BIOMEDICAL ABSTRACT INDEX

UNIVERSITY OF MISSOURI, COLUMBIA

UNIVERSITY OF MISSOURI, ST. LOUIS

UNIVERSITY OF MISSOURI, KANSAS CITY

UNIVERSITY OF MISSOURI, COLUMBIA

WIRELESS PATIENT POSITIONING & WARMING DEVICE

Prevention of hypothermia during operation is a significant requirement for any surgical case. Difficulty in meeting this necessity is increased in small patients (such as small animals and infants) that have large surface-to-volume ratios. An unrelated requirement for pre-op to post-op patient care is positioning and stabilizing patients on operating tables while minimizing the risk of pressure sores.

The invention addresses deficiencies associated with current convection- and conduction-based patient warming devices – such as the need for external power, increased risk of infection, wire clutter, and noise. Additionally, combining the functions of warming and positioning into a single wireless device adds to its convenience and ease of use.

When a patient is placed on the wireless positioning and warming device, its outer silicone-rubber shell gently conforms to the individual's body and holds its shape when air is removed from a bead-filled chamber. Over five hours of warming is provided via an exothermic reaction within a sodium acetate-filled cavity. When the procedure is complete, air is returned to the bead-filled chamber and a built-in heating pad is used to melt the sodium acetate crystals for reuse. Design variables are optimized for safe surface temperature, maximal heating time, and maximal conformity.

Potential Areas of Application: Hypothermia prevention and patient positioning during veterinary and human surgery. Conforming/heated seating for outdoor sports and recreation. Emergency patient transportation
Patent Status: Provisional patent filed May 21, 2012
Inventor(s): Josh Arnone, Paul Dale. Keith Branson. John Dodam. Charles Sweat, Jr.. Khushbu Jain
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

AUQUAGEN: BOVINE MUCOSAL IMMUNITY ENHANCER

PM ELEVATOR PITCH

Vision: An innovative biotech company, passionately creating rational science based solutions rapidly, to cater underserved/unmet needs for the health & well-being of animals, fish & birds

Technology: A peptide sequence has been isolated from a gut associated lymphoid tissue cDNA expression library which upregulates the expression and secretion of immunoglobulin alpha (IgA), the predominant antibody type in mucosal secretions, tears, saliva and theupper respiratory tract. The factor is novel, is unrelated to any molecule in the database (EST tagged sequences are homologous but function is unknown) and the material may have great impact as an adjuvant for oral or nasal vaccines.

Potential Areas of Application: Global Livestock industry, Bio-defense vaccines, Bovine Respiratory disease complex vaccines, Enhancement of efficacy of oral and nasal vaccines
Patent Status: US Patent 6,930,167
Inventor(s): Gopin Raj
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

AORTIC EMBOLIC PROTECTION SYSTEM

The current rate of in-OR stroke during transcatheter aortic valve implantation (TAVI) is approximately 22%. There is also a 10-40% rate of neurological dysfunction in patients with infective endocarditis, including aortic valve endocarditis. This includes stroke, transient ischemic attack, encephalitis (brain infection), brain abscess, and meningitis (infection of the tissues covering the brain and spinal cord). The current treatment for endocarditis is non-operative and consists of long-term antibiotic treatment. This is because replacing a valve during an active infection is not safe as there is a very high risk for the new valve to become infected.

Currently, in regards to TAVI, no FDA approved solutions are available for use in the United States, and only three devices are available in Europe; however, serious deficiencies have been identified in each of the devices (*e.g.* inadequate seal between implant and intima, contact with the main vessel junctions increasing risk of irritation, etc.. Furthermore, there is no FDA-approved device available to decrease the rate of neurological dysfunction associated with infective endocarditis.

The proposed solution, when temporarily deployed in the aortic arch via catheter, deflects emboli down the descending aorta preventing any neurological dysfunction such as stroke. The device safely conforms to the aortic arch while maintaining a superior seal with the intima (*i.e.* aortic tissue), yet has minimal contact with the tissue, which reduces the risk of tissue irritation – especially at the main vessel junctions. While in place, additional catheters – such as those carrying valve implants – can be passed through the device. Ease of deployment and retraction with X-ray-assisted positioning ensures convenient and effective use. Additionally, the device is structurally optimized to minimize the risk of arterial rupture and of the device slipping once placed, and it safely accommodates human aortic geometry variation.

Potential Areas of Application: Transcatheter aortic valve implantation, Infective endocarditis
Patent Status: Provisional patent filed on May 8, 2012
Inventor(s): Josh Arnone. Raja Gopaldas. Charles Sweat, Jr.. Khushbu Jain
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

ANTI-BIOFILM LOW TEMPERATURE PLASMA COATING

Biofilm formation on or within indwelling medical devices such as catheters, artificial cardiovascular implants, prosthetic joints and contact lenses pose a critical problem for medical care. Biofilm-associated bacteria are particularly resistant to antibiotic treatment compared to planktonic organisms. In addition to the difficulty of treating biofilm with conventional antibiotic therapy, treating biofilm is further complicated by the rising antibiotic resistance among staphylococci. Approximately 1 million nosocomial infections are associated with indwelling devices annually in the United States and incurring enormous healthcare cost. Among these biofilm-forming bacteria, Staphylococcus aureus and Staphylococcus epidermidis are most commonly found on implantable cardiovascular devices.

