (AR) catalyzes the reduction of a wide range of aldehydes. The substrates of the enzyme range from aromatic and aliphatic aldehydes to aldoses such as glucose, galactose, and ribose. The reduction of glucose by AR is particularly significant during hyperglycemia Increased flux of glucose via AR has been etiologically linked to the development of secondary diabetic complications. AR is an excellent catalyst for the reduction of lipid peroxidation-derived aldehydes. The resulting glutathione conjugates suggest, that in contrast to its injurious role during diabetes, under normal glucose concentration, AR may be involved in protection against oxidative and electrophilic stress. The antioxidant role of AR is consistent with the observations that in a variety of cell types AR is upregulated by oxidants such as hydrogen peroxide, lipid peroxidation-derived aldehydes, advanced glycosylation end products, and nitric oxide. The expression of the enzyme is also increased under several pathological conditions associated with increased oxidative or electrophilic stress such as iron overload, liver disease, heart failure, myocardial ischemia, vascular inflammation, restenosis, and cancer.

The role of aldose reductase in several diseases and conditions requires elucidation, as patients with these diseases and conditions continue to require new treatments. There is a critical need for preventative and therapeutic methods involving aldose reductase and aldose reductase inhibitors.

SOLUTION

This novel technology provides compositions and methods for utilizing aldose reductase inhibitors (ARis) to treat and ameliorate inflammation.

POTENTIAL IMPACT

The technology will expand treatment options for patients with a myriad of inflammatory pathologies, leading to better health outcomes. The technology will help reduce costs associated with the treatment of general or disease-specific inflammation.

PATENT DETAILS

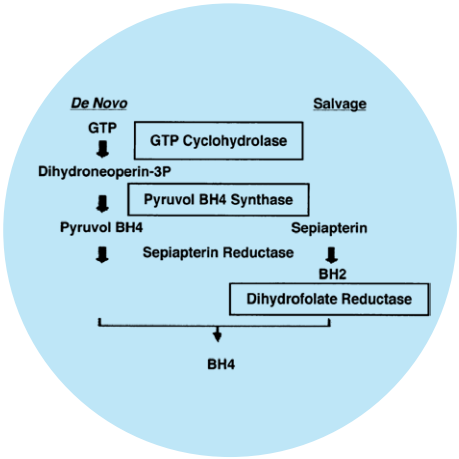
Gastroparesis Relief

PATENT TITLE

Treatment of Esophageal Motility Disorder Using Sepiapterin, Tetrahydrobiopterin and Derivatives Thereof

PATENT # US 9,486,456

INVENTORS | Pankaj J. Pasricha, Pandu R. R. Gangula



PROBLEM

Gastroparesis is a devastating disease affecting predominantly young women. Although a variety of diseases are associated with gastroparesis, the two most common subtypes are diabetes and idiopathic diabetic gastropathy, a syndrome of delayed gastric emptying leading to nausea, vomiting, postprandial fullness, abdominal pain, and early satiety. Because of its chronic and often intractable nature, the disorder has a tremendous impact on both patients and society. Long standing and poorly controlled diabetes results in the disturbance of several gastric functions such as gastric myoelectric activity, antroduodenal motor activity, gastric emptying, and gastric visceral sensation.

Normally, gastric motility is regulated by neurons of the enteric nervous system located in the muscle wall. These neurons are either excitatory (releasing acetylcholine) or inhibitory (releasing nitric oxide and vaso-active intestinal peptide). In diabetic gastric dysfunction, antral motility, and the coordination of pressures between antrum and duodenum are diminished resulting in associated negative symptoms. There is a critical need for better treatments.

SOLUTION

This novel technology provides methods and compositions for restoring gut motility by administering a pharmacologically effective amount of sepiapterin, tetrahydrobiopterin (BH4), sex steroid hormone, or derivative compound(s). The technology stimulates steroid receptors in the patient, thereby restoring gut motility.

POTENTIAL IMPACT

The technology overcomes the biggest barriers to the development of effective therapies for gastroparesis with methods and compositions targeted directly at pathogenesis and/or pathophysiology. The technology provides new effective treatment options and greatly expands access to these treatments, reducing both the clinical and societal burdens associated with the disorder.

PATENT DETAILS

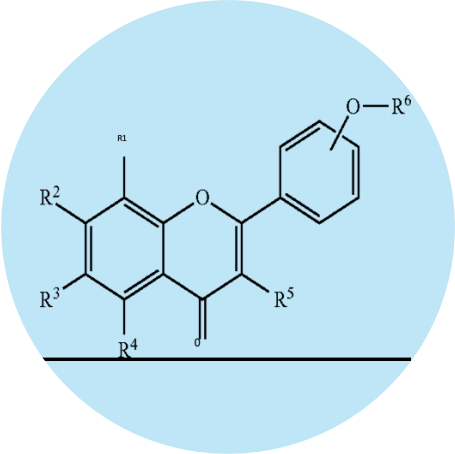
Apigenin Analogs

PATENT TITLE

Apigenin Analogs, Compositions, and Methods Related Thereto

PATENT # US 9,868,715

INVENTORS | Jia Zhou, Mark Hellmich, Csaba Szabo



PROBLEM

Chronic pancreatitis (CP) is a progressive, non-curable disorder of the pancreas. Pathologically, both the endocrine and exocrine pancreas undergo progressive and often irreversible morphological changes, including glandular fibrosis. Current treatment options for CP are limited to supportive and palliative care. Patients with advanced disease can be managed with endoscopic and/or surgical pancreatic decompression, denervation, resection, bypass, or transplantation. Overall, patients have a poor quality of life, and are burdened by chronic abdominal pain, increased hospitalizations, impaired digestion, diarrhea, weight loss, diabetes, complications like pseudocysts, and an increased risk of pancreatic cancer.

Accumulating evidence suggests that activated pancreatic stellate cells (PSC) play an important role in chronic pancreatitis (CP), and inhibition of the activated PSC is considered as a potential strategy for the treatment and prevention of CP. Therefore, the development of effective, safe, and affordable therapeutic agents remains a critical need.

SOLUTION

This novel technology provides methods and compositions related to O-alkylaminotethered apigenin derivatives to enhance the potency and drug-like properties including aqueous solubility. These apigenin derivatives suppress proliferation and induce apoptosis in PSC which reduce the PSC-mediated fibrosis in CP.

POTENTIAL IMPACT

The technology provides new treatment options which are highly potent and orally active agents for the prevention and treatment of various forms of fibrosis and cancers. These molecules may also be useful research tools and therapeutics as cystathionine-synthase (CBS) inhibitors to target H2S-signaling for a wide range of human diseases. The technology will expand access to treatment, help improve the lives of millions of patients, and help reduce the $4+ billion annual associated costs.

PATENT DETAILS

Group V – RNA Virus Treatment with Hydrogen Sulfide Donors

PATENT TITLE

Methods for Treating Viral Infections Using Hydrogen Sulfide Donors

PATENT # US 9,504,701

INVENTORS | Antonella Casola, Oliver Escaffre, Alexander Freiberg, Roberto Garofalo

PROBLEM

Viral infections are very common, cause substantial suffering, and cost hundreds of millions of dollars of economic loss every year. The prevention of viral infections is typically accomplished by administering antiviral vaccines. However, vaccines still cannot solely prevent an outbreak or epidemic because viruses easily mutate rendering the vaccine ineffective. Some treatments such as interferon or interleukin-2 therapy can inhibit virus replication and improve cell-mediated immune function, but are expensive and are associated with adverse reactions in some instances.

Group V negative-sense single-stranded RNA viruses comprise many human pathogens. These viruses have significantly higher mutation rates compared to DNA viruses, generally. The higher mutation rates correlate with faster rates of developing resistance to treatments. Thus, there is a constant need for additional treatments for these viruses.

SOLUTION

A series of hydrogen sulfide releasing compounds has been developed to treat Group V negative-sense single-stranded RNA virus illnesses, including those from Pneumovirus, Paramyxoviridae, Bunyaviridae, and Filoviruses.

POTENTIAL IMPACT

The development of this group of viral therapeutics will help provide a new treatment option to support vaccine efforts to combat this group of devastating viruses. This novel technology will help support virus specific vaccines as a hedge against viral mutation.

PATENT DETAILS

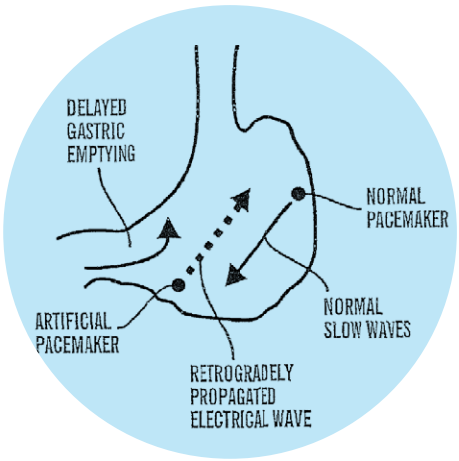
Gastrointestinal Electrical Stimulation

PATENT TITLE

Gastrointestinal Electrical Stimulation

PATENT # US 8,761,903

INVENTORS | Jiande Chen, Pankaj Jay Pasricha



PROBLEM

Controlled motility is one of the most critical physiological functions of the human gut. Without coordinated motility, digestion and absorption of dietary nutrients cannot take place. The gut needs to generate not just simple contractions but coordinated contractions to produce transit of luminal contents. Coordinated gastric contractions are necessary for the emptying of the stomach. The patterns of gastric motility are different in the fed state and the fasting state. In the fed state, the stomach contracts at its maximum frequency, 3 cycles/min (cpm). When the stomach is empty the pattern of gastric motility changes. The gastric motility pattern in the fasting state undergoes a cycle of periodic fluctuation.

Gastric myoelectrical activity consists of slow waves and spike potentials. The slow wave is omnipresent and occurs at regular intervals. The gastric slow wave determines the maximum frequency, propagation velocity and propagation direction of gastric contractions. When a spike potential is superimposed on the gastric slow wave a strong contraction occurs.

Abnormalities in gastric slow waves lead to gastric motor disorders and have been frequently observed in patients with functional disorders of the gut. Gastric myoelectrical abnormalities include uncoupling and gastric dysrhythmia and can lead to significant impairment in gastric emptying. Gastric emptying plays an important role in regulating food intake. Several studies have shown that gastric distention acts as a satiety signal to inhibit food intake and rapid gastric emptying is closely related to overeating and obesity.

Obesity is a major risk factor for many chronic diseases and there is a critical need for additional feasible and suitable means to treat obesity and other gastrointestinal disorders.

SOLUTION

This novel technology provides methods for treating obesity and other gastrointestinal disorders by utilizing a stimulatory electrode to generate non-naturally occurring gastrointestinal action.

POTENTIAL IMPACT

The technology overcomes many of the limitations associated with current treatment methods. The technology is much less invasive than stomach banding surgery and is faster than simply over-the-counter pharmaceutical treatments. The technology will enhance and greatly expand treatment options and outcomes for patients.

PATENT DETAILS

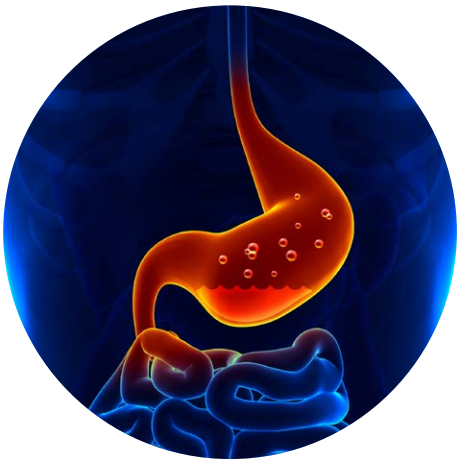
Gastrointestinal Ablation

PATENT TITLE

Antagonists of the Transient Receptor Potential Vanilloid 1 and Uses

PATENT # US 8,211,941

INVENTORS | Pankaj J. Pasricha, Jiande Chen, Rami Hawari



PROBLEM

Vomiting is the expulsion of gastrointestinal contents through the mouth brought about by the descent of the diaphragm, forceful contractions of abdominal muscles and chest wall muscles, while relaxing the gastric cardia. Nausea is the behavioral and emotional state that usually leads to the unpleasant need to vomit. Nausea usually precedes and follows vomiting, but it can sometimes be isolated or occur only after vomiting starts.

The nausea/vomiting reflex is triggered by either peripheral or central stimuli. The peripheral stimuli activate the chemoreceptor and/or mechanoreceptors in the gastrointestinal wall. Inflammation and tissue injury, bowel obstruction, or abnormal gastrointestinal motility activates mechanoreceptors. Toxins and culprit food contents are responsible for activating the chemoreceptor. The signal from these stimuli is carried by the afferent nerve fibers in the sensory vagus and abdominal splanchnic nerves. These nerve fibers converge onto the vomiting center and the sensory vagus nucleus.

Resiniferatoxin, and associated analogues, are exogenous ligands for the transient receptor potential cation channel subfamily V. Resiniferatoxin induces the desensitization effect and neuronal ablation with minimal initial activation of the TRPV-1 neuron. Resiniferatoxin and associated derivatives have been reported as potential analgesics through desensitization of theses neurons.

