FALL 2011

TECHNOLOGY HIGHLIGHTS

Children's Hospital LOS ANGELES℠

THE SABAN RESEARCH INSTITUTE

OFFICE OF TECHNOLOGY TRANSFER

Non-confidential Summaries of Technology available for Commercialization at Children's Hospital Los Angeles

1000
mL
900
800
700
600
500
400
300
APPROXIMATE VOLUME

TABLE OF CONTENTS

About Children's Hospital Los Angeles Page 2
The Saban Research Institute Page 3
Office of Technology Transfer Page 4
Temporary Bone Filler Page 6
Oral Solution of Known Compound for Treatment of Diseases, Including Sickle Cell Disease Page 7
Inhibitors of a Known Therapeutic Target to Treat Brain Injury and Improve Associated Cognitive Deficits Page 8
Electrophysiological Diagnosis and Treatment for Asthma Page 9
A Novel Population of Stem Cells Derived From Peripheral Blood of ECMO Patient Page 10
Prediction of Survival in Metastatic Neuroblastoma Based on 14 Genes Expressed by Tumor and Tumor-Associated Inflammatory Cells Page Page 11
Non-Invasive Substance Detection Using Eye Measurements Page 12
Non-Invasive Intracranial Pressure Monitor Page 13
Novel Pacemaker Device Page 14
EMAP II Inhibitors to Treat Cardiovascular Disease Page 15
Stem Cell-Based Therapy for Chronic Kidney Disorders Page 16
Novel Chimeric Protein as New Class of Anti-HIV Compounds Page 17
High Throughput Assay to Screen Compounds that Inhibit Enveloped Viruses Page 18
An Ultrasound-Activated MRI Contrast Agent and Drug Delivery System Page 19
Novel Therapeutic Target for Gliomas and Medulloblastomas Page 21
Oral Formulation of Fenretinide with Improved Bioavailability Page 22
Combination Therapy for Cancer: Oral Fenretinide and Microtubule Inhibitors Page 23
Combination Therapy for Cancer: Oral Fenretinide and Ketoconazole Page 24
Adipocyte-Secreted Factor Attracts Leukemia Cells Page 25
RNAi Therapy for Brain Tumors Page 26
Clinical Radiology Software for MR Urography Page 27
Diagnostic Target for Ewing's Family Tumors Page 28
Diagnostic Kit for Functional Disorders Page 29
Novel Research Tool for Neuron Culture: The Neuron Chip Page 30
Minimal Lentiviral System Page 31
Project AIM (Adult Identity Mentoring): A Program to Reduce Sexual Risk and Substance Abuse Risk Among Youth Page 32
Kids N Fitness© Evidence-Based Weight Management Program Page 33
Medical Emergency Communication Book Page 34

ABOUT CHILDREN'S HOSPITAL LOS ANGELES

OUR MISSION

We create hope and build healthier futures.

OUR HISTORY

Founded in 1901, Children's Hospital Los Angeles is one of the nation's top children's hospitals and is acknowledged worldwide for its leadership in pediatric and adolescent health. Children's Hospital is one of only 11 in the nation–and the only one in California–named to the national Honor Roll of children's hospitals in the 2011 *U.S. News & World Report* rankings for clinical excellence.

Children's Hospital Los Angeles is a premier teaching hospital and has been affiliated with the Keck School of Medicine of the University of Southern California since 1932.

FAST FACTS

- Admits approximately 11,000 children each year
- 66,000 Emergency Department visits per year
- 4,200 employees and approximately 600 medical staff
- The only freestanding Level 1 Pediatric Trauma Center in Los Angeles County approved by the County Department of Health Services and accredited by the Committee on Trauma of the American College of Surgeons
- Performs nearly 15,500 pediatric surgeries each year, including more complex surgical procedures than any other hospital in Southern California

THE SABAN RESEARCH INSTITUTE OF CHILDREN'S HOSPITAL LOS ANGELES

The Saban Research Institute of Children's Hospital Los Angeles is among the largest, most productive pediatric research facilities in the United States, with 100 investigators engaged in 186 laboratory studies, clinical trials and community-based research and health services.

It is one of the few freestanding research centers in the nation that combines scientific inquiry with patient clinical care and is dedicated exclusively to children. Originally established in 1992, the Children's Hospital Los Angeles Research Institute became The Saban Research Institute in 2003 following a $40 million gift in support of pediatric research made by Cheryl Saban, PhD, Haim Saban and The Saban Family Foundation. The Saban Research Institute maintains strong scientific and strategic affiliations with the University of Southern California (USC) and, in particular, the Keck School of Medicine of USC. All of the Institute's principal investigators (clinical investigators, physician/scientists and PhD/scientists) are USC faculty and many have collaborative projects with scientists at the Keck School of Medicine and other departments at USC. The Institute's researchers also are involved in collaborative projects with academic institutions in other cities in the U.S. and abroad.

FAST FACTS ABOUT THE SABAN RESEARCH INSTITUTE

- In 2010, The Saban Research Institute received more than $23 million in funding from the National Institutes of Health, and $37 million in total funding
- 200,000 square feet of dedicated research space
- Holds 152 active patents

OFFICE OF TECHNOLOGY TRANSFER AT CHILDREN'S HOSPITAL LOS ANGELES

Technology transfer is the process of transferring novel technologies, discoveries and ideas generated from the hospital's research labs and clinical practice to the outside world for society's benefit.

Research programs at Children's Hospital Los Angeles are significantly funded from top national and regional funding agencies such as the National Institutes of Health and the California Institute of Regenerative Medicine. Research at Children's Hospital has led to a number of breakthroughs in the form of therapeutics, diagnostics, research tools and medical devices. Children's Hospital is committed to translating these discoveries and innovations into products and services for the benefit of society by partnering with industry to make these products and services widely available. The hospital understands that such breakthroughs cannot be made available to the public without the cooperative efforts of both the public and private sectors, and takes pride in fostering inter-institutional partnerships that lead to strengthening the economy, creating jobs and above all, serving mankind.