It was estimated that S. aureus and S. epidermidis caused about 40-50% of prosthetic heart valve infections, most of which are caused by S. epidermidis, and 50-70% catheter biofilm infections. 250,000-500,000 primary blood stream infections resulted from the 150 million intravascular devices implanted in the US annually. Each episode of these infections can increase health care cost by $4,000 to $56,000, which could cost US healthcare system 1-2 billion dollars per year. Approximately 87% of blood stream infections were caused by staphylococci. Taken together, S. aureus and S. epidermidis in biofilm exert a staggering burden on the healthcare system.

As a result, novel therapeutic strategies beyond treatment with conventional antibiotics are urgently needed to address the morbidity and mortality resulting from biofilm formation. There is currently no anti-biofilm drug in the market.

By coating biomaterials used in making these devices with our special technology, we found that bacteria biofilm formation on the coated materials was greatly decreased. We also found that bacteria on the coated materials were more susceptible to antibiotic treatment. As a result, our technology holds a great promise in decreasing the risk of indwelling medical device related infections and could increase the efficacy of current antibiotic therapy. The coating technology we developed is an environmentally friendly process involving no chemical waste. Our technology could offer an inexpensive and simple way to coat medical devices to prevent and treat biofilm formation by S. epidermidis on medical devices.

Potential Areas of Application: Prevent and treat biofilm on medical devices
Patent Status: Patent Pending
Inventor(s): Sun HM, Chen M
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

EGCG CONJUGATED GOLD NANOCEUTICAL FOR TREATMENT OF PROSTATE CANCER

Epigalo Catachein Gallate (EGCG) stabilized radioactive gold nanoconjugate serves a novel therapeutic nanoceutical for use in the treatment of various forms of human cancers including head and neck, breast, prostate cancer and other solid tumors. Our therapeutic gold nanoparticulate formulation is unique, as we have discovered a 100% green nanotechnology process for the production of radioactive gold nanoparticles. In this process, gold salt is converted into the corresponding gold nanoparticles without the intervention of any toxic chemicals.

Potential Areas of Application: Thernastic agent for treatment of cancer
Patent Status: Patent Pending
Inventor(s): Kattesh V. Katti, Raghuraman Kannan, Chathy S. Cutler, Charles Caldwell, Ravi Shukia, Nripen Chanda, Ajit Zambre, Kavita K. Katti, Anandhi Upendran
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

TISSUE-SELECTIVE TARGETED GENE TRANSFER MODALITY FOR TREATING CORNEAL DISEASES

Corneal scarring is the third leading cause of blindness according to World Health Organization's recent report. It is also a common complication of laser eye surgery, a procedure that is frequently used worldwide, to correct refractive errors and corneal dystrophies. At present, no gene therapy treatment exists to cure corneal scarring and corneal neovascularization. Our invention defines a method that efficiently delivers therapeutic genes to the corneal stroma in a highly targeted manner. This tissue-targeted gene therapy approach is highly beneficial for treating corneal fibrosis and corneal neovascularization in vivo without compromising normal corneal function.

Potential Areas of Application: Treatment of corneal scarring
Patent Status: Provisional Filed
Inventor(s): Rajiv Mohan
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

AAV-MEDIATED DECORIN GENE THERAPY FOR CORNEAL FIBROSIS

Corneal scarring is the third leading cause of blindness according to World Health Organization's recent report. At present, no agents exist that are proven to clinically cure corneal scarring without causing serious side effects. We identified a natural gene, decorin, to neutralize fibrosis-causing transforming growth factor b in the cornea. Our invention significantly inhibited fibrosis and myofibroblast formation in the cornea of rabbit eyes *in vivo* by the targeted decorin gene therapy with adeno-associated virus serotype 5. Further, our interventional therapy deemed safe because it did not cause damaging immune reac-

tion, cell death, toxicity, abnormal healing or changes in corneal collagens.

Potential Areas of Application: Treatment of vision impairment and eye disease
Patent Status: Patent Pending
Inventor(s): Mark Estes, Amy Austin, Karen Haas
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

SMALL MOLECULE INHIBITORS WITH ANTINEOPLASTIC AND ANTIANGIOGENIC ACTIVITIES

The molecule NAD^+ is extensively utilized in cellular processes including cell signaling and respiration. The drug AP0866, a potent inhibitor of Nampt, the first and rate-limiting enzyme of the mammalian NAD^+ recycling pathway, is currently being tested in several Phase I and Phase I/II clinical trials against several forms of cancer. In the present invention, we have developed a new class of Nampt inhibitors. The concentration dependent activities of these agents have been tested in-vitro and directly compared with those of AP0866 against six human tumor cell lines including: breast, colon, glioma, prostate, pancreatic, and lung cancer. Several of these agents demonstrate significantly higher activity than AP0866 in vitro, exhibiting significantly lower IC_{50} values, as well as higher cancer cell anti-proliferative effects.