SOLUTION

This novel technology provides methods for the treatment of acute or chronic nausea and/or vomiting by administering resiniferatoxin or associated derivatives. The technology utilizes localized ablation of vagal afferent nerves in the stomach or other regions of the gastrointestinal tract. The technology can also be utilized for the treatment of obesity and insulin resistance.

POTENTIAL IMPACT

The technology offers new lower cost and less invasive treatments for nausea, vomiting, obesity, and insulin resistance. The technology will increase access to treatment and provide better health outcomes than the current treatment standards.

PATENT DETAILS

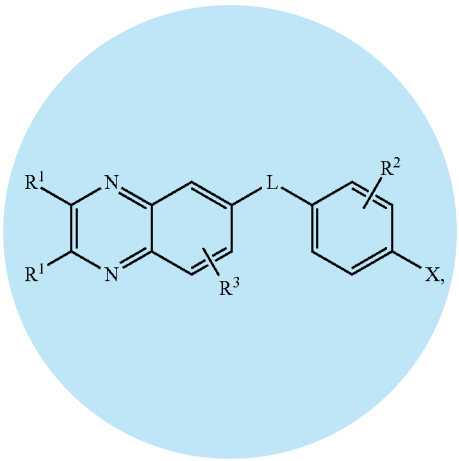
Kinase Inhibitors for Cancer

PATENT TITLE

Substituted Quinoxalines as Kinase Inhibitors

PATENT # US 9,353,094

INVENTORS | Amarnath Natarajan, Qianyi Chen, Vashti C. Bryant, Rajkumar Rajule



PROBLEM

NF-KB has been shown to regulate the expression of over 200 immune, growth and inflammation genes. NF-KB is constitutively active in proliferating T cells, B cells, thymocytes, monocytes and astrocytes. The clinically silent onset of pancreatic cancer (PC) has been attributed to the upregulation of pro-inflammatory pathways such as NF KB. NF-KB is constitutively active in most tumor cell lines, and many tumor tissues derived from patients, but not in normal tissues. A similar observation was made in PC cell lines and pancreatic adenocarcinoma which showed constitutively activated RelA (p65 subunit of NF-KB), but not in normal pancreatic tissues or immortalized/non-tumorigenic pancreatic epithelial cells. Studies also showed that PC cell lines had increased levels of NF-KB subunits compared to non-malignant proliferating intestinal cells. Inhibiting constitutive NF-KB activity suppresses growth, angiogenesis, and metastasis of PC. NF-KB driven pro-inflammatory pathways lead to a subset of PC's and modulating the NF-KB activity is a viable therapeutic strategy for this subgroup.

The activity of IKB kinase (IKKB) is regulated by multiple phosphorylation events. IKKB, like other kinases has an activation loop. Phosphorylation of two serine residues on the loop leads to the activation of IKKB. IKKB also has a stretch of serine residues at the C-terminus and IKKB activation leads to autophosphorylation of the C-terminus serine residues. Unlike phosphorylation of the activation loop, phosphorylation of the C-terminal residues dampens kinase activity. Therefore, phosphorylation of the C-terminal serine residues not only makes IKKB activation transient but also provides docking sites for phosphatases to dephosphorylate the serine residues on the activation loop. The lack of antibodies specific to the various states of IKKB makes this a challenging problem. A need exists for IKKB inhibitors and methods of treating IKKB mediated disorders.

SOLUTION

This novel technology provides composition and methods for treating various IKKB dependent conditions such as pancreatic cancer.

POTENTIAL IMPACT

The technology greatly expands the access to treatment for a variety of cancers and inflammatory diseases that overcome many of the limitations to current chemotherapy treatment options. The technology will help reduce overall health care costs while providing better health outcomes.

PATENT DETAILS

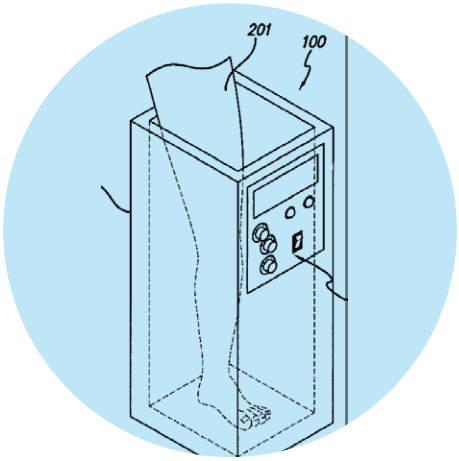
Heart Disease Bath

PATENT TITLE

Ultrasonic Bath to Increase Tissue Perfusion

PATENT # US 9,050,448

INVENTORS | Robert J. Siegel, Yochai Birnbaum, Huai Luo



PROBLEM

Peripheral Vascular Disease (PVD), also referred to as Peripheral Arterial Disease (PAD), is a general term for diseases caused by occlusion or obstruction of peripheral arteries. PVD is a common disease affecting numerous patients that may lead to morbidity and suffering. The occlusion of peripheral arteries via the processes of atherosclerosis, inflammatory response, embolism, thrombus formation and diabetes mellitus may all result in PVD. PVD may cause acute or chronic ischemia in the surrounding tissues, particularly in an extremity of the affected person. The acute or chronic ischemia may result in pain, loss of sensation, sores, wounds or ulcers, and tissue loss in the affected extremity. Ischemia is characterized by an absolute or relative shortage of blood supply to a tissue because of constricted or blocked blood vessels supplying the tissue.

Current treatment options include invasive arterial bypass surgery, peripheral arterial balloon angioplasty, and stent placement. However, in many patients and especially in those with diabetes mellitus, the occlusive disease affects small blood vessels that are not amenable to mechanical revascularization. Current technology tends to have limited long-term success with high recurrence rates. The most severe cases require amputation of the extremity. There is a critical for non-invasive treatment options for ischemia and/or PVD.

SOLUTION

This novel technology provides methods for enhancing tissue perfusion, enhancing development of collateral blood vessels and/or enhancing collateral circulation in an extremity.

POTENTIAL IMPACT

The technology is less invasive than current treatment standards while effectively treating small blood vessels. The technology is scalable and will enable new health care facilities to provide the treatment. This greater access to care will help prevent the unneeded amputation of a patient's extremity.

PATENT DETAILS

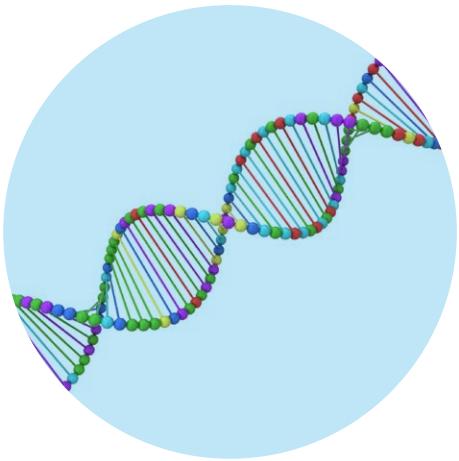
IKK Modulation of NF-kB

PATENT TITLE

IKK Gamma Gene Products and Methods for Making and Using Same

PATENT # US 7,521,534

INVENTORS | Allan R. Brasier, Tao Hai, Thomas G. Wood, Yuanfen Wei



PROBLEM

Nuclear factor kB (NF-kB) is a family of inducible transcription factors controlling expression of genes that play important roles in airway inflammation and other inflammatory conditions and diseases, atherosclerosis, blood pressure, and immune response. Under normal conditions, the NF-kB complex is inactivated in the cytoplasm by binding inhibitors. These inhibitors of NF-kB are referred to as IkB. Upon cellular stimulation with angiotensin II, oxidized low density lipoproteins, cytokines, or viral pathogens, IkB is phosphorylated and degraded, liberating NF-kB, which enters the nucleus and activates the expression of target genes. IkB kinase ("IKK") is a multi-subunit complex that transduces upstream activating signals into the rate-limiting phosphorylation of IkB. Several studies have demonstrated that IKK is required for NF-kB activation.

SOLUTION

This novel technology provides systems and methods to modulate NF-kB activation for the treatment, prevention, or management of inflammatory conditions and diseases.

POTENTIAL IMPACT

The technology provides a novel therapeutic for the treatment of a myriad of inflammatory conditions and diseases. The technology expands access to new treatments, helps reduce the complexity and redundancy of treatments, and provides better health outcomes for patients.

PATENT DETAILS

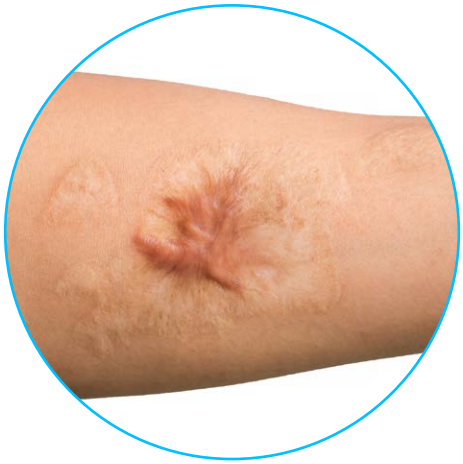
Hypertrophic Scarring Treatment

PATENT TITLE

N-(2-Aminoethyl) Ethanolamine (AEEA) and Analogs to Treat Hypertrophic Scarring and Liposomal Topical Delivery

PATENT # US 10,285,956

INVENTORS | Paul Boor, Ludwik Branski



PROBLEM

Hypertrophic scarring is a common, important complication in any healing process; however, it is a critical determinant of outcomes in recovery from major burns. Up to 90% of severely burned patients have hypertrophic scarring (estimated at nearly a million/year).

More specifically, hypertrophic scars (HS) are exuberant, pathological growths of scar tissue resulting in bulky, inelastic masses that restrict movement and cause a multitude of morbidities. However, there is little effective treatment for HS, other than surgical revision, and this problem remains a major issue in burn wound therapy.

SOLUTION

A novel pharmaceutical liposome formulation has been developed for the treatment of dermatitis, hypertrophic scarring, scarring from burns, keloid scarring, acne scars, body piercings and tattoo scars, burn scars, scars associated with Classic Type Ehlers-Danlos syndrome, scars from thermal radiation, traumatic skin or eye injuries that involve the deep layers of the dermis.

POTENTIAL IMPACT

This novel formulation is a first-in-class therapeutic that fills a treatment gap for scarring that can be disfiguring, drastically affect a patient's self-esteem, and adversely affect their mobility. Such treatments can provide non-surgical remedies to a multitude of scar types.

PATENT DETAILS

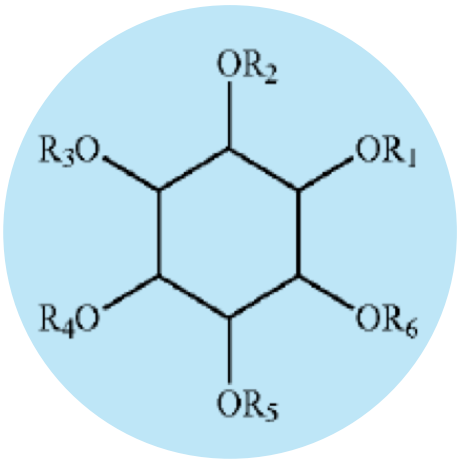
Inositol Hexakisphosphate Analogs

PATENT TITLE

Inositol Hexakisphosphate Analogs and Uses Thereof

PATENT # US 9,200,015

INVENTORS | Tor C. Savidge, Petril Urvil, Dhananjaya Nauduri, Numan Oezguen, Catherine Schein, Werner Braun



PROBLEM

Clostridium difficile is a Gram-positive, spore-forming anaerobic bacillus that is a common cause of nosocomial antibiotic-associated diarrhea and is the etiologic agent of pseudomembranous colitis. The disease ranges from mild diarrhea to life threatening fulminating colitis. Antibiotic use in patients results in a reduction of the commensal gut microflora. C. difficile is resistant to most antibiotics, which gives it a competitive advantage over normal bacterial flora resulting in its proliferation and toxin production.

Several reports have described clinical improvement following use of passive antitoxin immunotherapy with normal pooled intravenous immunoglobulin to avoid surgery and prevent death. More recently, passive immunotherapy using human IgG monoclonal antitoxins was reported to be effective in preventing recurrent C. difficile infection. However, it did not confer protection against toxin activity, and the length of hospitalization was not significantly reduced. Other options, such as probiotics and anion-exchange resins, have limited efficacy and are potentially harmful. Complementary therapy is therefore urgently warranted to neutralize toxin activity. Experimental therapy currently under clinical development includes toxin-absorbing polymers and new antibiotics. There remains a critical need for alternative therapies for C. difficile infections.

SOLUTION

This novel technology provides inositol hexakisphosphate-based compounds for the effective treatment of C. difficile infections and neutralization of its toxins. These compounds are degradation resistant allosteric activators of C. difficile exotoxin cleavage.

POTENTIAL IMPACT

The technology will greatly expand the access to effective treatments for C. difficile. These treatments obviate the need for invasive and expensive surgical procedures currently used. The technology will greatly reduce the costs associated with treatment and disease-associated economic losses.

PATENT DETAILS

Inflammatory Lung Disease Ease

PATENT TITLE

Methods for Treating Epithelian Mesenchymal Transition Related Diseases

PATENT # US 10,292,986

INVENTORS | Bing Tian, Allan Brasier

PROBLEM

Chronic epithelial injury is a hallmark of inflammatory lung disease. Mucosal repair is mediated by a cell state transition of normal epithelial cells, known as Type II epithelial-mesenchymal transition (EMT), responsible for myofibroblast expansion, epithelial trans-differentiation, and subepithelial fibrosis. Currently, very little is known about the factors initiating type II EMT.