OFFICE OF TECHNOLOGY TRANSFER STAFF

JESSICA L. ROUSSET is director of the Office of Technology Transfer at The Saban Research Institute, managing all intellectual property matters for Children's Hospital Los Angeles. She is co-director of the Center for Scientific Translation of the Southern California Clinical and Translational Science Institute and co-director of the Southern California Center for Technology and Innovation in Pediatrics (SC-CTIP), a pediatric medical device consortium. She received her master's degree in biochemical engineering at the Institut National des Sciences Appliquées in Lyon, France. Prior to joining the Office of Technology Transfer at Children's Hospital Los Angeles, Jessica worked as a licensing professional at The Scripps Research Institute in La Jolla, Calif. She also held positions in research and development, clinical development and business development at GlaxoSmithkline Biological's vaccine division located in Brussels, Belgium. Jessica is a member of the Association of University Technology Managers (AUTM), the Los Angeles Venture Association (LAVA), the Southern California Biomedical Council (SoCalBio) and the Licensing Executives Society (LES).

PHONE: 323.361.4531 • EMAIL: JROUSSET@CHLA.USC.EDU

JOY VICK, coordinator, manages the office's financial activities, oversees all administrative duties and is the liaison on all copyrighted product marketing and sales. She was educated at Wayne State University in Detroit, Mich., with an undergraduate degree and graduate work in Biological Sciences, as well as a law degree. A former practicing attorney and entrepreneur, her interests in business development, intellectual property law and biology brought her into the world of technology transfer.

PHONE: 323.361.8368 • EMAIL: JVICK@CHLA.USC.EDU

BRIAN BENSON is the business development program specialist at The Saban Research Institute, assisting the Business Development Group in developing essential strategies for expanding industry-sponsored partnerships, research and licensing for Saban Research Institute inventors. He is project manager of the Southern California Center for Technology and Innovation in Pediatrics, a pediatric medical device consortium. Prior to joining the Business Development Group, Brian was the business outreach officer at the California NanoSystems Institute at the University of California, Los Angeles. He also held positions as crew chief, product development specialist and marketing strategist with several automotive racing teams. He received his bachelor of science degree in Entrepreneurship from Loyola Marymount University in Los Angeles, Calif. Brian is a member of the Los Angeles Venture Association (LAVA).

PHONE: 323.361.7397 • EMAIL: BBENSON@CHLA.USC.EDU

THERESA WEBSTER, administrative assistant, handles all clerical tasks for the office and is the liaison for the office's communications and marketing activities. Theresa graduated from the University of Las Vegas, Nevada with an undergraduate degree in International Business. A working background in research grants and an interest in science, technology and business development have propelled her into the technology transfer environment.

PHONE: 323.361.2186 • EMAIL: TWEBSTER@CHLA.USC.EDU

NEW

TEMPORARY BONE FILLER

CHLA ID: 2010-005

INVENTOR
David Skaggs, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
An implantable device for temporarily filling a hole in a bone.

BACKGROUND
Bone surgery, such as spinal fusion surgery, craniofacial reconstruction/trauma and dentistry, can require that holes be made in the bone. For example, patients who have undergone surgery involving the placement of a screw into a bone will have a hole in the bone when the screw is removed. In situations where removal of the screw is permanent, bone can regrow and close the hole over time. However, there are situations where temporary removal of a screw is necessary, such as when an infection develops at the site of implantation of the screw. Frequently, after treatment and clearance of the infection, a new screw is implanted at the same site as the original screw. During the infection clearing period, which generally lasts a minimum of six weeks but often up to six months or more, new bone typically forms and fills the space left by the removed screw. The newly formed bone is harder and denser than the original bone, making it much more difficult for the surgeon to drill into the new bone in order to put in a new screw. This difficulty also results in increased risks associated with the surgery, particularly damage to surrounding tissue if a drill or other tool or implant is diverted to a different location.

TECHNOLOGY DESCRIPTION
This invention addresses the need for a temporary bone filler that is highly biocompatible, decreases and/or abolishes bone growth, can be easily removed and helps clear infection. The device will facilitate subsequent surgeries at the same site and prevent possible complications during re-implantation of a screw.

APPLICATIONS
- Spinal fusion surgery and other non-spine applications
- Implant site infection, implant rejection, necessity of removing implants due to untoward sequlae (spine implants that led to paralysis), poor soft-tissue healing over implants, etc.

ADVANTAGES
- No such device currently addresses this issue
- Can be provided as part of a kit

DEVELOPMENT STAGE
- Design specifications in progress

IP PROTECTION
PCT application filed

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

DAVID SKAGGS, MD

NEW

ORAL SOLUTION OF KNOWN COMPOUND FOR TREATMENT OF DISEASES, INCLUDING SICKLE CELL DISEASE

CHLA ID: 2011-001

INVENTOR
Edward Gomperts, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
A novel formulation of a known compound for treating diseases including cardiovascular, inflammatory, sickle cell and other diseases. The novel formulation is designed to safely administer therapeutic levels of the known compound in a liquid form.

BACKGROUND
The selected compound exhibits medical properties and has shown promise in treating a variety of diseases. Given its potential toxicity and narrow range between efficacious and toxic doses, the primary challenge in using this compound as a therapeutic agent is to deliver known levels that do not cause harm. In addition, delivery must be easy for the patient.