Potential Areas of Application: Anti-cancer therapy, Diabetes, Arthritis
Patent Status: Patent Pending
Inventor(s): Mark Lee, Yulia Sevryugina
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

DETECTING MICRORNA (MIRNA) USING NANOPORE SINGLE MOLECULE DETECTION

MicroRNAs (miRNAs) are a class of short (~18-24-nt) non-coding RNA molecules that regulate gene expression at the post-transcriptional level. Aberrant expression of miRNAs has been found in all types of tumors. Most notably, specific miRNAs are released from the primary tumor into blood circulation, making the detection of circulating miRNAs a powerful tool for noninvasive cancer detection, diagnosis, staging, and monitoring.

We developed a robust nanopore sensor that selectively detects single molecules of circulating miRNAs derived from primary cancer. The nanopore is a fabricated 2-nm molecular pore. Such a tiny pore can generate a signature current signal when a miRNA molecule is specifically captured in it. These signals function as fingerprints that enable us to identify a specific miRNA and quantify its concentration. The prototype has demonstrated the capability to discriminate single nucleotide difference between miRNAs. In clinical tests, we have differentiated miRNA levels in blood between lung cancer patients and healthy people.

Due to the label-free single molecule detection without nucleic acids amplification, the nanopore sensor is higher selective, precise and accurate over the gold standard RT-PCR and microarray. The nanopore array in development would achieve high throughput capability for detecting miRNA profile.

Potential Areas of Application: Detection of any nucleic acids fragments, including all microRNAs and pathogenic DNAs or RNAs, Study of nucleic acid folding/unfolding reactions. Study of miRNA mechanism and principle of regulation Study single nucleotide polymorphisms (SNPs). Study of oligonucleotide-protein and oligonucleotide-drug interactions for drug discovery and development. Biomarker characterization. Diagnostics, prognostics and theranostics.
Patent Status: PCTUS201144082
Inventor(s): Li-Qun Gu, Yong Wang
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

TREATMENT OF TYPE I DIABETES BEFORE AND AFTER EXPRESSION OF PREDISPOSITION MARKERS

Research at the University of Missouri has resulted in a novel technology to treat type I diabetes. This technology uses the unique approach of antigen specific therapy. A peptide from glutamic acid decarboxylase (GAD) autoantigen was genetically expressed on an immunoglobulin molecule and the resulting Ig-GAD was able to restore normoglycemia in hyperglycemic, non-obese diabetic (NOD) mice. This regimen triggered regeneration of endogenous beta cells without assistance of exogenous insulin or stem cell infusion.

Potential Areas of Application: Treatment of type I diabetes before or after expression of predisposition markers
Patent Status: Patent Pending
Inventor(s): Habib Zaghouani, Randal Gregg, Renu Jain
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

A NOVEL PROTEIN TARGET FOR ANTI-CANCER THERAPEUTICS

Targeted therapies are transforming the way people treat cancer. With help from cancer biochemistry and computational modeling technologies, it is now possible to discover new therapeutic targets within cancer cells and then design small molecule drug candidates that selectively interfere with their role in cancer.

The current invention is a novel protein target for anticancer therapeutics. It also includes pharmaceutical compositions and a method of treating cancer using such

compositions. Known inhibitors of this target have been used in other therapeutic areas and supply proof of principle for chemotherapeutic use.

Potential Areas of Application: Cancer treatment, Chemotherapy
Patent Status: Patent Pending
Inventor(s): X. Zou, S. M. Hyder, Y. Liang, S. Z. Grinter, S. Y. Huang
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

DNA METHYLATION BIOMARKERS IN LYMPHOID AND HEMATOPOIETIC MALIGNANCIES

Leukemias and lymphomas are a part of the broad group of malignancies of the lymphoid and hematopoietic systems. Accurate and rapid identification of leukemias and lymphomas, especially subtypes of non-Hodgkin's lymphoma (NHL), is essential to successful treatment because clinical outcome and therapy options vary greatly among them. Aberrant DNA methylation often shows abnormal patterns, unique to specific cancer types, and thus can be used as biomarkers for detections of specific cancers. However, until recently only a few individual genes were known to be methylated in either leukemias or lymphomas.

This invention comprises a set of genetic sequences whose pattern of DNA methylation can be used as biomarkers to identify and differentiate various subtypes of human lymphomas and leukemias for purposes of early detection, diagnosis, prognosis, staging, monitoring of responses to therapies, and sensitive detection and prediction of relapse. Based on this invention, a commercial kit capable of implementing non-invasive test can be generated for treatment and management of cancers such as NHL, chronic lymphocytic leukemia (CLL), multiple myeloma (MM), acute myelogenous leukemia (AML), and acute lymphoblastic leukemia (ALL). This novel invention also provides targets and methods for therapeutic epigenetic treatments of various lymphomas or hematologic malignancies.