Chronic lung disease is the second largest cause of mortality worldwide. A pathological hallmark of asthma is disruption of the epithelial cell. Upon exposure to respiratory viruses or environmental oxidants, resident epithelial cells undergo epigenetic and phenotypic changes to produce pro-inflammatory mediators, express extracellular matrix, and expand the myofibroblast population. These phenotypic changes are associated with enhanced motility, resistance to reactive oxygen species (ROS) and expression of fibrotic genes, processes together known as Type II EMT. Although important in tissue repair, unregulated EMT plays a critical cellular role in the progression of chronic human pulmonary fibrotic diseases, diseases including atopic asthma, chronic obstructive pulmonary disease (COPD), and idiopathic pulmonary fibrosis (IPF). EMT has also recently been observed in chronic airway disease associated with cystic fibrosis or severe respiratory syncytial virus (RSV), a risk factor for the development of allergic asthma later in life.

This evidence suggests that EMT plays important roles in the pathogenesis of airway remodeling in response to environmental stressors. There is a critical need for additional methods and compositions for treating EMT related to fibrosis, asthma, or COPD.

SOLUTION

The novel technology provides methods and compositions for treating lung diseases such as asthma or COPD. These compositions include combinations of BRD4 inhibitors and CDK9 inhibitors which are required for Type II EMT formation.

POTENTIAL IMPACT

The technology offers new treatment options for patients with lung diseases such as asthma and COPD. The technology expands access to care and can help reduce the overall clinical and societal costs associated with this type of lung disease.

PATENT DETAILS

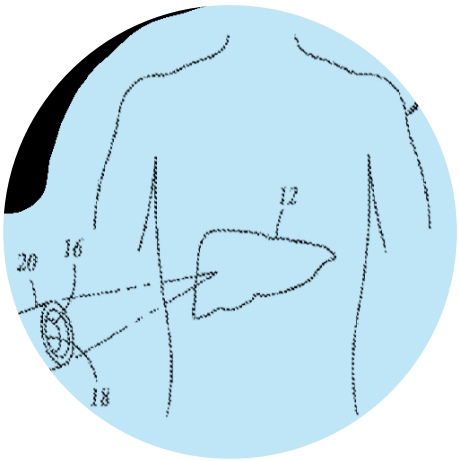
Hepatic Electrical Stimulation

PATENT TITLE

Hepatic Electrical Stimulation

PATENT # US 8,417,331

INVENTORS | Pankaj Jay Pasricha, Jiande Chen



PROBLEM

Although the liver has been known to have a nerve supply for a longtime, relatively little is known about its physiological role. There is recent experimental evidence that neuronal reflexes consisting of the afferent vagus from the liver, and efferent sympathetic nerves to adipose tissues, may regulate energy expenditure, systemic insulin sensitivity, glucose metabolism, and fat distribution between the liver and the periphery.

Expression of peroxisome proliferator activated receptor (PPAR)-g2 in mouse liver markedly decreased peripheral adiposity. These changes were accompanied by increased energy expenditure and improved systemic insulin sensitivity. Hepatic vagotomy and selective afferent blockage of the hepatic vagus revealed that the effects on peripheral tissues involve the afferent vagal nerve. By providing electrical stimulation to the liver parenchyma, it was hypothesized that the ascending limb of this reflex could be stimulated and achieve the same effects.

SOLUTION

This novel technology provides methods of hepatic electrical stimulation for the treatment of risk factors of metabolic syndrome.

POTENTIAL IMPACT

This technology provides a new treatment option that greatly expands the patients access to care. The technology can help reduce costs and increase quality consistency for the treatment of metabolic syndrome risk factors.

PATENT DETAILS

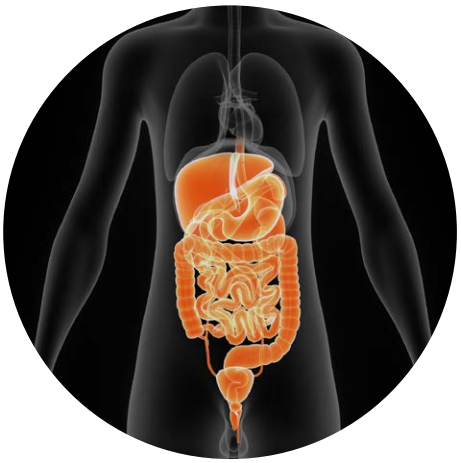
Irritable Bowel Syndrome (IBS) Relief

PATENT TITLE

Treatment Of Irritable Bowel Syndrome and Related Bowel Disease

PATENT # US 8,273,729

INVENTORS | Pankaj J. Pasricha



PROBLEM

Irritable Bowel Syndrome (IBS) is characterized by painful defecation and altered stool frequency/consistency and has a reported prevalence between 15-25%. Unlike most other diseases of the gastrointestinal tract, IBS is not characterized by any specific, currently known histopathological changes, but rather is a functional disorder characterized by disturbed gut motility and/or abdominal pain perception linked to cytokines and/or other inflammatory cascades.

The precise pathophysiology of IBS is not well understood. Nevertheless, there is a heightened sensitivity to visceral pain perception, known as peripheral sensitization. This sensitization involves a reduction in the threshold and an increase in the gain of the transduction processes of primary afferent neurons, attributable to a variety of mediators including monoamines, substance P, and variety of cytokines and prostanoids. Also implicated in the etiopathology of IBS is intestinal motor dysfunction (gut dysmotility) which leads to abnormal handling of intraluminal contents and/or gas.

IBS represents a therapeutic challenge to both clinicians and developers of pharmaceuticals. The uncertainty and variety of causes, as well as the variable nature of symptomatic expression greatly complicates the task of treating this disorder. Current treatment options for IBS and/or related conditions do not adequately address the complexities of IBS.

SOLUTION

This novel technology provides methods and compositions for luminally active anti-inflammatory or immunosuppressive compounds for treatment of irritable bowel syndrome and related disorders.

POTENTIAL IMPACT

The technology overcomes the limitations of the current treatment standards. The technology provides a more directed approach to IBS treatment while reducing associated adverse reactions. The technology will help provide greater access to care and better health outcomes for patients.

PATENT DETAILS

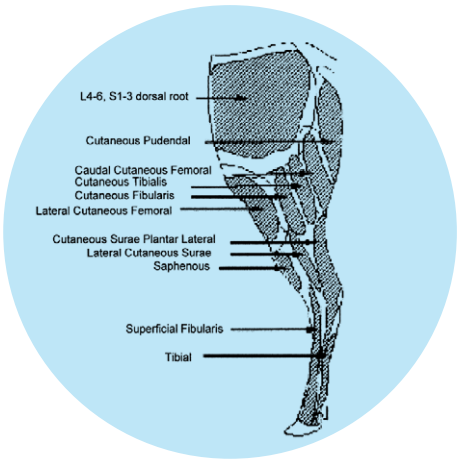
Large Animal Pain Model

PATENT TITLE

Model of Experimentally Induced Chronic Pain and Uses Thereof

PATENT # US 8,212,104

INVENTORS | Denise M. Wilkes, Li-Yen M. Huang



PROBLEM

The prevalence of chronic pain is common and will continue to grow due to the increasingly aging population. Chronic pain consists of either nociceptive or neuropathic pain or both. Neuropathic pain is caused by a lesion in the peripheral nerve and/or dysfunction of the central nervous system which produces symptoms often described by patients as burning, tingling, hot stabbing and shock-like in the absence of nociceptive stimulus.

There are many causes of neuropathic pain. Even though there is no universal classification system, neuropathic pain can be divided into categories based on etiologies and anatomy such as trauma, infection, and compression syndromes. Evidence suggests that the current treatments for neuropathic pain conditions are inadequate.

An increasing interest in pain research has been to develop treatments of neuropathic pain based on mechanisms instead of a diagnostic approach. A mechanistic approach might provide more effective treatments. Much of the current knowledge of the mechanisms of neuropathic pain is based on animal models.

Rat models are limited in predicting efficacy and safety in clinical trials because of several factors: the size difference between rats and humans, the lack of genetic diversity of inbred strains, and the relatively short lives which might limit the development, and consequent measurement, of longitudinal effects.

Lack of available large mammalian model limits the ability to study efficacy and safety of therapeutic alternatives prior to clinical trials.

SOLUTION

This novel technology provides the first large mammalian neuropathic pain model utilizing sheep to investigate and assess neuropathic pain behavior.

POTENTIAL IMPACT

The technology overcomes limitations of previous pain models since the sheep spine closely approximates the size and dimensions of the human spine, which allows the use of existing clinical delivery systems. The sheep model also allows testing of equivalent weight-based drug doses and has a more equivalent lifespan. The technology will allow for better approximation of human reaction and drug response.

PATENT DETAILS

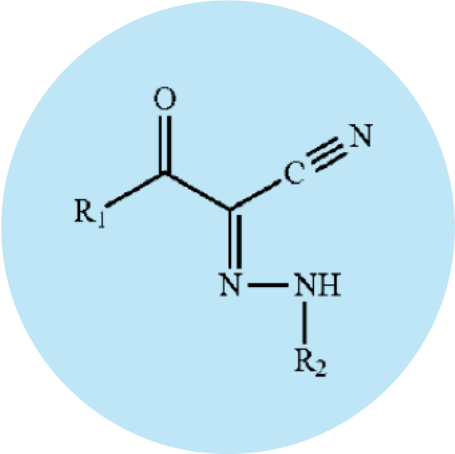
Non-Opioid Pain Management

PATENT TITLE

Methods and Compositions for Treating Chronic Pain

PATENT # US 9,737,512

INVENTORS | Xiaodong Cheng, Fang Mei, Annemieke Kavelaars, Cobi J. Heijnen



PROBLEM

Pain can be exerted in different forms and normally serves as a warning signal to protect the body from harmful stimuli or promote healing after injury. However, under pathological conditions, pain is sensed without harmful stimuli and can be persistent. Chronic pain is a long-lasting pain that persists longer than the temporal course for natural healing of the underlying causative injury or disease. It serves no beneficial or protective function. Chronic pain is a major debilitating disorder that affects one-third of the general population during their adult lifespan.

Cancer pain is one of the most common types of chronic pain and demonstrates nociceptive components due to tumor growth and neuropathic components due to tumor induced nerve damage. It can further involve structural damage, nerve entrapment, inflammatory processes, the production of inflammatory prostaglandins and cytokines, and tissue damage.

The cyclic AMP signaling pathway is the first pathway identified in regulating pain sensitivity. Studies suggests that the cAMP receptor is more closely related in regulation of acute pain while cAMP sensors contribute to development of chronic pain. To date, the main analgesics employed for treatment of chronic pain are opioids and non-steroidal anti-inflammatory drugs (NSAIDS). Both classes of drugs can produce severe side-effects. NSAIDS can cause gastric ulceration and renal damage and opioids can cause nausea, constipation, confusion, and dependency problems.

There is a critical need to identify new pharmaceutically active compounds that interfere with key steps of the chronic pain process and for the treatment and prevention of chronic pain.

SOLUTION

This novel technology provides methods and pharmaceutical compositions of an exchange protein activated by cAMP (EPAC) inhibitor such as ESI-09 for treating chronic and neuropathic pain in patients.

POTENTIAL IMPACT

The technology overcomes the negative side effects and addictive potential of opioids. The pain relief provided is not susceptible to development of analgesic resistance associated with opioids, which complicates their utility for long-term therapy. The technology offers new and improved treatments for chronic pain without the risk of addiction and associated societal impacts.

PATENT DETAILS

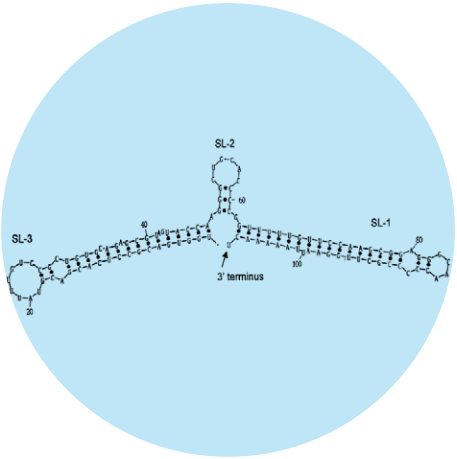
Hepatitis C Virus Proxy

PATENT TITLE

3' Sequence of the GB Virus B (GBV-B) Genome

PATENT # US 7,244,585

INVENTORS | David V. Sangar, Stanley M. Lemon



PROBLEM

Chronic hepatitis C is a major threat to public health. Serologic surveys suggest that over 4 million Americans are chronically infected with the responsible virus, hepatitis C virus (HCV). These individuals are at increased risk of developing progressive hepatic fibrosis leading to cirrhosis and loss of hepatocellular function, as well as hepatocellular carcinoma.

Efforts to better understand HCV and to develop new therapeutics have been stymied by two overwhelming technical deficiencies: 1) the nonexistence of a high permissive cell line that supports replication of the virus and 2) the absence of a permissive animal species other than chimpanzees, which are endangered and therefore available on a limited basis.