Patients suffering from inflammatory diseases (Crohn's disease, ulcerative colitis, rheumatoid arthritis, multiple sclerosis, systemic inflammation), ischemic diseases (coronary, organ, neural or shock-induced ischemia), cardiovascular diseases (ischemia/reperfusion, vascular disease), sepsis and others will potentially benefit from the use of the compound as a therapeutic agent. It also will be of great benefit to manage and prevent crises in patients with sickle cell disease, which affects an estimated 70,000 to 100,000 subjects in the United States. The life expectancy of these patients is only about 40 years and a large percentage experience sickle cell crises several times a year, resulting in strokes, organ damage and poor health. Currently, only chronic transfusions have been shown to reduce the number of crises and prevent strokes, although they don't prevent silent strokes that result in cognitive impairment. Transfusion programs are cumbersome, costly and put patients at risk for iron-overload. Hydroxyurea treatment reduces the number of crises but does not prevent strokes, may have secondary effects in some patients, and poor compliance with the medication occurs in the adult sickle cell population. While bone marrow transplantation can cure the disease, best results are obtained when the donor is a sibling. High-cost and co-morbidities also limit the use of this curative procedure.

TECHNOLOGY DESCRIPTION
The invention delivers a known compound in a liquid formulation in an amount that is sufficient to reduce or eliminate at least one clinical symptom in the affected patient. The new formulation will reduce the number of sickle cell crises experienced by the patient. The treatment may be repeated one or more times during a prescribed time period to provide a multi-dose treatment regimen and/or to provide a chronic treatment regimen.

APPLICATIONS
- Sickle cell disease
- Inflammatory, ischemic, cardiovascular diseases
- Sepsis and others

ADVANTAGES
- Can be accurately delivered orally
- Palatable formulation to encourage compliance

DEVELOPMENT STAGE
- Formulation in development
- In vitro data
- Safety and efficacy experiments in an animal model

IP PROTECTION
Provisional patent application filed

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

EDWARD GOMPERTS, MD

NEW

INHIBITORS OF A KNOWN THERAPEUTIC TARGET TO TREAT BRAIN INJURY AND IMPROVE ASSOCIATED COGNITIVE DEFICITS

CHLA ID: 2011-002

INVENTOR

Robert J. Brown, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY

A novel method for treating the loss of neurocognitive function in subjects suffering from an injury/trauma, disease, disorder or degeneration of the brain. Provides, for the first time, a link between cognitive function of the brain and activity of the known therapeutic target.

BACKGROUND

In the last few years, various modalities have been successfully developed to treat trauma, injuries, disorders and degeneration of the brain; however, novel treatments are still needed to improve associated cognitive deficits. For example, there is no proven or accepted therapy for the treatment of long-term neurocognitive deficits such as those occurring in children with brain tumors who have received whole brain irradiation as therapy.

Any chronic or long-term loss of cognitive function resulting from global hypoxia, anoxia or inflammation, radiation damage (both therapeutic radiation and radiation from nuclear weapons or accidents), stroke, age-related dementia, lupus, multiple sclerosis, drowning, heart attack (MI), traumatic closed-head brain injury, concussion or coma could benefit from this novel treatment. A common element in these various types of injuries to the brain is the activation of inflammatory pathways. It is believed that inhibition of a specific pathway will have a beneficial effect on cognitive function.

ROBERT J. BROWN, MD

TECHNOLOGY DESCRIPTION

A person suffering from an impairment of cognitive function would be administered an inhibitor with a known therapeutic target. The cause of the impairment in brain function need not be limited to trauma or injury and can be any disease, disorder or degeneration of the brain that results in a cognitive defect.

The amount of inhibitors of the known therapeutic target administered is an amount sufficient to result in a reduction in the level, severity or occurrence of at least one clinical symptom of the impairment. Improvement can be measured using neurocognitive testing, including standardized measures of memory such as verbal, long-term and working memory, processing speed, executive functioning and planning, measures of the level of N-acetylaspartate (NAA) or assessment of the presence of specific biomarkers in cerebrospinal fluid or serum that indicate neurogenesis and brain repair. The novel method is directed at chronic impairment, and it is anticipated that multiple doses of the inhibitors of the known therapeutic target will be used over time to achieve significant response. Preliminary studies show that these inhibitors improve cognitive function in brains showing chronic loss of functionality. Such an activity has not been recognized previously. Experiments in animal models will aim at investigating the underlying mechanisms.

APPLICATIONS

- Curative treatment of loss of cognitive function due to various causes
- Prophylactic treatment of loss of cognitive function due to degenerative diseases

ADVANTAGES

- No other treatment currently in place for chronic, long-term cognitive deficits
- Prophylactic effect

DEVELOPMENT STAGE

- Limited human clinical data

IP PROTECTION

Provisional patent application filed

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

NEW

ELECTROPHYSIOLOGICAL DIAGNOSIS AND TREATMENT FOR ASTHMA

CHLA ID: 2011-008

INVENTOR

Edwin C. Jesudason, MD (Children's Hospital Los Angeles; University of Liverpool)

TECHNOLOGY SUMMARY

A novel method of diagnosing and treating asthma using electrophysiological mapping based on a novel paradigm of asthma pathophysiology.

BACKGROUND

Asthma is the most common chronic childhood disease in the U.S. and an increasing problem in emerging economies. Asthma is often incurable and current palliative therapy relies on steroids and bronchodilators. This therapy relies on our current understanding of the pathophysiology of the disease involving airway inflammation, allergy, bronchospasm and airway smooth muscle (ASM) remodeling. Thermoplasty, a novel therapy for severe drug refractory disease, indiscriminately destroys the ASM. In recent years, ASM has been shown to play a key role during prenatal lung development, especially through airway peristalsis, the spontaneous phasic propagation of waves of ASM contractility. Dr. Jesudason and his group showed that this ASM contractility appears to be coupled to lung growth, is underpinned by calcium waves and preferentially arises from discrete pacemaker sites within the proximal airway before distal propagation.

Based on these findings, Dr. Jesudason proposes a novel paradigm where a hierarchy of proximal pacemakers persists in postnatal lungs and where asthma is an intrinsic pacemaker dysrhythmia resulting in abnormal airway contractility. This can then be secondarily influenced by allergy and inflammation. Rhythmicity in asthma is visible in diurnal symptom variations as well as the exaggeration of normal rhythmic fluctuations in airway calibers (homeokinesis). While destroying ASM, thermoplasty may work by inadvertently ablating the dominant proximal pacemakers to render distal airways quiescent. This would explain how a therapy delivered to larger proximal airways (thermoplasty) is effective for a disease of the small airways (asthma).