Potential Areas of Application: Medicine, Oncology, Chemotherapy
Patent Status: Patent Pending
Inventor(s): Charles Caldwell, Huidong Shi, Farahnaz Rahmatpanah, Kristen Taylor, Doug Laux, Dieter Duff, Guo Juyuan
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

SYNTHESIS OF AVASTIN CONJUGATED GOLD NANOPARTICLES

Gold nanoparticles possess unique properties including preferential binding to leaky blood vessels, ability to bind to a variety of ligands, with no evidence of cellular toxicity, making them an excellent platform for targeted sustained release delivery of drugs and peptides. Avastin is a humanized monoclonal antibody specifically targeting vascular endothelial growth factor that has found widespread use in inhibiting intraocular neovascularization that occurs in macular degeneration and proliferative diabetic retinopathy.

The current invention provides the conjugation of gold nanoparticles (AuNP) with Avastin (Av) to yield AvAuNP nanoconjugates. AvAuNP nanoconjugate is a potential clinical therapeutic agent and has demonstrated excellent ability to deliver Avastin for sustained release of therapeutic dose within the eye.

Potential Areas of Application: Treatment of age related Macular Degeneration, Diabetic Retinopathy
Patent Status: Patent Pending
Inventor(s): Dean Hainsworth, Ravi Shukla, Kattesh V. Katti, Kannan Raghuraman
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

MODULATION OF SPHINOGOSINE 1-PHOSPHATE-METABOLIZING ENZYMES FOR THE TREATMENT OF INFLUENZA

Influenza virus continues to cause tremendous morbidity and mortality on an annual basis. While vaccines exist to help prevent infection, there are only a handful of drugs approved for treating the infected individual. Moreover, the virus has evolved, in many cases, to become resistant to these treatments. The current discovery identifies sphingosine-1-phosphate pathway as critical for virus replication. Blocking sphingosine kinase activity or over expressing sphingosine 1-phosphate lyase strongly inhibited virus propagation. Therefore, modulation of this pathway could lead to new points of pharmaceutical intervention.

Potential Areas of Application: Inhibit Influenza virus replication
Patent Status: Patent Pending
Inventor(s): Bumsuk Hahm, Young-Jin Seo, Stephen Alexander
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

BIOCOMPATIBLE POROUS TITANIUM FOR BONE REPAIR

Arthritis and trauma are a major problem and one of the leading causes of physical disabilities, necessitating billion-dollar expenditures annually in medical care and rehabilitation. Many times replacing a joint is necessary; our invention describes a method for the preparation of porous titanium (Ti) implants for the repair of diseased or damaged bone. These Ti implants have the requisite mechanical properties to match the strength and elastic modulus of bone. The Ti implants are also coated with a layer of bioactive glass to improve their biocompatibility

and the interfacial bonding with bone. This results in a stronger, longer lasting solution.

Potential Areas of Application: Repairing diseased or damaged bone
Patent Status: Patent Pending
Inventor(s): B.S. Bal, T.S. Huang, M.N. Rahman
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

INTRAVITREAL INJECTION DEVICE

With the discovery of new drugs to treat macular degeneration and other retinal diseases, the prevalence of intraocular injections for treatment of those diseases has skyrocketed. Current ophthalmologic practice relies on a free hand injection of the medicines using a syringe. This difficult procedure poses a significant challenge to the novice and expert alike. A preferred approach would be to use a device that would guide the needle into the eye in a specific and reproducible manner. This new device will allow reproducible delivery to the eye in a position and orientation-specific manner using current syringes.

Potential Areas of Application: Intravitreal injection using syringe loaded medicines
Patent Status: Patent Pending
Inventor(s): Chetan Rasiklal Soni, Nathan Heseman
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

ALTERATIONS IN RNA BINDING PROTEINS TREAT BREAST CANCER

Human breast cancer is broadly divided into two different subtypes: estrogen receptor positive (ER+) and estrogen receptor negative (ER-). The majority of women with breast cancer are ER+ (85%), whereas the remainder is ER- (15%). Patients with ER+ breast cancer can be treated with the drug tamoxifen, but for unknown reasons, many of them develop drug resistance. In contrast, there are no specific treatments for women who are ER-. These patients are usually treated with surgery and chemotherapy, but the tumor eventually recurs resulting in the death of the patient. Hence, there is a need to develop therapies to treat ER- breast cancer, as well as ways of overcoming the development of tamoxifen resistance in ER+ breast cancer. Posttranscriptional gene regulation by RNA binding proteins (RBPs) and microRNAs (miRNAs) regulate gene expression at the level of mRNA stability and translation.

The current invention alters the expression of breast cancer genes at the posttranscriptional level which can block tumor growth by over 90% in difficult to treat breast cancers.