Presently, those 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, due to the technical difficulties of working with HCV. Alternatively, they are using isolated proteins or RNA segments of HCV for biochemical and structural studies. This approach precludes functional studies of virus replication and its inhibition.

SOLUTION

GBV-B is a hepatotropic flavivirus that has a unique phylogenetic relationship to human HCV and can serve as a surrogate virus in drug discovery efforts related to hepatitis C antiviral drug development. This novel technology utilizes a previously unidentified 3' terminal sequence (259 nucleotides) of the GB virus B (GBV-B) genome to maximize the utility of GBV-B as a chimera target and/or proxy for HCV.

POTENTIAL IMPACT

The technology provides new opportunities to screen drug candidates for the preventative and therapeutic treatment of HCV, overcoming the dangers and complications of utilizing native HCV and the limitations associated with using less biologically similar viruses as surrogates.

PATENT DETAILS

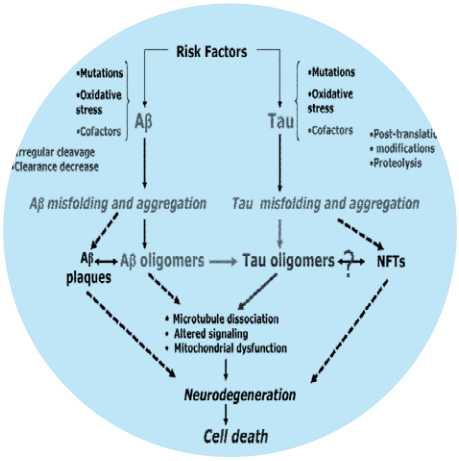
Neurodegeneration Regeneration

PATENT TITLE

Methods of Treating Brain Injury

PATENT # US 10,266,585

INVENTORS | Rakez Kayed



PROBLEM

Pathological aggregation of the microtubule-associated protein Tau and accumulation of neurofibrillary tangles (NFT) or other inclusions containing Tau are defining histopathological features of Alzheimer's disease (AD) and many neurodegenerative diseases collectively known as tauopathies, including Pick's disease (PiD), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and frontotemporal lobar degeneration (FTLD). The correlation between neurofibrillary tangles (NFT) and disease progression has been studied extensively with conflicting results, and the mechanisms linking the pathological aggregation of Tau with synaptic dysfunction and neurodegeneration are poorly understood.

In the case of Alzheimer's, current therapies are focused on symptomatic treatment of the loss of cholinergic transmission, which results from neurodegeneration. Although the available treatments delay progression of the disease for up to six to twelve months, they do not prevent it. The discovery of drugs that could prevent the aggregation of Tau, which leads to neurodegeneration, would provide a more effective strategy for prophylaxis or for inhibiting the progression of the disease. The clinical diagnosis of Alzheimer's is difficult to make, especially in early stages of the disease. Today, the diagnosis is based on a typical medical history combined with the exclusion of other causes of dementia. Certain clinical centers can have a diagnostic accuracy of 85-90% compared with the neuropathological diagnosis. In the early stages of the disease the clinical picture is vague and definite diagnostic markers have not yet been identified. The development of biochemical diagnostic markers is important for several reasons: to support the clinical diagnosis, to allow clinicians to give adequate information to patients and their relatives, to initiate pharmacological treatment and caregiving, and in various aspects of clinical research. There is a critical need for a technique that enables earlier detection of markers of Alzheimer's disease.

SOLUTION

This novel technology provides methods and pharmaceutical compositions of Tau oligomers and Tau oligomer-specific antibodies for the detection, diagnosis, and treatment of neurodegenerative diseases such as Alzheimer's.

POTENTIAL IMPACT

The technology uses Tau oligomers as an early biomarker for tauopathies to identify pathogenic or potentially pathogenic conditions.

The technology provides improved diagnostic capabilities and expands treatment options for those suffering neurodegenerative diseases.

PATENT DETAILS

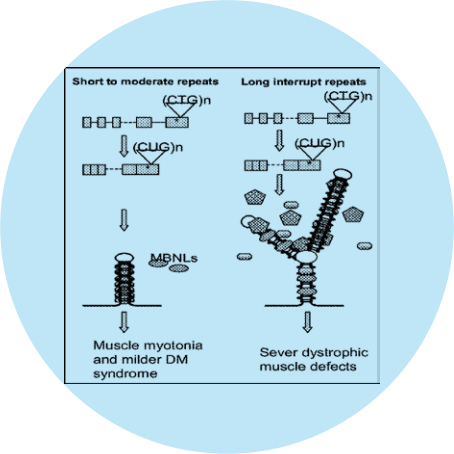
Nucleotide Repeat Intervention

PATENT TITLE

Methods and Compositions Involving Nucleotide Repeat Disorders

PATENT # US 8,771,965

INVENTORS | Partha Sarkar, Tetsuo Ashizawa, Weidong Xu



PROBLEM

Myotonic dystrophy is characterized by the severe dysfunction of skeletal and smooth muscle structure and function. Delayed muscle differentiation and hypotonia are the pre-dominant features in myotonic dystrophy type 1 (DMI) whereas myotonia, atrophy and muscle weakness are the features in adult onset DMI. DMI genetic mutation is the expansion of a CTG repeat in the 3' untranslated region of DMPK and DM2 (myotonic dystrophy type 2) genetic mutation is the expansion of a CCTG repeat in the first intron of ZNF9.

In DMI, the length of the CTG repeat shows a strong correlation with the complexity and severity of disease phenotypes. In contrast, DM2 phenotypes are more subtle and DM2 patients do not develop congenital muscle defects. In DMI, transcription of the mutant DMPK allele produces mRNA encoding expanded CUG sequences; in DM2, the transcription of ZNF9 produces mRNA that carries expanded CCUG sequences. The CUG and CCUG RNA cause cellular toxicity, but the mechanism by which expanded CUG and CCUG RNA cause such cellular toxicity has not been elucidated.

There is a critical need to recapitulate the physiological context of DMI to identify key proteins involved in DMI to allow for the identification and development of appropriate therapeutic and preventative agents for the disease. DMI represents an example of a disease associated with repeat sequences in nucleic acid molecules. Many other diseases and disorders do not have cures, cannot be prevented, or are not effectively treated.

SOLUTION

This novel technology provides methods and compositions for identifying candidate therapeutics and preventative agents for treating and/or preventing diseases, disorders, and conditions involving trinucleotide repeats. Such diseases include DMI and DM2.

POTENTIAL IMPACT

The technology helps elucidate the trinucleotide repeat disease mechanisms behind their associated pathologies to identify and develop drug candidate. The technology provides a foundation for new treatments to diseases that are currently untreatable. The technology will expand the understanding of trinucleotide repeat diseases and disorders and provide hope to disheartened patients.

PATENT DETAILS

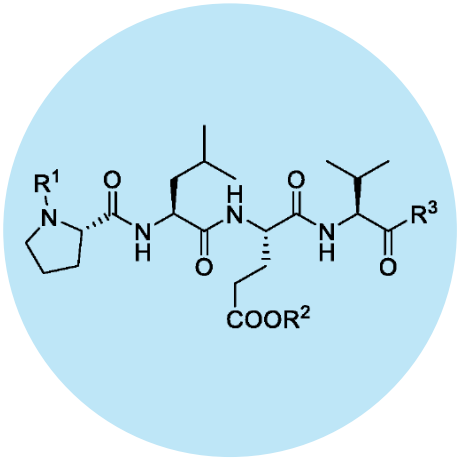
Non-opioid Pain Medication

PATENT TITLE

Novel Non-Opioid Anti-Pain Medication

PATENT # (PENDING)

INVENTORS | Fernanda Laezza, Jia Zhou, Jin Chung, Pingyuan Wang, Jun-Ho La, Oluwarotimi Folorunso, Aditya Singh



PROBLEM

Opioid drugs help reduce post-operative pain; however, their euphoric affects have led to an epidemic of misuse and abuse. In the US, official reports indicate over 115 deaths per day from opioid addiction with an estimated total economic burden of $78.5 billion per year. These trends have only been exacerbated by the COVID pandemic.

SOLUTION

A novel non-opioid medication has been developed for the treatment of pain. This new medication is non-addictive while showing capacity to manage chronic inflammation and post-operative pain. In addition, the novel medication does not affect normal sensory function or produce a significant euphoric affect.

This novel medication has unique positive and negative allosteric modulation properties and acts as a FGF 13-1b inhibitor and as a FGF 13-1a mimic, giving it unique and broad function.

POTENTIAL IMPACT

A non-opioid, non-active pain medication with the capacity to cover severe post-operative pain would be a game changer. Not only would it be a treatment alternative to opioid drugs that cause many unpleasant side effects, but it would also help reduce the opportunity for post-treatment addiction that causes tens of thousands of deaths and places unneeded financial burdens across all aspects of the economy.

PATENT DETAILS

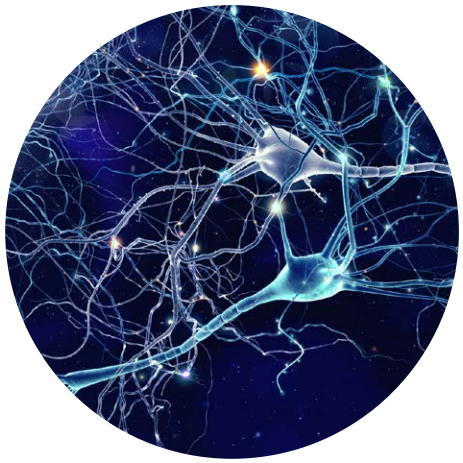
Neuronal Stem Cell Production

PATENT TITLE

Method of Producing Region-Specific Neurons from Human Neuronal Stem Cells

PATENT # US 8,058,063

INVENTORS | Ping Wu



PROBLEM

Many neurological disorders result from the loss of neurons through disease or injury, and these cells are not intrinsically replaced. Such neurological disorders include Parkinson's disease (PD), Alzheimer's disease (AD), multiple sclerosis, Huntington's disease, and amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease). A new strategy for the treatment of such disorders is to replace the damaged or lost neurons by implanting healthy neurons. A potential therapeutic approach for treating AD, ALS and spinal cord injuries is to replace lost cholinergic neurons by the implantation of new, healthy cholinergic neurons.

While such cells could serve as a source of new neurons to ameliorate many neural disorders, a critical issue is how to direct these pluripotent or multipotent stem cells toward a specific cell lineage. Treating spinal cord injury, AD or ALS using a cell replacement strategy requires the differentiation of cholinergic neurons from these stem cells. Human cells can differentiate into specific neuronal types when grafted into either developing central nervous system (CNS) or neurogenic areas. However, these cells remain undifferentiated or become mainly glial cells when transplanted into non-neurogenic regions of the adult CNS. This indicates that in vitro priming prior to grafting is necessary.

SOLUTION

This novel technology includes a method of producing neurons by adhesively culturing neural stem cells and/or progeny in vitro with a mixture including a mitogenic growth factor, a heparin-like agent and an extracellular matrix component and implanting the cultured stem cells and/or progeny into the mammalian spinal cord or brain, where they differentiate into neurons. The cells may be transplanted into the spinal cord or the medial septum of the brain where they differentiate into cholinergic neurons. Typically, of the neurons formed, at least 50% are cholinergic neurons. The stem cells can be implanted into various regions of the brain where they produce regional specific neurons.

POTENTIAL IMPACT

The technology provides a method to direct pluripotent or multipotent stem cells to differentiate into neurons of a specific lineage. The capabilities of self-renewal and multipotential differentiation render these stem cells an attractive and presumably unlimited donor source for cell replacement therapy to treat numerous neurological disorders

PATENT DETAILS

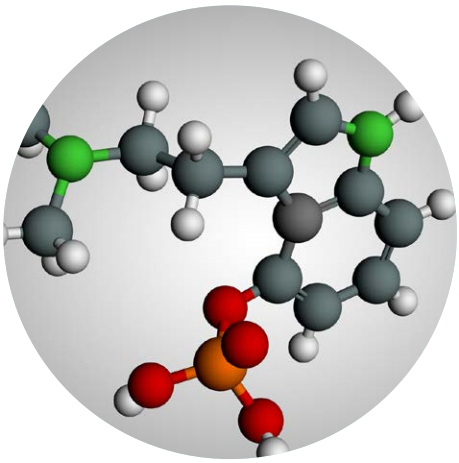
Novel Phenylketonuria Treatment

PATENT TITLE

Methods and Compositions for Treating Phenylketonuria

PATENT # US 8,440,182

INVENTORS | Reuben Matalon



PROBLEM

Phenylketonuria (PKU) is hyperaminoacidemia of phenylalanine (Phe) associated with an inborn error of phenylalanine metabolism, a mutation of the gene encoding phenylalanine 4-hydroxylase (PAH), which converts phenylalanine to tyrosine. A normal plasma phenylalanine level is approximately 0.05 mM and, untreated classic PKU patients have plasma phenylalanine levels above 1 mM.

The excessive levels of plasma phenylalanine observed in PKU combined with the relatively high affinity of phenylalanine for binding sites on carrier protein of the neutral amino acid transport system in the blood-brain barrier (BBB) leads to (1) accumulation of Phe and its neurotoxic metabolites, and (2) depressed levels of non-phenylalanine neutral amino acids entering the brain, resulting in disturbed brain development and function.