TECHNOLOGY DESCRIPTION

Dr. Jesudason proposes to use airway electrophysiology to detect and modulate airway contractility in vivo in asthma cases. After locating aberrant pacemaker activity in the airways, radiofrequency ablation can be used discretely on these sites in a minimally-invasive fashion. Implantable devices can also be used to monitor the electrophysiology of routine airway contractility to check for signs of an impending asthma attack and, where necessary, intervene to render the ASM refractory.

APPLICATIONS

- Long-term treatment and cure of asthma
- Monitoring and prevention of asthma attacks in chronic refractory asthma using implantable electrophysiological devices

ADVANTAGES

- A curative treatment to replace current asthma palliation

DEVELOPMENT STAGE

- Preclinical data

IP PROTECTION

Provisional patent application filed

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

EDWIN C. JESUDASON, MD

NEW

A NOVEL POPULATION OF STEM CELLS DERIVED FROM PERIPHERAL BLOOD OF ECMO PATIENT

CHLA ID: 2011-007

INVENTORS

Kim Chi Bui, MD (Children's Hospital Los Angeles; LAC+USC)
Barbara Driscoll, PhD (Children's Hospital Los Angeles)
Carolyn Lutzko, PhD (Children's Hospital Los Angeles; Cincinnati Children's Hospital Medical Center)

TECHNOLOGY SUMMARY

A novel population of stem cells has been isolated from the peripheral blood of patients on extracorporeal membrane oxygenation (ECMO). These cells have distinctive properties that may provide unique clinical benefits, specifically for lung and heart repair after injury.

BACKGROUND

Experimental studies have demonstrated that bone marrow progenitor cells can be recruited to injured lungs through an unknown mechanism. This process occurs rarely in normal tissue. Extracorporeal membrane oxygenation (ECMO) is used for cardiorespiratory support of neonates with meconium aspiration, primary pulmonary hypertension, asphyxia or other pulmonary disease. The goal of ECMO is to allow time for intrinsic repair of lungs and heart; thus, patients on ECMO represent a clinical model for the most severe acute lung and/or heart injury.

Since blood can be recovered from discarded ECMO circuits, it is possible, using appropriate methodology, to determine whether stem cells or progenitor cells are mobilized into the circulation of patients undergoing ECMO for severe cardiac and/or respiratory failure.

KIM CHI BUI, MD *BARBARA DRISCOLL, PhD*

TECHNOLOGY DESCRIPTION

An analysis of the blood from ECMO patients demonstrated mobilization of hematopoietic, mesenchymal and epithelial progenitors. The levels of colony-forming hematopoietic progenitors in ECMO blood was significantly higher than blood from patients in neonatal and pediatric intensive care units not placed on ECMO.

ECMO-derived mesenchymal cells have osteogenic, chondrogenic and adipogenic differentiation potential. ECMO samples gave rise to epithelial colonies that were CD45-negative and cytokeratin-positive, as expected for progenitor epithelial cells. Mesenchymal and epithelial progenitors were observed in ECMO samples but not in control samples.

This work leverages prior findings, previously reported in the literature, of host-graft chimerism with enhancement of host-derived cells being incorporated into donor tissues in areas of damage/inflammation versus uninjured tissues, demonstrating that circulating cells can incorporate into injured tissues.

ECMO-derived progenitors, in particular mesenchymal progenitors, may have a functional advantage over progenitors obtained routinely from bone marrow. Dr. Bui has banked the progenitor cells obtained from ECMO and shown that they remain stable after several passages in culture. She is pursuing the characterization of these cells.

APPLICATIONS

- Study of progenitor homing
- Repair mechanisms to injury

ADVANTAGES

- The unique properties of these cells may lead to the use of these cells or secreted factors as therapeutic candidates for tissue repair

DEVELOPMENT STAGE

- Stem cells banked and cultured for several passages; In vitro characterization studies underway (unpublished data)

IP PROTECTION

Confidential information

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

NEW

PREDICTION OF SURVIVAL IN METASTATIC NEUROBLASTOMA BASED ON 14 GENES EXPRESSED BY TUMOR AND TUMOR-ASSOCIATED INFLAMMATORY CELLS

CHLA ID: 2011-009

INVENTORS

Shahab Asgharzadeh, MD (Children's Hospital Los Angeles)
Robert C. Seeger, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY

A gene expression test that is able to predict risk of disease progression in metastatic neuroblastoma patients.

BACKGROUND

Neuroblastoma, an embryonal tumor of the peripheral sympathetic nervous system, is one of the most common solid tumors in children, with approximately 40 percent of patients presenting with metastatic disease at diagnosis. Age at diagnosis is the most important clinical variable for assigning patients with metastatic, MYCN non-amplified, neuroblastoma (NBL-NA) to an intermediate- or high-risk group. Children diagnosed with metastatic NBL-NA before 18 months of age have greater than 90 percent overall survival after receiving only moderate intensity chemotherapy. By contrast, patients diagnosed at greater than or equal to18 months of age have poor outcomes. Having the means to identify individuals at extremely high-risk for disease progression among this population of clinically indistinguishable patients diagnosed after 18 months of age would be valuable for the management of their therapy. Furthermore, understanding the mechanisms underlying this age-dependent clinical behavior would also be invaluable.

SHAHAB ASGHARZADEH, MD

TECHNOLOGY DESCRIPTION

A molecular prognostic test based on a 14-gene signature that can predict disease progression in patients diagnosed at greater than or equal to18 months of age. The technology employed in this assay is the same as that currently used in OncotypeDx for prognosis of breast cancer.