Potential Areas of Application: Gene Therapy, Cancer Therapy
Patent Status: Patent Pending
Inventor(s): Ulus Atasoy, Matt Gubin, Robert Calaluce
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

HELICAL CONSERVATIVE SHOULDER PROSTHESIS

Shoulder replacement surgery is required to supply function to joints damaged by traumatic injury, use injuries or disease. Over 60,000 replacements are performed in the US annually. Presently, the ball (or head) of the replacement joint rests on top of the humerus and is connected to a long shaft (or stem) that penetrated down into the intramedullary canal of the bone.

This invention does not require the stem insertion into the intramedullary canal for stabilizing the ball thus the device does not require reaming into the intramedullary canal. One size stem will fit multiple patient geometries decreasing the need for precise sizing and leading to decreased need for variable manufacturing and inventory.

Potential Areas of Application: Shoulder implant for shoulder arthritis, post trauma, or medical conditions
Patent Status: Patent Pending
Inventor(s): Matthew Smith
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

FACILE GAS-INDUCED TRANSFORMATION OF PHARMACEUTICAL POLYMORPHS/ORGANIC SOLIDS

Gas pressurization can be used to convert polymorphs of pharmaceutical agents with ease. Current processing methods are often lengthy and can involve the use of high temperature at great expense to the industrial sector. Our facile method of polymorph transformation eliminates the need for such measures, and offers vast potential for streamlining the processing of pharmaceutical agents, with a concomitant savings in energy costs while potentially creating new pharmaceutical entities and patent extensions.

Potential Areas of Application: Pharmaceutical manufacturing
Patent Status: Patent Pending
Inventor(s): Jerry Lee Atwood, Jian Tian, Scott John Dalgarno
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

HUMAN ZONA PELLUCIDA GLYCOPROTEINS, THEIR OLIGOSACCHARIDES, AND THEIR USE IN CONTRACEPTION AND IN THE DIAGNOSIS OF HUMAN INFERTILITY

To fertilize the human egg (oocyte), human sperm must first bind on the surface of the oocyte. The sperm binds to the oocytes via both the carbohydrate and protein portion of the glycoprotein. A human glycoprotein that is the equivalent to that on the oocyte can be used as a contraceptive agent by acting as a decoy. The carbohydrate sequences from these glycoproteins can also be used as agents, either singly or conjugated to polymers or other supports, for multiple uses including methods in the field of human infertility diagnosis. This discovery takes advantage of the unique species specific interactions between human sperm and oocytes.

Potential Areas of Application: Large potential in the natural contraceptive market. Species-specific sperm binding assays.
Patent Status: Patent Pending
Inventor(s): Gary Francis Clark, William Shu Biu Yeung, Philip Chi Ngong Chiu, Anne Dell, Poh-Choo Pang, Kay-Hooi Khoo
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

CLOSED LOOP RESPIRATORY DEVICE WITH DYNAMIC ADAPTABILITY

This invention describes a device for automatically controlling SpO2 concentrations in the blood of premature infants and other patients in need of respiratory support. This dynamically adaptable device will respond to changing patient conditions where tight O2 control is desired or in situations of reduced staff monitoring capabilities.

Potential Areas of Application: Neonatal intensive care units, General respiratory control situations
Patent Status: Patent Pending
Inventor(s): Ramak R. Amjad, Roger C. Fales, Timothy Keim
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

RIP-CHIP PROFILING OF BREAST CANCER SUBTYPES

The correlation between steady state mRNA levels and protein products is known to be poor. Posttranscriptional gene regulation, provided in part by microRNAs and RNA binding proteins, is becoming recognized as an important form of cellular control, especially as the significance of these regulators is better appreciated. Several RNA binding proteins are over-expressed in a variety of malignancies, including breast cancer. They have been shown to play a role in increased invasiveness of malignancy and poor prognosis for many cancers, as well as being implicated in tamoxifen resistance in breast cancer. Moreover, they have been described to control the expression of genes involved in transformation, and may serve as tumor maintenance genes.

The current invention enables the identification, en masse, of in vivo targets of RNA binding proteins from cancer cells. This RIP-Chip technique allows one to identify en masse in vivo mRNA targets that interact with different RNA binding proteins.

Potential Areas of Application: Cancer diagnostic tests, Cancer therapeutics
Patent Status: Provisional patent filed
Inventor(s): Ulus Atasoy, Robert Calaluce, J. Wade Davis
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

DNA METHYLATION BIOMARKERS FOR RARE CANCER CELL DETECTION

Multiple Methylation Sensitive Enzyme Restriction PCR (MSR-PCR) is a highly sensitive and specific novel PCR assay, which is suitable for detection of rare cancer cells including circulating various tumor cells (CTCs) in blood. Approximately 90% of cancer deaths are caused by metastasis in which the hematogenously spread cancer cells subsequently grow at distant organs. Emerging evidence indicates that the disseminating CTCs present in the peripheral blood and bone marrow represent an early rather than a late event in cancer development. Early detection of CTCs and characterization of the molecular signature of metastatic clones provide vital insight information for early diagnosis. Furthermore, monitoring CTCs during the entire course of treatment, especially after surgical resection and chemotherapy, provides objective information for personalized clinical management to avoid unnecessary therapeutic related toxicity.