Although a diet low in phenylalanine can reduce plasma phenylalanine levels in classic PKU below 0.3 mM and ameliorate the mental retardation associated with untreated PKU, dietary compliance can be problematic, leading to a rise in plasma phenylalanine levels and to both loss in intelligence and white matter changes in the brain. In addition to requiring patient compliance, therapies based on dietary restriction also require that the patient know the level of phenylalanine present in a particular food.

There is a critical need for new methods and compositions for treating phenylketonuria and other conditions and disorders associated with phenylalanine metabolism.

SOLUTION

This novel technology provides methods and compositions for treating conditions and disorders associated with phenylalanine, such as phenylketonuria, with phenylalanine 4-hydroxylase or a phenylalanine ammonia lyase.

POTENTIAL IMPACT

The technology overcomes the compliance issues associated with dietary based treatment options. The technology expands access to treatment by providing additional pharmaceutical treatment options other than use of neurotransmitter precursors such as tyrosine and tryptophan. This treatment expansion will help reduce overall costs and improve health outcomes for patients.

PATENT DETAILS

Non-adjuvant Immunotherapy

PATENT TITLE

Methods and Compositions Related to Immunogenic Fibrils

PATENT # US 9,849,174

INVENTORS | Joel H. Collier, Jai S. Rudra

PROBLEM

The development of vaccines and other immunotherapies has been challenged by imprecise antigen display and the use of heterogeneous immune adjuvants whose mechanisms of action are complex and incompletely understood. Synthetic peptides are useful as antigens because their precise chemical definition allows one to specify the exact epitopes against which an immune response is to be raised. However, peptides are poorly immunogenic by themselves and require co-administration with strong adjuvants, a process that sacrifices the chemical definition that peptides possess initially and complicates their development and regulatory approval. Although several adjuvants have been investigated for peptide immunotherapies, current strategies such as particulates, oil emulsions, toll-like receptor ligands, and other biologically-sourced materials use chemically or structurally heterogeneous materials, making characterization and mechanistic understanding challenging. This situation has motivated the pursuit of self-adjuvanting or adjuvant-free systems.

There is a critical need for additional immunogenic compositions to induce immune responses for treating microbial infection and other pathogenic conditions.

SOLUTION

This novel technology provides methods and compositions for inducing an immune response using immunogenic fibrils.

POTENTIAL IMPACT

The technology provides a novel way to generate immune responses without the use of adjuvants, overcoming the current limitations of reduced specificity associated with adjuvant use. The technology will help simply therapeutic development and reduce associated costs to the patient and the manufacturer.

PATENT DETAILS

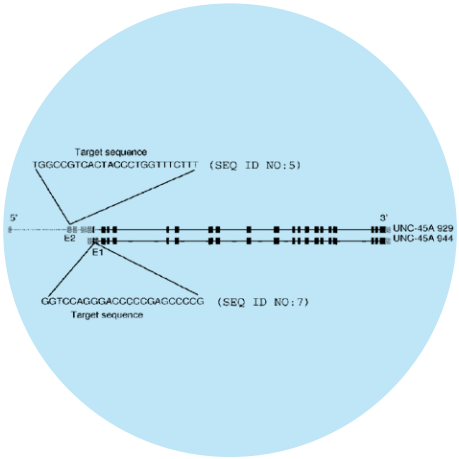
Metastasis Blocker for Cancer

PATENT TITLE

UNC-45A Splice Variants Based Cancer Diagnostics and Therapeutics

PATENT # US 9,127,273

INVENTORS | Henry Fredric Epstein, Wei Guo, Daisi Chen, Ram Singh



PROBLEM

Approximately 90% of breast cancer deaths are caused by metastasis to bones, liver, lungs, or brain with an average survival time of 2 years. Cancer metastasis is tightly related to cell motility including cell invasion and migration in breast cancer where UNC-45 functions as a molecular chaperone for myosin motors.

The UNC-45 family of molecular chaperones is necessary for the proper functions of myosins, the motor proteins of the actin cytoskeleton and the contractile thick filaments of the muscle and heart. Two genes have been discovered which encode UNC-45 chaperones. One encodes UNC-45A that is essential for embryonic development, cell migration, and cell division. UNC-45A is also necessary for cell migration and proliferation in metastatic human ovarian cancer cells.

Mutations in UNC-45/Cro 1p/She4p (Diml p) domain (UCS) proteins result in phenotypes related to defects in myosin folding and assembly. These mutations advance metastasis and lead to negative health outcomes.

SOLUTION

This novel technology provides UNC-45A splice variants used in cancer therapeutics and diagnostics. The technology selectively suppresses or down regulates the 929 amino acid residue splice variant of UNC- 45A utilizing short/small interfering RNAs (siRNA) and short/small hairpin RNAs (shRNA).

POTENTIAL IMPACT

The technology greatly expands the treatment options for late-stage cancers and the resulting metastasis into neighboring tissues and organs. The technology complements and can be used in conjunction with existing treatments. The technology offers hope where hope currently does not exist.

PATENT DETAILS

Medulloblastoma Treatment

PATENT TITLE

Methods of Using Thrombin Derivatives to Treat Medulloblastoma

PATENT # US 10,220,078

INVENTORS | Darrell Carney, Carla Kantara, Stephanie Moya

PROBLEM

Medulloblastoma is the most common malignant brain tumor in children, accounting for 25-30% of primary central nervous system (CNS) tumors. Current available treatment protocols include surgical removal, fractionated radiation therapy (RT), and intensive chemotherapy treatment. Although, such an intense treatment regimen yields a promising average 5-year survival rate of 60-80%, nearly all survivors experience hindered quality of life and long-term cognitive dysfunction.

Regardless of the specific signaling pathway involved in medulloblastomas, the underlying cause of this type of cancer seems to arise from the dysregulation of normal stem/progenitor cells during development. In essence, when normal stem cells lose their homeostatic proliferative functions, they develop a mutated phenotype and transform into cancer stem cells (CSCs). CSCs are a subpopulation of cancer cells within tumors with the ability to perpetually self-renew and differentiate, providing tumors with a limitless supply of cancer cells. To date, available conventional treatment therapies are only efficient in targeting the tumor bulk and fail to eradicate the tumor-initiating CSCs residing within the bulk. Such therapies allow for the survival of CSCs post-treatment and result in the repopulation of tumors and relapse of the disease. However, if CSCs can be specifically targeted and eradicated with treatment, then tumor recurrence can be eliminated. Therefore, it is important to develop cancer therapeutics capable of identifying and targeting CSCs to prevent cancer relapse.

SOLUTION

This novel technology provides methods and compositions for using Thrombin peptide TP508, also known as rusalatide acetate or Chrysalin®, for the treatment of Medulloblastoma.

POTENTIAL IMPACT

TP508 exerts protective effects on normal neural stem/progenitor cells, promote neurogenesis, reduce cognitive dysfunction post-radio-therapy, and targets CSCs to tumor shrinkage in vivo. The technology offers new therapies to overcome chemo-therapy resistance and horrible side effects of other current treatment. The technology will increase access to care and improve health outcomes for patient.

PATENT DETAILS

HIV Therapeutic

PATENT TITLE

Small Molecule BRD4 Modulators for HIV Epigenetic Regulation

PATENT # US 10,975,059
 # US 10,633,363 (ASSOC.)

INVENTORS | Haitao Hu, Jia Zhou, Zhiqing Liu

PROBLEM

Human immunodeficiency virus-1 (HIV) causes persistent and latent infection, posing a major obstacle for eradication of the virus. While anti-retroviral therapy (ART) is highly effective in controlling HIV replication and reducing viremia, it cannot eradicate the virus and manifests significant limitations. Low levels of HIV replication continuously occur in ART-suppressed individuals and the latent reservoir is capable of rapidly producing infectious virus when ART is discontinued. The effects of residual HIV infection remain evident even under ART, including a range of metabolic, immunologic, and neurologic co-morbidities. In addition, ART treatment requires life-long administration to achieve sustained viral suppression.

SOLUTION

The Bromodomain and Extra-Terminal Domain (BET) protein family member BRD4 is an important epigenetic regulator that localizes to DNA via binding acetylated histones and participates in the control of cellular and integrated HIV gene transcription through multiple functional activities.

A novel lead compound has been developed that selectively targets BRD4 but intriguingly induces a functional impact on HIV transcription. This lead compound can suppress HIV transcription and viral replication. Functional analysis shows that this compound can potently suppress HIV in various cellular models, including transformed cell line and human primary PBMCs.

POTENTIAL IMPACT

With the expanded usage of ART, HIV has become more drug resistant, which also erodes the efficacy of ART. This technology can be used in conjunction with ART to target latent HIV reservoirs for eradication. This will provide a multi-pronged approach to the treatment of HIV.

PATENT DETAILS

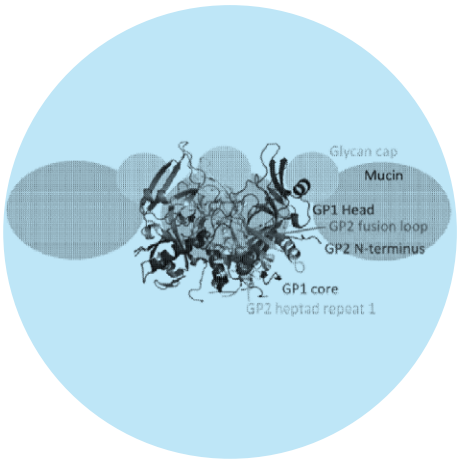
Marburg Virus Neutralizing Antibodies

PATENT TITLE

Antibody-Mediated Neutralization of Marburg Virus

PATENT # US 11,084,869

INVENTORS | James E. Crowe, Jr., Andrew I. Flyak, Alexander Bukreyev, Philipp Ilinykh



PROBLEM

Marburg virus (MARV) and Ebola virus (EBOV) are members of the family Filoviridae, which infect humans and non-human primates causing a hemorrhagic fever with mortality rates up to 90%. There have been a dozen outbreaks of Marburg virus infection in humans reported to date. There is no licensed treatment or vaccine for filovirus infection.

Recently, several studies showed that filovirus glycoprotein (GP)-specific neutralizing antibodies (nAbs) can reduce mortality following experimental inoculation of animals with a lethal dose of EBOV. The primary target of these nAbs, the filovirus surface GP, is a trimer composed of three heavily glycosylated GP1-GP2 heterodimers.

The GP1 subunit can be divided further into base, head, glycan cap and mucin-like domains. During viral entry, the mucin-like domain and glycan cap mediate binding to multiple host attachment factors present on the cell membrane. After the virus enters the host cell by micropinocytosis, the GP is cleaved by host proteases that remove approximately 80% of the mass of the GP1 subunit, including the mucin-like domain and glycan cap. After cleavage of GP in the endosome, the receptor-binding sites on GP become exposed, and the GP1 head then can bind to its receptor. Subsequent conformational changes in GP facilitate fusion between viral and endosomal membranes.

SOLUTION

This novel technology provides methods and compositions of Marburg virus glycoprotein antibodies for use in viral detection and treatment.

POTENTIAL IMPACT

The technology offers hope for enhanced Marburg virus detection and first -n-class effective vaccine against Marburg virus. The use of glycoprotein targeting is more specific to receptor-binding and viral function. The technology will greatly improve outcomes for patients while providing frontline clinical tools for the fight against hemorrhagic fevers such as Marburg and Ebola.

PATENT DETAILS

Myocardial Reperfusion Combo-Therapy

PATENT TITLE

Reducing Myocardial Reperfusion Injury by the Combination Therapy of Protein Kinase A Activation and B1-Adrenergic Receptor Blockade

PATENT # US 8,415,384

INVENTORS | Ming-He Huang, Kenichi Fujise, Barry F. Uretsky

PROBLEM

Currently, there are 5 million American with congestive heart failure, with nearly 500,000 new cases being diagnosed every year. Because of the direct costs of care for heart failure, estimated up to $38 billion per year, the Centers for Medicare and Medicaid Services targeted heart failure as the disease most worthy of cost-effective management.

In addition, acute myocardial infarction (MI) is the leading killer in the United States accounting for 54% of total cardiovascular disease-related deaths. Although reperfusion therapy during acute MI with percutaneous coronary intervention (PCI) or thrombolysis salvages myocardium that would ultimately die without reperfusion, rapidly restoring blood flow to myocardium can also cause lethal injury to vulnerable myocardial cells. The restoration of blood flow can lethally compromise oxygen-deprived cells. Reperfusion injury may offset the optimal salvage of myocardium achieved by PCI and/or thrombolysis.

There is a critical need for additional compositions and methods for the treatment of cardiovascular disorders and myocardial reperfusion injury.

SOLUTION

This novel technology provides combination therapy methods for treating cardiac and cardiovascular disorders and conditions, such as reperfusion injury after acute myocardial infarction (MI). The technology limits infarct-size through pharmacological post-ischemia conditioning reperfusion injury, and post-ischemia conditioning.

POTENTIAL IMPACT

The technology provides a novel treatment option for reducing myocardial reperfusion injury. The technology can expand treatment to reduce a leading cause of death in the U.S. while greatly reducing the associated health care costs.