Analysis of the quantitative expression of 44 genes that were chosen for their previously known involvement in neuroblastoma in tumors from patients diagnosed before or after 18 months of age identified the 14-gene signature that was validated in two international cohorts of patients diagnosed at greater than or equal to18 months of age. The signature recognizes a subset of individuals at extremely high risk for disease progression.

Most of the genes in the signature are tumor-related; however, others suggest new targets for therapy that are greatly needed to improve outcomes in patients diagnosed at greater than or equal to18 months of age.

APPLICATIONS

- Neuroblastoma diagnosis for improved treatment

ADVANTAGES

- Can be set-up as a clinical assay
- Can help the management of clinically indistinguishable patients

DEVELOPMENT STAGE

- Identification of the 14-gene signature
- Data analysis and validation of the signature

IP PROTECTION

Confidential information

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

NON-INVASIVE SUBSTANCE DETECTION USING EYE MEASUREMENTS

CHLA ID : 2000-009

INVENTORS

Mark Borchert, MD (Children's Hospital Los Angeles) and James Lambert, PhD (JPL/Caltech)

TECHNOLOGY SUMMARY

Provides methods and apparatus for quantifying substances in the blood and brain by non-invasively allowing access to the anterior chamber of the eye for measurement of a given substance.

BACKGROUND

The ability to measure a given substance in blood and bodily fluids has many applications, including managing critically ill patients, determining the presence of intoxicants and managing chronic diseases such as diabetes mellitus. It also can be used to determine levels of therapeutic agents in the blood and brain during the drug development process.

Monitoring a particular compound in bodily fluids typically requires invasive techniques, such as a pin prick or blood draw. Using non-invasive techniques would have many advantages, including better subject compliance, elimination of infection risk and no requirement for specialized staff. In addition, multiple measurements could be more easily accomplished.

TECHNOLOGY DESCRIPTION

The device generates an excitation laser beam at a selected wavelength. This laser beam is focused onto the anterior chamber of the subject's eye. This illuminates the eye's aqueous humor, vitreous humor or one or more conjunctive eye vessels.

Detection of a Raman spectrum from the illuminated portion of the eye is then used to determine—via a proprietary algorithm—the blood or CSF concentration of a given substance.

Substances that can be detected using this approach include glucose, ethanol, macular pigments and therapeutic drugs such as amphotericin B.

APPLICATIONS

- Management of type II diabetes
- Law enforcement monitoring of alcohol blood levels
- Monitoring of macular degeneration
- Monitoring drug levels in a research or clinical setting, including the amount of drug crossing the blood-brain barrier

ADVANTAGES

- Non-invasive
- Able to detect a broad array of substances
- Able to measure drug crossing the blood-brain barrier

DEVELOPMENT STAGE

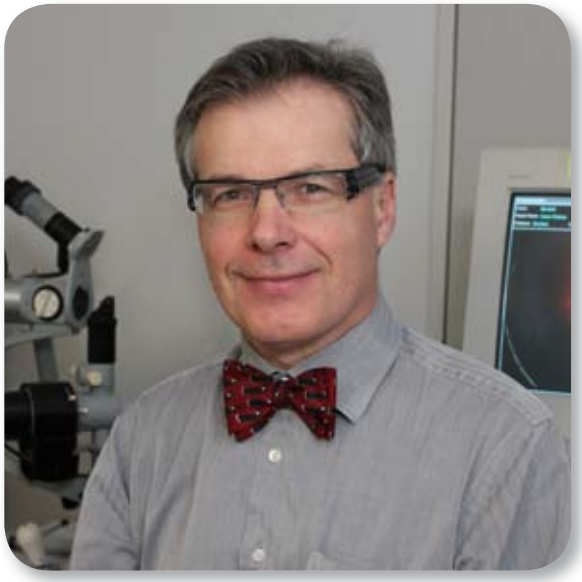
- Phase I clinical trial is ongoing

IP PROTECTION

Issued U.S. Patents 6,181,957; 6,424,850; 6,961,599; 6,574,501; 7,398,119; 7,593,763; Mexico Patent MX252339 (granted); 2717315.2 (pending)

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531



MARK BORCHERT, MD

NON-INVASIVE INTRACRANIAL PRESSURE MONITOR

CHLA ID: 1997-006

INVENTORS
Mark Borchert, MD (Children's Hospital Los Angeles) and James Lambert, PhD (JPL/Caltech)

TECHNOLOGY SUMMARY
Provides a method and apparatus to measure intracranial pressure in a non-invasive way, using images of the eye.

BACKGROUND
Intracranial pressure (ICP) is exerted by the cranium on the brain tissue, cerebrospinal fluid (CSF) and the brain's circulating blood volume. ICP is a dynamic phenomenon that constantly changes during such activities as exercise, coughing, straining, arterial pulsation and the respiratory cycle.

Brain trauma and other neurological conditions, including brain tumors, can cause elevated ICP. This elevated pressure can be fatal if prolonged, so it must be monitored and treated.

Currently, ICP is usually measured with a spinal tap, which involves puncturing the subarachnoid space of the spinal cord. For many diseases, this must be done repeatedly to monitor treatment results or disease progression. Such invasive monitoring involves risk and discomfort and is not always feasible.

This technology measures ICP in a simpler, non-invasive and far less-painful way. It would benefit the 375,000 Americans who are hospitalized annually with non-fatal brain injuries.

TECHNOLOGY DESCRIPTION
Provides a non-invasive method for measuring ICP by imaging the patient's eye with Optical Coherence Tomography (OCT).

Obtains an approximation of ICP by using OCT images to monitor changes of the optic nerve head. Elevated ICP causes the optic nerve head to swell.

OCT can detect the preclinical signs of this swelling, called papilledema. These signs are dependent on relative ICP and intraocular pressure (IOP).

Thus, ICP can be calculated by measuring the preclinical signs of papilledema, using OCT combined with IOP measurements.