A universal cancer diagnostic kit for detection of occult circulating tumor cells (CTCs) at early state of cancer development can be generated from our newly developed MSR-PCR conjugated a panel of tumor-specific DNA methylation biomarkers disclosed in this invention. Detectible malignancies include hematopoietic tumors (leukemia, lymphoma, myelodysplastic syndrome, multiple myeloma), carcinoma (breast cancer, colorectal cancer, prostate cancer, ovarian cancer and lung cancer) and melanoma. This novel invention can not only save lives from early detection and diagnosis, but also improve the quality of life in diagnosed cancer patients during the entire course of medical treatment.

Potential Areas of Application: Preventive medicine, Cancer screening, Oncology, Chemotherapy, personalized cancer therap.
Patent Status: Provisional patent filed
Inventor(s): Michael Xia Wang, Kristen Taylor, Charles William Caldwell, and Srilatha Nalluri
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

EGFR-SURE: DIAGNOSTIC KIT

Epidermal Growth Factor Receptor (EGFR) is a biomarker for cancer in tissue. EGFR is overexpressed in the cell membrane of a variety of malignant neoplasms, including colorectal adenocarcinoma, non-small cell lung carcinoma, head and neck carcinoma, and glioblastoma. Many targeted anticancer therapeutic approaches are aimed at the inhibition of EGFR. For example, EGFR inhibitor *Cetuximab* is currently used for treating colorectal carcinoma in humans. For the therapy to be effective, precise determination of the EGFR expression levels within the cell membrane is important, because only EGFR-dependent (EGFR positive) tumors respond to these therapeutic approaches. Clinically available Dako's EGFR-PharmDx (current gold standard) immunohistochemistry kit is not sufficiently accurate in the determination of EGFR expression in tumor tissues. Therefore, patients showing an EGFR negative expression have responded to EGFR-therapy treatment. Our team at MU has developed a proprietary nanotechnology based histological cancer detection kit (*EGFR-Sure)* for identifying and quantifying EGFR-expression in a tissue sample. *EGFR-Sure* is a platform technology.. *EGFR-Sure*'s technology can be extended to other biomarkers in cancers by careful variation in the peptide sequence. According to an article published in *Genetic Engineering & Biotechnology News (GEN),* the tissue-based diagnostics market will most likely double by 2016 growing from the $1.029 billion in 2009 to $2.278 billion in 2016. Tissue-based diagnostics continues to be important for tumor analysis and for diagnosing other diseases. With an expanding rise of cancer patients, tissue diagnostics is likely to experience significant growth.

Potential Areas of Application: Tumor analysis and diagnosing other diseases
Patent Status: Patent Pending
Inventor(s): Raghuraman Kannan
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

ROTATOR CUFF BONE-TENDON ALLOGRAFT

Rotator cuff problems occur when one or more tendons that connect shoulder muscles to bone become torn, leading to pain and dysfunction of the arm. The tears may occur as the result of acute trauma to the shoulder, particularly in athletes, or from chronic wear and tear, especially in the elderly. Rotator cuff problems are commonly associated with activities that require repetitive overhead motions or forceful pulling motions. In the US alone, there are more than 50,000 rotator cuff surgeries per year. While smaller, single-tendon tears can often be managed successfully non-operatively or by direct arthroscopic repair, the majority of tears involve larger defects, multiple tendons, and/or a degenerative component that leaves the muscle-tendon unit severely dysfunctional and predisposes the shoulder to arthritis. For these more severe tears, surgical reconstruction is typically required to restore function to the arm. Current surgical repairs entail the use of suture and bone anchors or soft tissue scaffolds to address the tissue defects and associated dysfunction. However, these techniques are not designed to be "spanning" or "structural" grafts and therefore are not able to replace irreparable tendon tissue, re-establish the critical bone-tendon and tendon-muscle junctions, and restore full shoulder function.

The current invention developed by researchers at the University of Missouri provides a FDA-approved biomaterial for use in rotator cuff repair as well as a method that when used in rotator cuff repair will potentially result in the overall function of a repaired rotator cuff that is similar to a healthy uninjured rotator cuff.

Potential Areas of Application: Rotator cuff surgical repair and reconstruction; Glenoid bone reconstruction
Patent Status: Non-Provisional Application filed
Inventor(s): James L. Cook
Contact: Harriet Francis, UMC, francish@missouri.edu, 573-884-0374

ACL GRAFTS PRODUCED BY CONJUGATING NANOMATERIALS WITH ACELLULAR BIOLOGICALLY DERIVED TISSUE

There is a critical need for new graft materials for ligament reconstruction. Current problems experienced by many ACL reconstruction patients is joint instability caused in part by lack of cellular integration and remodeling, leading to deterioration of the graft. Thus there is a critical need for new graft materials that promotes cellularity, integration, and recapitulation of natural joint function.