PATENT DETAILS

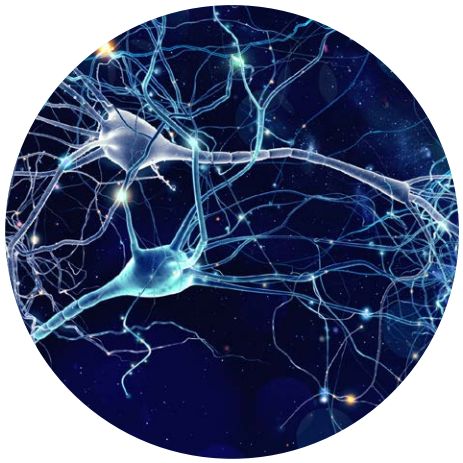
Multiple Sclerosis Therapeutics

PATENT TITLE

Soluble Interleukin-7 Receptor (sIL7R) Modulating Therapy to Treat Autoimmune Diseases and Cancer

PATENT # US 11,118,186

INVENTORS | Mariano Garcia-Blanco, Gaddiel Galarza-Munoz, Shelton Bradrick



PROBLEM

Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by self-reactive immune cell-mediated damage to neuronal myelin sheaths in the central nervous system (CNS) that leads to axonal demyelination, neuronal death and progressive neurological dysfunction. Currently, there is no cure for the disease and available treatments can only slow down disease progression, often by globally suppressing the immune system, causing a plethora of adverse side effects that can be severe or lethal.

SOLUTION

Since the expression of sIL7R exacerbates MS, novel therapeutics have been developed that arrest MS development, by directly targeting the production of sIL7R.

This antisense oligonucleotide therapy targets a genetic sequence of a particular gene that is causative of a particular disease with a short oligonucleotide that is complementary to a target sequence. Typically, a strand of nucleic acids is designed (DNA, RNA or a chemical analogue) that binds to the messenger RNA (mRNA) or pre-mRNA of the target sequence. In the case of splice-modulating antisense oligonucleotides, the complementary nucleic acid is designed to bind a specific sequence in a pre-mRNA that modifies the exon content of the resulting mRNA and consequently in this case, reduces the production of sIL7R.

POTENTIAL IMPACT

These novel therapeutics for MS have the potential to become an extremely affective frontline treatment for as many as 60% of MS patients. In addition to MS, this novel therapeutic has broader potential for the treatment of other autoimmune disease and cancers.

PATENT DETAILS

Personalized Medicine Approach to Chronic Liver Disease

PATENT TITLE

Systems and Methods for Spectral Imaging Characterization of Macrophages for Use in Personalization of Targeted Therapies to Prevent Fibrosis Development in Patients with Chronic Liver Disease

PATENT # (PENDING)

INVENTORS | Heather Stevenson-Lerner, Omar Saldarriaga

PROBLEM

Cirrhosis and hepatocellular carcinoma (HCC) represent increasing health and economic burdens in the U.S and around the world. Non-alcoholic fatty liver disease/ steatohepatitis (NAFLD/NASH), hepatitis C virus (HCV) and autoimmune hepatitis (AIH) are common etiologies. In the United States, NAFLD is predicted to increase from 83.1 million cases in 2015 to 100.9 million in 2030. Although direct-acting antivirals (DAA) are now available to treat HCV, the CDC estimates that the incidence of HCV infection is on the rise due to the opioid epidemic and will go largely unnoticed in the absence of comprehensive screening.

SOLUTION

A new system and method for studying intrahepatic macrophages has been developed. This screening system permits the study of intrahepatic macrophages and their interaction with other components of host immunity in human liver tissue. The system assesses and determines a patient's intrahepatic macrophage profile to be able to predict their risk of developing adverse clinical outcomes.

POTENTIAL IMPACT

This novel technology provides a launchpad platform for the development of truly personalized therapeutic inventions around an individual patient's intrahepatic macrophage profile. In doing so, a trial-and-error approach can be avoided to insure the best clinical outcome for the patient.

PATENT DETAILS

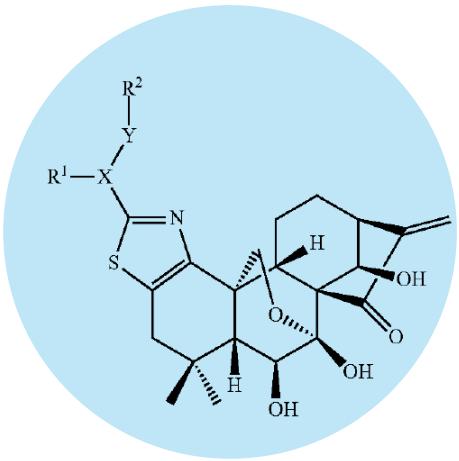
Oridonin Analogs

PATENT TITLE

Oridonin Analogs, Compositions, and Methods Related Thereto

PATENT # US 10,072,022

INVENTORS | Jia Zhou, Chunyong Ding, Qiang Shen



PROBLEM

Natural products have a profound impact upon both chemical biology and drug discovery, and the great structural diversity of natural products at various levels has always served medicinal chemists as a source of inspiration in their search for new molecular entities with pharmacological activity. Natural tetracyclic diterpenoids, especially diterpenoids with an enone system in ring D such as oridonin and eriocalyxin B, constitute an important class of natural products which exhibit considerable pharmacological activities including anti-tumor and anti-inflammatory effects.

Oridonin is a natural product (isolated from the herb rabdosia rubescens) that is used in Chinese traditional medicine for its antitumor, antibacterial, antiviral, and anti-inflammatory effects. Structurally, the highly oxygenated oridonin is primarily characterized with an a, -unsaturated ketone moiety in ring D and a 6-hydroxyl-7-hemiacetal group, which is stereo-chemically rich and densely functionalized. To date, reported structure modifications are primarily focused on the 1-0 and 14-0 positions, likely due to the ease of synthesis. There is a critical need for development of additional oridonin analogs.

SOLUTION

This novel technology provides methods and compositions of Oridonin analogs that are used for antitumor and anti-inflammatory therapeutics.

POTENTIAL IMPACT

The technology expands treatment options for patients suffering from various forms of cancer and inflammatory diseases. With the introduction of these new therapeutics, patients will have greater access to cheaper treatment options.

PATENT DETAILS

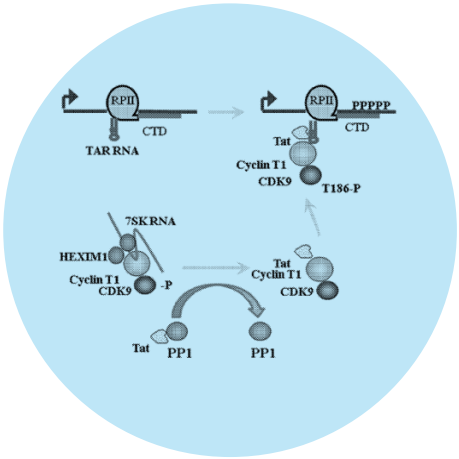
Protein Phosphatase-I Inhibitors

PATENT TITLE

Inhibitors of Protein Phosphatase-I and Uses Thereof

PATENT # US 9,447,047

INVENTORS | Sergei Nekhai, Alexander Bukreyev



PROBLEM

The viral family Filoviridae, which includes Marburg (MARV) virus and five species of Ebola virus (EBOV), causes severe hemorrhagic fever in humans, with lethality up to 90%. Outbreaks of EBOV and MARV infections occur in Central Africa on a regular basis. Sequences of EBOV identified in wild apes during the recent outbreaks in Gabon and The Democratic Republic of Congo (DRC) demonstrated circulation of several lineages of the virus and recombination events between the viruses. Similarly, sequence analysis of MARV isolated during the outbreak in the DRC demonstrated the simultaneous circulation of multiple genetic lineages with up to 21% nucleotide divergence. Sequence analysis of multiple MARV isolates in bats also demonstrated the simultaneous circulation of multiple diverse lineages of the virus, including those identical or almost identical to human isolates. These data suggest a broad distribution and significant diversity of filoviruses. There is an urgent need for development of treatments against filoviruses.

SOLUTION

This novel technology provides compounds and methods used to treat, inhibit, and/or prevent filovirus infection. The technology inhibits dephosphorylation of transcription elongation factors encoded preventing viral replication.

POTENTIAL IMPACT

The technology provides a first in class front-line treatment for a board range of deadly filoviruses including Ebola and Marburg. The technology will greatly increase the access to this much needed treatment and help prevent needless deaths associated with these dangerous viral outbreaks and help prevent a worldwide pandemic.

PATENT DETAILS

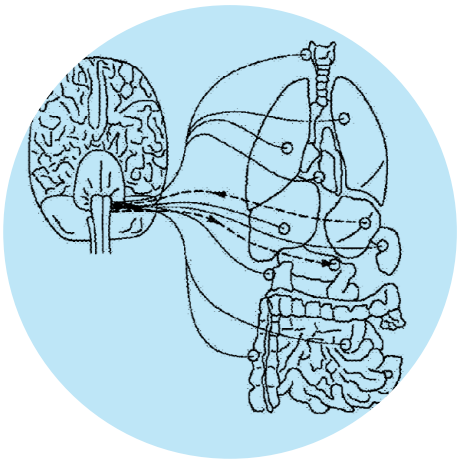
Pancreatitis Electrical Stimulation

PATENT TITLE

Gastrointestinal Electrical Stimulation for the Treatment of Pancreatitis

PATENT # US 8,326,427

INVENTORS | Pankaj Pasricha, Jlande Chen



PROBLEM

Acute pancreatitis is a sudden inflammation that occurs over a short period of time. In most cases, acute pancreatitis is caused by gallstones or heavy alcohol use. Other causes include medications, infections, trauma, metabolic disorders, and surgery. Endoscopic retrograde cholangiopancreatography (ERCP) has been used for the diagnosis and treatment of pancreatic diseases. This procedure is performed on an outpatient basis under sedation. ERCP is associated with a 5%-10% risk of pancreatitis. The risk is increased in those cases where cannulation of the ducts is difficult, or the pancreas is normal. A prior history of ERCP-induced pancreatitis is also a risk factor. Other less common risks include bleeding, infection, and perforation. Particularly in the setting of pancreatic disease, it is a specialized procedure that should be performed only by experienced endoscopists.

Pharmacologic means of decreasing pancreatic secretion have been attempted with limited success because of the dose-limiting side effects encountered with the drugs, their lack of specificity, or their lack of availability. The vagus nerves are strongly implicated in the pathophysiology of pancreatitis. Atropine is a drug that blocks parasympathetic (vagal) nerve endings. Atropine is a desirable treatment for acute pancreatitis patients to down-regulate pancreatic activity. Unfortunately, for many patients, this drug cannot be used due to its many side effects. A critical need exists for an additional feasible and suitable means to treat pancreatitis.

SOLUTION

This novel technology provides methods of preventing acute pancreatitis. The technology uses stimulatory electrodes to produce repetitive trains of short pulse electrical stimulation for suppressing the inflammatory response in the pancreas.

POTENTIAL IMPACT

The technology overcomes the side effects associated with pharmacological interventions. The technology provides preventative therapy options not possible with other treatments. The technology will lead to better health outcomes for patients.

PATENT DETAILS

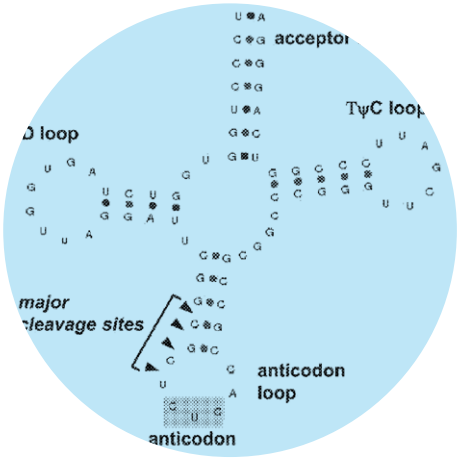
RSV Therapeutics

PATENT TITLE

Compounds and Methods for Altering RSV Replication Rate

PATENT # US 10,219,492

INVENTORS | Xiaoyong Bao, Yong Sun Lee



PROBLEM

During the last decade, significant attention has been directed towards identification of small non-coding RNAs (sncRNAs) and their biological functions. sncRNAs are 16-35 nucleotides (nts) long and of several classes including microRNA (miRNA), small interfering RNA (siRNA), piwiinteracting RNA (piRNA), etc. Among them, miRNA and siRNA are the most extensively studied, and both suppress gene expression by complementary binding to target mRNAs. The role of sncRNAs in regulating antiviral innate immune responses has just emerged and is largely unexplored.

Respiratory tract infections (RTis) are the second leading cause of death worldwide in children less than 5 years old. The majority of RTis are caused by viruses, among which a paramyxovirus called respiratory syncytial virus (RSV) figures prominently. Nearly all children have had RSV infection by 2-3 years of age. RSV infection also increases the morbidity and mortality rate in immunocompromised patients and the elderly, resulting in a substantial health burden. There is currently no specific treatment or vaccine for RSV infection.

SOLUTION

This novel technology provides methods and pharmaceutical compositions of oligonucleotides that decrease the replication rate of RSV; thereby, providing new therapeutic treatments.

POTENTIAL IMPACT

The technology provides a new frontline treatment of RSV, which is currently wreaking havoc in US emergency departments. The technology helps to overcome access to care issues associated with monoclonal antibody preventative treatment, available to <3% of the at-risk infant population. The technology will also help reduce the immediate clinical and societal burdens related to RSV.