APPLICATIONS
- Brain injuries
- Brain tumors
- Other neurological conditions

ADVANTAGES
- Simple
- Non-invasive
- Less painful

DEVELOPMENT STAGE
- The correlation between ICP and mean nerve fiber layer thickness has been demonstrated through a pilot study conducted in humans
- Seeking to partner with an OCT device manufacturer to test the device in a Phase I clinical trial

IP PROTECTION
Issued US Patent 6,129,682

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

CHLA ID : 2009-001

NOVEL PACEMAKER DEVICE

INVENTORS
Yaniv Bar-Cohen, MD (Children's Hospital Los Angeles); Ramen Chmait, MD (USC); Michael Silka, MD (Children's Hospital Los Angeles); Mark Sklansky, MD (Children's Hospital Los Angeles /UCLA) and Gerald Loeb (USC)

TECHNOLOGY SUMMARY
A novel fetal cardiac pacemaker that also can be used in infants, children and adults.

BACKGROUND
Despite 30 years of efforts to pace the fetal heart and improve overall fetal survival, there has yet to be a successful fetal pacemaker. To date, fetal pacemakers have been designed based on the same concepts used for adult pacemakers. Specifically, designs for fetal pacemakers have used an electrode connected to a battery unit via a long lead. The electrode is contacted with the fetal heart tissue, and the battery unit is placed outside of the uterus. This design has uniformly met with rapid failure due to movement of the fetus in the uterus. This movement dislodges the electrode from the fetal heart tissue.

YANIV BAR-COHEN, MD

TECHNOLOGY DESCRIPTION
Provides a solution to the need for an improved fetal cardiac pacemaker. Also serves as an improved cardiac pacemaker suitable for infants, children and adults. When used in a fetus, the pacemaker can be implanted in utero without significant harm to the developing fetus or the mother. It can function for extended periods of time without dislodging or otherwise failing. When designed for infants, children or adults, the pacemaker can be implanted quickly and under conditions that might otherwise preclude successful implantation of a pacemaker. Like the fetal version, this pacemaker can be implanted without significant harm to the patient and can function for extended periods of time. The implantation method used for this device already is being applied in fetal surgery. The inventors are a team of clinical experts who are dedicated to putting this device into clinical use: Dr. Ramen Chmait, director of Fetal Therapy and Minimally Invasive Fetal Surgery at the CHLA-USC Institute for Maternal-Fetal Health (IMFH), is a leading surgeon in the country in the area of fetal surgery. Dr. Mark Sklansky, formally director of Fetal Cardiology for the IMFH and for the Heart Institute at Children's Hospital, is a pioneer of three-dimensional fetal cardiac imaging. Dr. Michael Silka and Dr. Yaniv Bar-Cohen are pediatric electrophysiologists with expertise in pacemaker therapy. Dr. Gerald Loeb is director of the Medical Device Development Facility and professor of Biomedical Engineering at USC, with expertise in implantable stimulators that are similar in structure and function to the proposed fetal pacemaker.

DEVELOPMENT STAGE
- Prototype built and animal testing on-going

IP PROTECTION
PCT application pending

APPLICATIONS
- Cardiac pacing of fetuses in utero
- Cardiac pacing of patients in an urgent care setting, particularly where venous access is difficult

ADVANTAGES
- First-ever fetal pacemaker
- Minimally invasive implantation
- Closed system

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

EMAP II INHIBITORS TO TREAT CARDIOVASCULAR DISEASE

CHLA ID : 2000-002

INVENTORS

Margaret Schwarz, MD (Children's Hospital Los Angeles), Fangrong Zhang, PhD (National Jewish Medical Center), Sarah Gebb, PhD (National Jewish Medical Center)

TECHNOLOGY SUMMARY

Targets Endothelial Monocyte Activating Polypeptide (EMAP II) to promote cardiac tissue regeneration in patients suffering from myocardial infarction or pulmonary hypertension.

BACKGROUND

Cardiovascular disease is the leading cause of mortality in the United States, causing 41 percent of all deaths. Following coronary artery occlusion, myocardial recovery depends on the heart's ability to develop collateral circulation and revascularize the infarcted myocardium.

Growth factors such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) promote myocardial revascularization following myocardial infarction. But while much is known about these factors, little is known regarding the molecular mechanisms that counteract these stimuli.

EMAP II is an anti-angiogenic factor in tumor vascular development and could be a negative modulator of lung vascular growth.

TECHNOLOGY DESCRIPTION

Provides methods of facilitating vascular growth in cardiac muscle by inhibiting EMAP II. This is important for patients afflicted with myocardial ischemia, atherosclerosis and other myocardial diseases, such as cardiopathy or cardiac hypertrophy.

Pre-clinical data using an anti-EMAP II antibody suggest therapeutic benefits to this approach. In preclinical animal studies, the cardiac muscle structure and function of treated animals showed significantly reduced damage and improved cellular regeneration after infarction.

Benefits of EMAP II inhibition also have been shown in an animal model of pulmonary hypertension by using an EMAP II receptor antagonist. This treatment has been shown to reduce the distal pulmonary vessel thickening.

APPLICATIONS

- Myocardial infarction
- Pulmonary hypertension

ADVANTAGES

- Provides an alternate target to VEGF or bFGF for promoting cardiac tissue regeneration

DEVELOPMENT STAGE

- Preclinical data

IP PROTECTION

US Patent 6,306,612; US Patent 6,857,749; US patent 7,264,803; pending US and foreign applications

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

STEM CELL-BASED THERAPY FOR CHRONIC KIDNEY DISORDERS

CHLA ID : 2008-018

INVENTORS

Laura Perin, PhD (Children's Hospital Los Angeles); Roger De Filippo, MD (Children's Hospital Los Angeles); David Warburton, DSc, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY

Use of amniotic fluid-derived stem cells (AFSCs) and/or renal progenitor cells to treat or prevent chronic inflammatory kidney disorders.