We have developed a patented technology where nanomaterials are conjugated to acellular tissue to provide a 3D tissue network that has enhanced remodeling and controlled degradation, promotes cellular in-growth, and provide good mechanical behavior. Our transformative technology utilizes a functionally graded nano-graft. HaNPs are conjugated at the ends of a graft to promote osseointegration while AuNPs are conjugated throughout the graft to promote cellular migration and remodeling.

There are approximately 350,000 ACL reconstruction surgeries per year which involve autograft or allografts and the acute care associated with ACL surgeries is estimated to be $6 billion annually in the US. Our nano-grafts will compete based on proprietary intellectual property for soft tissue implants.

Potential Areas of Application: ACL reconstruction surgeries
Patent Status: Patent Pending
Inventor(s): Sheila Grant, Richard White
Contact: Paul Hippenmeyer, UMC, HippenmeyerP@missouri.edu, 573-882-0470

1-CLICK DECISION SUPPORT

Clinical practice is complex. This is demonstrated by the statistic that only 56% of guideline-based recommended chronic disease care and only 55% of guideline-based recommended preventive care are delivered to patients in the U.S. Evidence-based chronic disease and preventive care guidelines should be utilized by clinicians to guide decision-making and healthcare delivery to all patients. There are hundreds of high quality web-based guidelines available for routine patient care, such as: complex drug dosing algorithms, chronic disease treatment algorithms, and heart disease, fracture and cancer risk calculators. The Health Information Technology for Economic and Clinical Health (HITECH) Act and "meaningful use" requirement provides incentive that will drive widespread adoption of decision support systems. However, among the barriers to adoption of existing systems are issues with usability, which prevent successful implementation of these systems.

MedSocket provides a patented clinical decision support solution with 1-Click Decision Support (1-CDS). The 1-CDS system connects busy, practicing clinicians to the best evidence-based practices with unprecedented speed and simplicity. Issues such as lack of integration into the electronic health record and busy clinical workflow, as well as frequent changes in treatment algorithms, create barriers to clinical decision support system utilization. 1-CDS eliminates these issues by automatically displaying evidence-based guidelines and clinical decision support tools in the workflow of busy, practicing clinicians.

1-CDS was successfully piloted at the University of Missouri Health System and demonstrated improvements in health care decisions, enhanced efficiency, decreased health care costs, and improved patient outcomes. The University of Missouri develops and maintains treatment algorithms for some of the most common and expensive conditions in the U.S. MedSocket is obtaining exclusive rights to these algorithms. With 1-CDS, clinicians have the power to connect to treatment algorithms and medical calculators directly from a patient's electronic health record. This technology will potentially improve patient care, save money, and increase provider satisfaction by saving time and reducing medical errors.

Potential Areas of Application:
Clinical decision support, Health information technology Health care services, namely, alerts and guidelines relating to patient diagnosis, procedures and treatment Medical services, namely, automated evaluation of laboratory results and provision of treatment guidelines
Patent Status: U.S. Patent Application No. 12/572412
Inventor(s): Karl Kochendorfer, MD, FAAFP; Jared S. Coberly, MD
Contact: Paul Hippenmeyer
hippenmeyerp@missouri.edu. 573-882-0470

UNIVERSITY OF MISSOURI, ST. LOUIS

COMPOUNDS TO FIGHT MICROBIAL SEPSIS AND ALZHEIMER'S

The invention provides a series of novel Lipid A analogues that are structurally simple, synthetically accessible, and capable of blocking the cellular receptor within the signal stransduction pathway. Sepsis is a potentially deadly, medical condition characterized by a whole-body inflammatory response by the immune system to bacterial endotoxins in the blood stream. Severe sepsis includes the presence of organ dysfunction. Endotoxins (Lipopolysaccharide or LPS) are a major component of the cell wall of gram-negative bacteria and are released from the bacteria as they are destroyed. LPS induces a strong response from normal immune systems; it binds the CD14/TLR4/MD2 receptor complex, which promotes the secretion of pro-inflammatory cytokines in many cell types, but especially in macrophages. LPS is composed of three structural regions, one of which (the Lipid-A region) is largely responsible for the toxic activity. This new class of compounds can serve as a Lipid A-like LPS antagonist, has potential as a therapeutic agent for microbial sepsis and a treatment for the inflammatory component of Alzheimer Disease.

Potential Areas of Application: Treat microbial sepsi. and the inflammatory component of Alzheimers
Patent Status: Patent Pending
Inventor(s): Alexei Demchenko, Michael Nichols, Sophon Kaeothip
Contact: Tamara Wilgers, UMSL,
WilgersT@umsl.edu, 314-516-6884

CHEMICAL TRANSFORMATION AND TRANSFECTION AGENTS TO DELIVER LARGE DNA AND OTHER MACROMOLECULES INTO CELL

The delivery of large molecules, such as DNA, into cells is critical to many fields of biological research including drug discovery, and drug and biofuel production, however many of the current technologies mediating this delivery have damaging effects on cellular systems or require complex and expensive reagents. In addition, there are no effective chemical methods for transporting sizes of DNA greater then 15kb into cellular systems, limiting research development and commercial applications. Researchers at the University of Missouri-St. Louis have identified cost-effective and easily prepared chemical agents that deliver DNA plasmid sizes of greater than 20kb into a variety of cell types, including bacteria and fungi, with low cell toxicity.