PATENT DETAILS

Respiratory Virus Treatment with Hydrogen Sulfide Donors

PATENT TITLE

Methods for Treating Viral Infections Using Hydrogen Sulfide Donors

PATENT # US 9,616,076

INVENTORS | Antonella Casola, Roberto Garofalo

PROBLEM

Respiratory infections, particularly upper respiratory infections (URIs) are very common and cause substantial suffering and hundreds of millions of dollars of economic loss every year. The majority of the pathogens contributing to upper respiratory tract infections are spread through air or through direct contact by touching of hands to infected surfaces and then touching hands to eyes, nose, or mouth. The nasopharynx, nasal passages, and sinus cavities all play an important role in filtering and housing the majority of these pathogens.

The prevention of viral infections is typically accomplished by administering antiviral vaccines. Vaccines still cannot solely prevent an outbreak or pandemic because viruses easily mutate rendering the vaccine ineffective. Some treatments such as interferon or interleukin-2 therapy can inhibit virus replication and improve cell-mediated immune function but are expensive and are associated with adverse reactions in some instances.

SOLUTION

A series of hydrogen sulfide releasing compounds have been developed to treat a series of virus including respiratory syncytial virus (RSV), Nipah virus, human metapneumovirus (hMPV), Influenzavirus A, Influenzavirus B, and Influenzavirus C.

POTENTIAL IMPACT

The development of these group of viral therapeutics will help provide a new treatment option to support vaccine efforts to combat this group of devastating viruses.

PATENT DETAILS

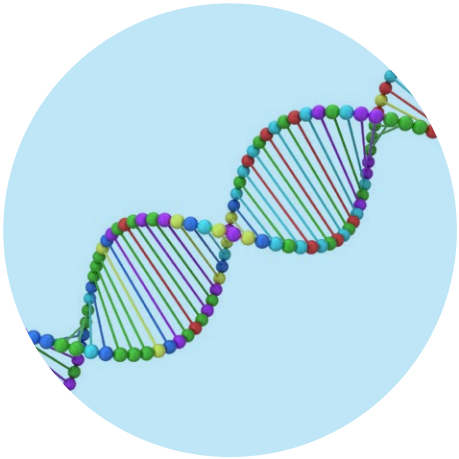
Reduced Risk Pain Management

PATENT TITLE

Upregulation of Opioid Receptors for Management

PATENT # US 8,546,348

INVENTORS | Li-Yen Mae Huang, Yanping Gu



PROBLEM

Chronic pain is a common complaint of patients who undergo surgical procedures or suffer from long term illness, including cancer, nerve injury, arthritis, or heart disease. Pharmacological agents used for treating chronic pain are often unsatisfactory because of the side effects accompanying the treatment. Opiates, at high doses, are apt to produce sedation, respiratory depression, and tolerance, which severely limit their use. Recently, genetic approaches have been attempted to manage the chronic pain. One strategy is to increase the production of endogenous μ-opioid receptor ligands by introducing opioid precursor genes for enkephalin and endorphin into DRG neurons or meninges surrounding the spinal cord through adeno or herpes viral vectors. So far, the success of this approach has been limited by transient expression of the target genes and potential possibilities of tolerance development.

SOLUTION

This novel technology provides methods and compositions for pain management by increasing the antinociceptive effect of opioids. Increases in associated levels of μ-opioid or δ -opioid receptors are achieved at the genomic level via specific nucleic acid constructs delivered through viral or bacterial vectors.

POTENTIAL IMPACT

The technology provides a new genomic approach to pain management that can effectively treat pain while reducing the risk of addiction development. The technology will help reduce costs associated with treatment, and subsequent opioid addiction, while providing better pain management for the patient.

PATENT DETAILS

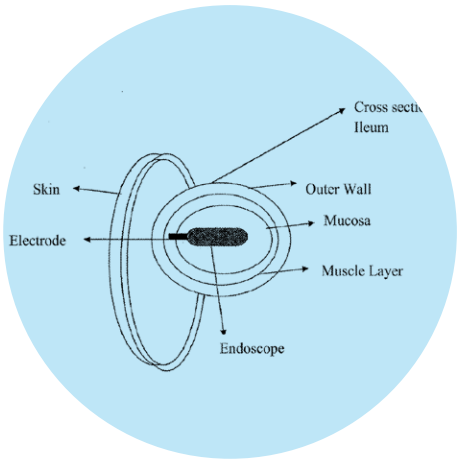
Reduced Risk Obesity Treatment

PATENT TITLE

Ileal Electrical Stimulation

PATENT # US 8,565,885

INVENTORS | Jiande Chen, Pasricha Pankaj Jay



PROBLEM

Electrical stimulation of the gastrointestinal (GI) tract is analogous to the pacing of the human heart. Organs of the GI tract have their own natural pacemakers, and the electrical signals they generate can be altered by externally delivering certain types of electric currents. Abnormalities in gastric slow waves lead to gastric motor disorders and have been frequently observed in patients with functional disorders, such as gastroparesis, functional dyspepsia, and anorexia. Therefore, electrical stimulation of GI organs is a valuable alternative to medication and surgical approaches in the treatment of GI dysfunctions.

Obesity is a complex, multifactorial and chronic condition characterized by excess body fat. Obesity results from an imbalance between energy expenditure and caloric intake. Although the causes of this imbalance are not completely understood, genetic and/or acquired physiologic events and environmental factors are important. The adverse health effects of obesity, and more particularly morbid obesity, have become well-known in recent years. Such adverse health effects include, but are not limited to, cardio-vascular disease, diabetes, high blood pressure, arthritis, and sleep apnea. Generally, as a patient's body mass index rises, the likelihood of suffering from the adverse health effects of obesity also rises.

Often, surgery has been the only therapy that ensures real results in patients who have exceeded BMI values by more than 40 kg/m2.

Modern surgical procedures generally entail either (1) the reduction of gastric compliance, with the aim of limiting the subject's ability to ingest food, or (2) the reduction of the food absorption surface by shortening or bypassing part of the digestive canal. The risk and invasiveness factors of currently available surgeries are often too great for a patient to accept in order to undergo surgical treatment. There is a critical need for less invasive, yet effective treatment procedures for the morbidly obese.

SOLUTION

This novel technology provides a method for the treatment of obesity using stimulatory electrodes targeting the vagal afferent and efferent activity of the distal small intestines.

POTENTIAL IMPACT

The technology overcomes the dangers associated with much more invasive surgical procedures such as stomach stapling. The technology expands obesity treatment for patients that do not meet the qualifications for current treatment options. The technology will provide greater access to care, reduce costs, and reduce risks of complications.

PATENT DETAILS

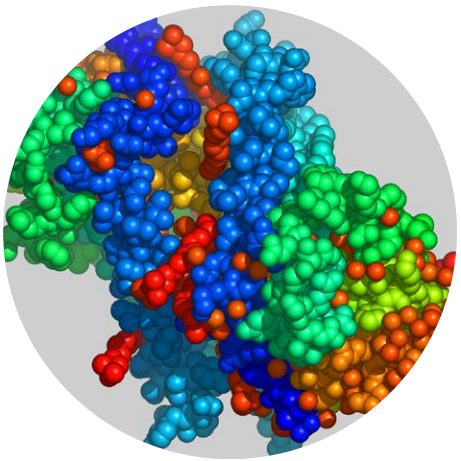
Restenosis Reduction

PATENT TITLE

Composition and Method for Treatment and Prevention of Restenosis

PATENT # US 7,101,852

INVENTORS | Kenichi Fujise, Zakar H. Mnjoyan



PROBLEM

Percutaneous transluminal coronary interventions (PCI) such as angioplasty are common practice today for relieving atherosclerotic blockage caused by fatty acid deposits in coronary arteries. A relatively common complication of angioplasty is restenosis, a re-narrowing of the blood flow due to uncontrolled proliferation of smooth muscle cells at the angioplasty site. Post-angioplasty restenosis was first treated by balloon re-dilatation and/or stents. However, close to 20% of patients developed restenosis within the stent (in-stent restenosis). In-stent restenosis was initially treated by repeat angioplasty, rotational atherectomy, laser angioplasty, and other techniques, but all yielded suboptimal outcomes.

Brachytherapy has been investigated for preventing restenosis after primary angioplasty, however, at least 15% of patients treated with brachytherapy still develop restenosis. It has been reported that brachytherapy only moderately reduced the recurrence rate of in-stent restenosis, at the expense of adverse radiation exposure both to patients and operators.

Although brachytherapy and sirolimus-eluting stents may effectively treat a selected group of patients with restenosis, those treatment modalities are likely to remain very expensive and exclusive. A lower-cost treatment that can significantly reduce the risk of restenosis is greatly needed.

SOLUTION

This novel technology provides therapeutic compositions for prevention of proliferative disorders, including restenosis, atherosclerosis, and cancer. These therapeutic compositions contain soluble proteins (PARISs) normally secreted by vascular smooth muscle cells (VSMC) that inhibit VSMC growth. Since it is well known in the field of cardiovascular medicine that VSMC cells play a critical role in restenosis and atherosclerosis, these PARISs containing therapeutics can be effectively employed to treat, deter, or even prevent restenosis and atherosclerosis progression.

POTENTIAL IMPACT

A 25-35% reduction in restenosis in the patient population would reduce health care costs by $1,400-$2,000 per patient, with a total savings in North America of $400-800 million a year. These novel therapeutics can expand access to treatment, reduce costs, and improve health outcomes.

PATENT DETAILS

siRNA Cancer Treatment

PATENT TITLE

siRNA Inhibition of PI3K, P85, P110, and AKT2 and Methods of Use

PATENT # US 8,198,252

INVENTORS | B. Mark Evans, Piotr G. Rychahou

PROBLEM

Phosphatidylinositol 3-kinase (PI3K), a ubiquitous lipid kinase involved in receptor signal transduction, includes 3 classes. The type I enzymes were originally identified in association with tyrosine kinases such as growth factor receptors and products of oncogenes. Class IA PI3Ks are strongly expressed in colonic epithelial carcinoma cell lines. The gene coding for p110δ (pik3cδ) is amplified in ovarian and breast tumors, implicating pik3cδ as a potential oncogene in these cancers. The promotion of cell survival by the activation of PI3K occurs by the inhibition of proapoptotic signals and the induction of survival signals, which contribute to the malignant transformation and tumor progression.

The activation of PI3K/Akt is associated with colorectal carcinoma and can convert differentiated human gastric or colonic carcinoma cells to a less differentiated and more malignant phenotype. The effects of PI3K on tumor growth and progression are thought to be mediated by Akt, a downstream effector of PI3K.

The Akt gene products, cytoplasmic serine/threonine (ser/thr)-specific protein kinases, are major downstream targets of numerous receptor tyrosine kinases signaling via PI3K. Akt is overexpressed in a few cancers, including colon, pancreatic, ovarian, and some steroid hormone-insensitive breast cancers. Akt phosphorylation in human colon carcinomas correlates with cell proliferation and apoptosis inhibition, as well as with different clinicopathologic parameters such as invasion grade, vessel infiltration, metastasis to lymph nodes, and tumor stage.

Inhibitors of proteins that are involved in PI3K/Akt signaling have been suggested as potential therapeutic agents.

SOLUTION

This novel technology provides RNA polynucleotide duplex methods and compositions that inhibit the expression of specific coding regions of certain cancers including colorectal cancer, breast cancer, and lung cancer.

POTENTIAL IMPACT

The technology overcomes current wortmannin limitations such as short half-life, solubility in organic solvents, and toxicity. The technology also overcomes nonspecific targeting of non-target genes (off-target effects), opening a vast opportunity for precision medicine.

PATENT DETAILS

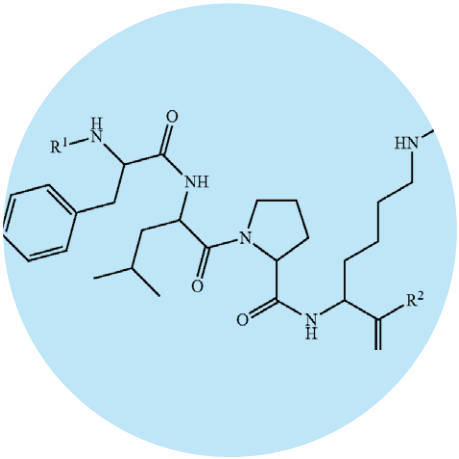
Sodium Channel Psychosis

PATENT TITLE

Fine-Tune Modulators of Neuronal Excitability for Neuropsychiatric Disorders

PATENT # US 10,889,543

INVENTORS | Fernanda Laezza, Jia Zhou, Zhiqing Liu, Syed Ali



PROBLEM

Psychiatric diseases and addictive behaviors are neural circuitry disorders that lead to dysfunction of high-order psychological domains. As indicated by the NIMH and NIDA, these diseases need targeted therapeutic remedies.

The pore-forming alpha subunit of the voltage-gated Na+ (Nav) channels (Navl.1-Navl.9) provides the basis for neuronal electrical excitability in the brain. These channels are regulated by several brain-specific accessory proteins. One of the critical accessory proteins is fibroblast growth factor 14 (FGF14) associated with several brain disorders. FGF14 binds directly to the C-tail of Nav channel and regulates neuronal excitability by controlling the channel expression and gating properties.