BACKGROUND

Many diseases lead to renal failure, and chronic kidney disease remains a global health threat. No matter what the underlying disease, fibrosis, or "non-reversible scarring," is the most important reason why End Stage Renal Failure (ESRF) occurs. Currently, the treatment of chronic kidney disease is centered on slowing its progression and reducing co-morbidities. The only currently available therapies include those that reduce hypertension, proteinuria, hyperlipidemia, hyperglycemia or the renin-angiotensin-aldosterone feedback system. Unfortunately, these therapies do not prevent ESRF for the majority of patients. The challenge of using stem cell therapy for chronic kidney disease is to achieve a level of efficacy—with or without significant donor cell incorporation—to halt the fibrosis process and improve kidney function.

TECHNOLOGY DESCRIPTION

The inventors have shown that AFSCs can ameliorate glycerol-induced acute tubular necrosis (ATN) in animals. They demonstrated that the main mechanism by which AFSCs are renal-protective in ATN is through a significant immunomodulatory effect.

They also demonstrated that injection of AFSCs is renoprotective (protects the kidney from progressive disease) in Alport syndrome mouse models. Mice injected with AFSCs demonstrated improved kidney morphology (including preservation of glomerular and tubular structures), as well as the restoration to normal of creatinine, BUN levels and glomerular filtration rate. In addition, treated mice showed an increased life span, thus slowing down the progression of the disease.

They have developed a proprietary methodology and know-how for extracting, characterizing and culturing AFSCs and renal progenitor cells from human amniotic fluid.

IP PROTECTION

PCT application filed WO 2010/047824 – National filings in the U.S., Europe, Canada, Australia, China, India and Japan.

APPLICATIONS

- Treatment of chronic kidney disease

ADVANTAGES

- May provide a shift from slowing disease progression to reversing it, significantly delaying ESRF or possibly avoiding ESRF entirely

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

LAURA PERIN, PhD, DAVID WARBURTON, DSc, MD, AND ROGER DE FILIPPO, MD

NOVEL CHIMERIC PROTEIN AS NEW CLASS OF ANTI-HIV COMPOUNDS

CHLA ID : 2008-020

INVENTOR
Paula Cannon, PhD
(Children's Hospital Los Angeles/USC)

TECHNOLOGY SUMMARY
A tetherin-based chimeric protein is used as a novel anti-HIV therapeutic agent.

BACKGROUND
"Tetherin" is a cellular protein that recently has been identified in human cells as an important restriction factor that inhibits the release of infectious viral HIV particles. It also inhibits the release of other enveloped viruses, such as Kaposi's sarcoma-associated herpesvirus (KSHV).

The HIV virus is known to encode proteins that inhibit the activity of tetherin, although the mechanism involved is not fully understood.

Tetherin is an important host defense protein against enveloped viruses.

TECHNOLOGY DESCRIPTION
Developed a chimeric protein that can still restrict HIV release when expressed in cells, but is resistant to the anti-tetherin protein expressed by HIV.

This chimeric protein represents a prototype of a new class of anti-HIV gene therapy candidates that is resistant to viral protein defense.

It is a fusion of human proteins, so it is not anticipated that it will cause an immune reaction when expressed by target cells.

Given that no other function for tetherin has been reported to date, this gene therapy candidate promises to have a good safety profile.

APPLICATIONS
- Anti-HIV gene therapy

ADVANTAGES
- Novel HIV target
- Less likely to trigger immune reaction

DEVELOPMENT STAGE
- Pre-clinical

IP PROTECTION
PCT application filed WO 2010/045570

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

PAULA CANNON, PhD

HIGH THROUGHPUT ASSAY TO SCREEN COMPOUNDS THAT INHIBIT ENVELOPED VIRUSES

CHLA ID : 2008-013

INVENTOR
Paula Cannon, PhD (Children's Hospital Los Angeles/USC)

TECHNOLOGY SUMMARY
A positive high throughput screen (HTS) to identify Vpu inhibitors as novel anti-HIV compounds.

BACKGROUND
The human protein "tetherin" recently has been identified as a cellular factor that "tethers" newly budded HIV particles at the surface of a cell, reducing the yield of infectious virions.

Tetherin also restricts the release of other enveloped viruses, such as filoviruses and arenaviruses. This suggests that it may be part of an intrinsic cellular defense against enveloped viruses.

HIV codes for two distinct proteins that counteract tetherin: the HIV-1 Vpu protein and the HIV-2 Env protein. The Kaposi's sarcoma-associated herpesvirus (KSHV), which can be a significant complication of HIV infections, also expresses an anti-tetherin factor, K5.

In all, at least three human pathogens encode proteins that target tetherin. This suggests that viral anti-tetherin factors are important new targets for therapeutic interventions.

TECHNOLOGY DESCRIPTION
Mapped the region of tetherin that interacts with Vpu and removes tetherin from the cell surface. This is the basis of Vpu's anti-tetherin activity.

Based on these findings, developed a tetherin-based assay that uses this region of tetherin to identify small molecule inhibitors of the tetherin-Vpu interaction. The assay is adaptable to a high-throughput screening format.

The screen uses a minimal region of tetherin that is fused to a reporter construct (e.g., eGFP and luciferase). This produces a cell surface signal that is down-regulated by anti-tetherin factors, such as Vpu and K5.

Inhibitors of anti-tetherin factors are identified when a signal is obtained. Anti-HIV activity of such hits can then be further characterized in vitro and in vivo—which may lead to the discovery of a new class of antiviral drugs.

APPLICATIONS
- HIV drug discovery

ADVANTAGES
- Positive screen
- Novel target

DEVELOPMENT STAGE
- A fluorescent reporter system using this construct is in the final stages of testing
- Testing is being conducted on equipment similar to what will be used in the high throughput screen

IP PROTECTION
PCT application filed WO 2010/028264

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

AN ULTRASOUND-ACTIVATED MRI CONTRAST AGENT AND DRUG DELIVERY SYSTEM

CHLA ID : 2009-010

INVENTORS

Andy Y. Chang, MD (Children's Hospital Los Angeles); Travis J. Williams, PhD (Children's Hospital Los Angeles); Emine Boz, PhD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY

We propose a new class of nanoparticles that can mask (via encapsulation) an MRI contrast agent or a therapeutic cargo, aggregate in a targeted tissue and then selectively release the cargo and/or activate MRI contrast upon treatment with ultrasound.