Potential Areas of Application: Gene therapy, Protein production, vaccine development and genetic engineering
Patent Status: U.S. Provisional Patent Application Filed
Inventor(s): George W. Gokel, Jason L. Atkins, Mohit B. Patel
Contact: Tamara Wilgers, UMSL,
WilgersT@umsl.edu, 314-516-6884

UNIVERSITY OF MISSOURI, KANSAS CITY

BIOCOMPATIBLE BONE CEMENT/BIOMATERIAL

A biocompatible polymer bone cement with numerous advantages over the currently used polymethyl methacrylates.

Currently available commercial bone cements are composed of polymethyl methacrylates and have several notable disadvantages including toxicity, lack of bioactivity, volumetric shrinkage, tissue necrosis, and the generation of heat upon polymerization. Due to the high temperatures produced during polymerization, antibiotic treatment with bone cement is very limited. Only tobramycin, gentamycin and vancomycin are heat-stable and can survive the high temperatures during the polymerization of PMMA's.

Researchers at the University of Missouri-Kansas City and Missouri University of Science & Technology have developed a chemically initiated cement that i. composed primarily of a monomer that has already proven very effective in commercial dental composites. Our extensive testing of this new cement has found that this system is biocompatible, has a peak exotherm that is below 45 degrees C, low shrinkage, and excellent mechanical properties. This system provides a biocompatible alternative to PMMA-based bone cements while maintaining good mechanical properties.

Potential Areas of Application: Bone repair, orthopedic surgeries, implants, etc.
Patent Status: Patent Pending
Inventor(s): Kilway, Kathleen V.; Bonewald, Lynda F.; Schuman, Thomas P.
Contact: James Brazeal, UMKC, brazealj@umkc.edu, 816-235-5091

PHOTO-ACTIVATED INSULIN DEPOT

Insulin users are burdened with a lifetime of injections and poor blood sugar control.

Alternatively, they are burdened with a lifetime of pump and cannula use, an effective but limiting solution. Therefore, there is a critical need for creating methods of administering insulin in a non-invasive, but precisely metered manner.

Researchers at the University of Missouri- Kansas City have conceived a material that allows insulin to be released in a controlled fashion using light from a shallow subcutaneous depot. Because daily insulin requirements are low (~1mg) but highly varying, a shallow subcutaneous reservoir of such materials allows for the effective, non-invasive control of blood sugar through transdermal irradiation and release of insulin in response to blood glucose levels. Such a reservoir could potentially contain weeks worth of insulin, loaded onto an insoluble resin, until a controllable light source could release the appropriate amount.

Potential Areas of Application: Diabetes Patients
Patent Status: Patent Pending
Inventor(s): Friedman, Simon; Karunakaran, Dipu; Jain, Piyush K..
Contact: James Brazeal, UMKC, brazealj@umkc.edu, 816-235-5091

LARIAT-SEQ

A new method to analyze RNA lariats by employing the high-throughput sequencing of purified RNA lariat populations.

UMKC Researchers have developed a new technology for the analysis of RNA lariats called Lariat-seq, which is high-throughput sequencing of purified RNA lariat populations. Lariat-seq can be used to investigate gene structure, identify alternative splicing patterns, map intron RNA branch points, compare gene transcription levels, and identify small RNAs encoded within intron lariats. In addition, Lariat-seq can identify the presence of other (non-lariat) covalent modifications in RNAs.

Lariat-seq increases the accuracy of genome annotation and simplifies the process of identifying lariat RNA branch points and the sites of some other covalent modifications of RNA. These advances will speed the development of diagnostics and drugs that target RNA features related to intron splicing as well as RNA covalent modifications that are not due to an RNA branch. Lariat-seq is a very sensitive method for basic and applied researchers to identify introns, branch point sequences , alternative splicing events, as well as the presence of covalent modifications in RNAs that are not due to an RNA branch. The sensitivity can be greatly enhanced by reducing RNA lariat debranching activity in the cells that are the source of the experimental RNA.

The sensitivity of Lariat-seq is an improvement over other methods for identifying introns and alternative splicing events. Furthermore, Lariat-seq is the only way to globally identify the lariat RNA branch point sequences within a heterogenous RNA population. Current methods require evaluation of one branch point at a time. Lariat-seq is also the only way to globally identify sites of covalent RNA modifications that are not due to an RNA branch within a heterogenous RNA population.

Potential Areas of Application: Analysis of RNA lariats
Patent Status: Patent Pending
Inventor(s): Menees, Thomas
Contact: James Brazeal, UMKC, brazealj@umkc.edu, 816-235-5091