Navl .6 is expressed throughout soma and axon of different neuronal cells, and Navl .6 has a significant contribution in persistent current, resurgent current, and repetitive neuronal firing. Both loss of function and gain of function from Navl .6 channel mutations are related to malfunction of neuronal excitability.

SOLUTION

This novel technology provides methods and compositions for selective pharmacological modulators of Navl .6 that can be used to treat psychiatric diseases and addictive behaviors.

POTENTIAL IMPACT

The technology represents a new line of potential therapies with subtype specific targeting of Navl .6 channels. The more targeted approach increases specificity and reduces unwanted side effects. This will greatly expand access to care and reduce the cost of care.

PATENT DETAILS

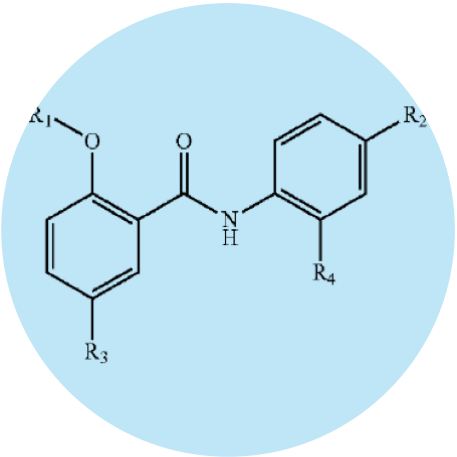
STAT3 Inhibitor for Cancer

PATENT TITLE

STAT3 Inhibitor

PATENT # US 9,562,002
 # US 9,884,863 (ASSOC.)

INVENTORS | Jia Zhou, Haijun Chen, Qiang Shen



PROBLEM

Signal Transducers and Activators of Transcription (STATs) are a family of transcription factors involved in the regulation of early embryonic development, the immune response, cell proliferation, differentiation, and apoptosis. Particularly, STAT3 activation promotes growth and survival of mammary tumors. High levels of activated STAT3 are often found to correlate with poor prognosis in human breast cancer patients in terms of metastatic progression. Therefore, STAT3 represents a promising target for the prevention and treatment of both ER-positive and ER-negative breast cancer and other cancers such as pancreatic, head/neck, prostate, and lung cancers. However, current strategies have not sufficiently inhibited STAT3 activity in cancer cells.

While peptide-based inhibitors can bind to STAT3 with high affinities, they suffer from the lack of cellular permeability due to both their peptidic nature and the negative charges on the phosphotyrosine group. Non-peptidic small-molecule inhibitors are relatively more cell-permeable, but most of the reported compounds such as static bind to STAT3 with weak affinities.

SOLUTION

Novel STAT3 inhibitors have been developed that are synthetic low molecular-weight compounds that specifically block STAT3 activation in cancer cells. These compounds display improved potency, specificity, and/or better drug-like properties such as water solubility and bioavailability. In some embodiments, these small molecules may be used as potent, orally active STAT3 inhibitors for the therapy, prevention, or treatment of various cancers including, but not limited to, breast cancers, pancreatic cancer, brain tumors, head/neck cancer, prostate, and lung cancers as well as inflammation.

POTENTIAL IMPACT

These novel STAT3 inhibitors overcome the cellular permeability challenges of peptide-based inhibitors, weak affinity challenges of non-peptide inhibitors, and bioavailability challenges of niclosamide. These new STAT3 inhibitors promise new, more potent, and targeted therapies for patients.

PATENT DETAILS

Tau Oligomer Antibodies

PATENT TITLE

Antibodies that Bind Tau Oligomers

PATENT # US 8,778,343

INVENTORS | Rakez Kayed

PROBLEM

Pathological aggregation of the microtubule-associated protein Tau and accumulation of neurofibrillary tangles (NFT) are defining histopathological features of Alzheimer's disease (AD) and many other neurodegenerative diseases collectively known as tauopathies. The correlation between neurofibrillary tangles (NFT) and disease progression has been studied extensively with conflicting results, and the mechanisms linking the pathological aggregation of Tau with synaptic dysfunction and neurodegeneration are poorly understood.

In the case of Alzheimer's disease, current pharmaceutical therapies are focused on symptomatic treatment of the loss of cholinergic transmission. Although the available treatments delay progression of the disease for up to a year, they do not prevent it. The discovery of drugs that could prevent the aggregation of Tau would provide a more effective strategy for prophylaxis or for inhibiting the progression of the disease.

The clinical diagnosis of Alzheimer's disease (AD) is difficult to make, especially in early stages of the disease. The development of biochemical diagnostic markers would support clinical diagnosis, allow clinicians to give adequate information to patients and their relatives, and initiate pharmacological treatment. There is a critical need for a technique that enables earlier diagnosis and treatment for Alzheimer's disease and other tauopathies.

SOLUTION

This novel technology provides compositions and methods related to Tau oligomers and Tau oligomer specific antibodies. The technology can be used in diagnosis, treatment, and prevention of neurodegenerative diseases such as Alzheimer's disease.

POTENTIAL IMPACT

The technology will provide a new standard for neurodegenerative disease diagnostics, treatment, and prevention. The technology does not require an immediate knowledge of the diverse upstream events that initiate the aggregation of Tau and will avoid negative side-effects of the current minimally effective treatment options.

PATENT DETAILS

Thrombin Dimers

PATENT TITLE

Thrombin Peptide Derivative Dimers

PATENT # US 7,919,457

INVENTORS | Darrell H. Carney

PROBLEM

Thrombin, a multi-functional enzyme known for its blood-clotting activity, has been recently reported to be an important cell-growth factor. Thrombin promotes angiogenesis, the development of new blood vessels, and endothelial cell proliferation. These processes are pivotal parts of wound healing.

Thrombin peptide derivatives are molecules having an amino acid sequence derived from thrombin, which are active at certain thrombin receptors. Because of their biological activity, these thrombin peptide derivatives show great potential as pharmaceuticals.

Strict regulations by the Food and Drug Administration (FDA) require a high degree of purity when biologically active agents are used as pharmaceuticals. Therefore, it is necessary to obtain active thrombin peptide derivatives that maintain their purity over extended time periods.

SOLUTION

This novel technology provides novel peptide dimers, pharmaceutical compositions comprising these peptide dimers, and methods for treating a subject with a thrombin receptor agonist

POTENTIAL IMPACT

Thrombin peptide derivative dimers retain activity toward thrombin receptors, can be prepared essentially free of monomer, and provide a similar level of activity toward the thrombin receptor. The thrombin peptide derivative dimers also retain their purity with minimal reversion to monomer. Therefore, it is possible to deliver inexpensive, precise, and reproducible dosages, even after storage for prolonged periods of time

PATENT DETAILS

Thrombin Peptide Derivatives

PATENT TITLE

Methods of Therapy Using Pharmaceutical Composition for Thrombin Peptide Derivatives

PATENT # US 7,875,588

INVENTORS | David W. Hobson, Roger S. Crowther, Darrell H. Carney, Andrew Po Kwan Tang

PROBLEM

Thrombin is a serine protease present in blood plasma in the form of a precursor, pro-thrombin. Thrombin is known for growth-promoting activity for a wide variety of cells from various tissues by activation of a specific cell surface receptor known as the non-proteolytically activated thrombin receptor. Thrombin has been shown to promote angiogenesis, the development of new blood vessels, and to stimulate endothelial cell proliferation.

Thrombin peptide derivatives are synthetic analogs of thrombin which have an amino acid sequence derived from thrombin and are active at the nonproteolytically activated thrombin receptor. Thrombin peptide derivatives show great potential as pharmaceuticals because of their therapeutic activity for the treatment of wounds, stimulating bone growth, cartilage growth, and promoting cardiac repair. Unfortunately, thrombin peptide derivatives are highly susceptible to dimerization.

There is a critical need to develop methods to maintain the purity of thrombin peptide derivatives over extended time periods and prevent or reduce dimerization, so that thrombin peptide derivatives have a long storage life to ensure delivery of precise and reproducible dosages, even after storage for prolonged periods of time.

SOLUTION

This novel technology provides pharmaceutical compositions that includes a thrombin peptide derivative and a dimerization inhibitor that retains the monomeric form of the thrombin peptide derivative essentially free of dimers.

POTENTIAL IMPACT

The technology provides advantages over the current standard pharmaceutical composition including a longer storage life for thrombin peptide derivatives. Therefore, it is possible to deliver precise and reproducible dosages with thrombin peptide derivatives, even after storage for prolonged periods of time. The pharmaceutical composition can be used in the treatment and/or prevention of diseases and/or conditions in which angiogenesis and cell proliferation would be beneficial.

PATENT DETAILS

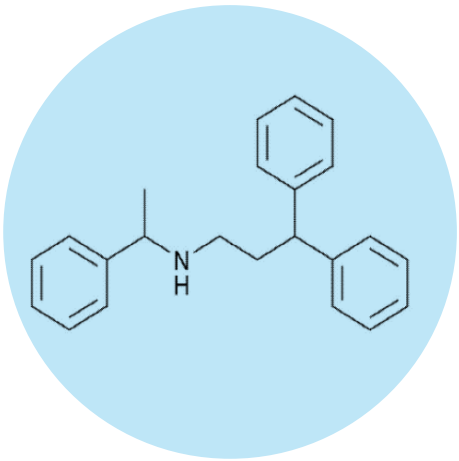
Treatment for K-Ras Mediated Disorders

PATENT TITLE

Methods and Compositions for Use With K-Ras Mediated Disorders

PATENT # US 9,474,730

INVENTORS | John F. Hancock, Dharini Van Der Hoeven, Kwang-Jin Cho



PROBLEM

Ras is the name given to a family of related proteins found inside human cells. All Ras protein family members belong to a class of proteins called small GTPase and are involved in cellular signal transduction. All Ras proteins are related in 3D structure and regulate diverse cell behaviors.

When Ras is switched on by incoming signals, it subsequently switches on other proteins, which turn on genes involved in cell growth, differentiation, and survival. As a result, mutations in Ras genes can lead to the production of permanently activated Ras proteins. This can cause inappropriate and overactive signaling inside the cell, even in the absence of incoming signals, which may permanently turn on genes involved in cell growth, differentiation, and survival. As a result, mutations in Ras genes can lead to the production of permanently activated Ras proteins.

Overactive Ras signaling can ultimately lead to cancer. Ras is the most common oncogene in human cancer mutations that permanently activate Ras and are found in 15% of all human tumors and up to 90% in certain types of cancer. The clinically most notable members of the Ras subfamily are H-Ras, N-Ras, and K-Ras, mainly for being implicated in many types of cancer. Inappropriate activation of the gene has been shown to play a key role in signal transduction, proliferation, and malignant transformation.

SOLUTION

This novel technology provides methods and compositions for inhibiting K-Ras signaling, blocking the association of K-Ras proteins with a plasma membrane, and providing methods of treating K-Ras mediated disorders.

POTENTIAL IMPACT

Inhibition or blocking of K-Ras association with the plasma membrane provides a much needed and improved method of inhibiting the signal transduction from oncogenic K-Ras. The technology will greatly expand access to new and improved therapies for cancer, such leukemias, colorectal cancers, pancreatic cancers, and lung cancers.

PATENT DETAILS

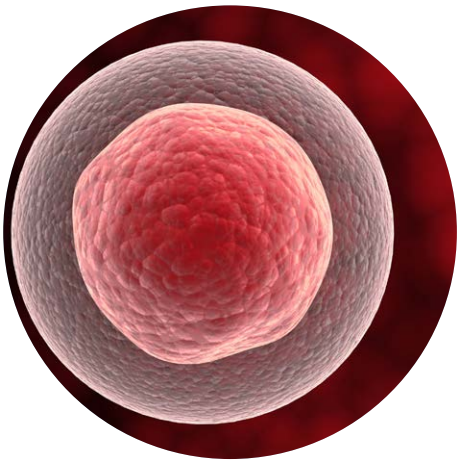
Unlimited Cell Production

PATENT TITLE

CD133+ Cells and Method for Expanding

PATENT # US 10,590,387

INVENTORS | Larry Denner, Randall J. Urban, Yvonne Bodenburg



PROBLEM

It was shown several years ago that human umbilical cord blood (UCB) CD133 + cells could be grown and expanded in culture for a limited time. These cells typically undergo asymmetric division producing CD133+ and differentiated CD133- daughter cells. While the CD133+ cells continue to expand, the ability to produce CD133+ daughter cells diminish over the course of several weeks, ultimately producing no new CD133+ cells. This limited number of CD133 + cells has presented an insurmountable barrier to their utility in transplantation settings. The purpose of the current effort was to overcome this limitation to grow high numbers of UCB CD133+ cells. Co-culturing freshly isolated human UCB CD133+ cells with human meschenchymal stem cells (MSCs) for a limited period followed by weekly removal of the CD133- daughter cells result in the selection of a population of CD133+ cells that will produce a sustained level of CD133+ daughter cells.

SOLUTION

This novel technology provides methods and compositions for producing and expanded populations of CD133+ cells in an unlimited manner.

POTENTIAL IMPACT

The technology will allow continual cell production that will enhance cell plantation in the transplant environment. This will reduce the need for donor search and long wait times associated with donor matching and selection. The technology will greatly expand the access to treatment and help reduce the cost associated with such transplantation.

PATENT DETAILS

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Intellectual Property Showcase:
Therapeutics

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

utmb Health

301 University Boulevard; Galveston, TX 77555