TECHNOLOGY DESCRIPTION

This nanoparticle technology is a platform technology with multiple applications such as the diagnosis and monitoring of vesicoureteral reflux disease (VUR) in children and targeted drug delivery to tissue.

Our nanoparticle is unique in the following ways:

- It contains a core that is radio-opaque, allowing for the imaging of tissue, including tumors, by X-ray or computed tomography.
- It has a protective shell that sequesters any cargo, such as a contrast agent or cytotoxin, from its environment. This shell can be selectively cracked open by applying an external source of energy such as ultrasound, to release its contents.
- The synthetic process of manufacturing these nanoparticles is such that the particles can be created to any given size with precision.

These properties enable simultaneous and targeted diagnosis and treatment of disease.

APPLICATIONS

VUR

VUR is the improper flow of urine from the bladder up to the kidneys, which leads to kidney infection, scarring, renal failure and the need for dialysis and renal transplant. There are 50,000 new cases of VUR each year in the U.S.

The gold standard for diagnosis and surveillance of VUR is the voiding cystourethrogram (VCUG). This procedure uses X-rays with an iodinated contrast medium to image the retrograde flow of urine. Its use results in undesired radiation exposure to the gonads, which can have long-term negative effects.

VCUG also requires a catheter to be placed through the urethra and into the bladder. This is extremely traumatic to children and their parents.

Some pediatric urologists advocate the use of nuclear voiding cystograms, which decrease patient radiation exposure by 10-fold, for follow-up studies. But most will use a VCUG as the initial study because it provides superior anatomic definition. According to the National Institutes of Health (NIH) 2006 Strategic Plan for Pediatric Urology, finding a catheter-free VCUG procedure is a national health research priority.

In this application, our gadolinium-containing nanoparticle has been designed to be sufficiently small to filter through the kidneys into the bladder in its masked and inactive state. Application of ultrasound to the bladder unmasks the gadolinium core, allowing the physician to monitor the flow of urine using MRI.

Our nanoparticle technology is used here to create a new contrast agent for VCUGs, leading to a novel system of detection that eliminates traumatic catheterizations and minimizes radiation exposure.

ANDY Y. CHANG, MD

AN ULTRASOUND-ACTIVATED MRI CONTRAST AGENT AND DRUG DELIVERY SYSTEM (CONTINUED)

CHLA ID : 2009-010

Cancer Therapy

Application in targeted drug delivery includes, but is not limited to, the delivery of chemotherapy. In this application, the nanoparticles are designed to take advantage of the enhanced permeability and retention (EPR) effect associated with cancer. Due to their rapid growth, tumors require the formation of large amounts of new blood vessels. However, these blood vessels are poorly constructed and porous. Similarly, the lymphatics, or waste system, are not well developed and do a poor job at removing the materials that have leaked out of the blood vessels and into the tumor beds. Leveraging the EPR effect is a proven viable approach allowing the nanoparticles to preferentially accumulate in the tumors over other parts of the body. The ability to deliver cytotoxins to the tumor bed will dramatically reduce systemic exposure to the cytotoxin, thereby decreasing the debilitating side effects. Cytotoxin efficacy can potentially increase by allowing for higher drug doses to be administered due to improved dose-related side effects.

Research Tool

Our nanoparticle can also be designed as a useful research tool to perform real time in vivo imaging of the biodistribution of a studied cargo.

ADVANTAGES

- Modular size of particles (5nm<D<200 nm): under 10nm the nanoparticles can pass through the kidneys and be safely voided
- Nanoparticles between 50 – 200 nm can optimize the EPR effect to selectively deliver drug to tumor beds
- Eliminates traumatic catheterizations
- Minimizes radiation exposure
- Mitigates systemic side effects
- Increases amount of drug being delivered to tumors

DEVELOPMENT STAGE

Nanoparticles have been synthesized and tested in vitro

IP PROTECTION

PCT application filed

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

TRAVIS J. WILLIAMS, PhD

NOVEL THERAPEUTIC TARGET FOR GLIOMAS AND MEDULLOBLASTOMAS

CHLA ID : 2010-004

INVENTORS
Anat Erdreich-Epstein, MD, PhD (Children's Hospital Los Angeles), Shahab Asgharzadeh, MD (Children's Hospital Los Angeles)

TECH SUMMARY
Novel predictive test to help determine appropriate therapy in medulloblastomas, gliomas and other tumors.

Novel therapeutic target for single or combination therapy to improve the outcome of these diseases.

BACKGROUND
According to the American Brain Tumor Association, primary brain tumors occur at a rate of 12.8 per 100,000 people. The problem seems to be most common in children ages 3 to 12, and in adults from 40 to 70.

In the United States, approximately 2,200 people younger than 20 are diagnosed annually with brain tumors. Although previously under-reported, increased awareness and better brain scanning techniques have led to people 85 and older being diagnosed and treated.

Tumors growing in the brain are difficult to treat. One type of treatment is external beam radiation, in which radiation passes through the brain to the tumor. Unfortunately, this exposes healthy brain tissue to potentially damaging radiation. Another treatment is surgical removal of the tumor, if possible, followed by chemotherapy. These treatments are difficult to endure, and pose risks to the patient.

Despite enduring the risks and discomforts of these treatments, many gliomas (tumors arising from glial cells) grow back.

TECHNOLOGY DESCRIPTION
An analysis of microarray data of children with medulloblastomas identified a gene that is highly correlated with outcome in children treated with chemotherapy and surgery only.

Examination of the Cancer Genome Atlas publicly available REMBRANDT database showed that high expression of this gene in gliomas was highly correlated with longer overall survival.

To investigate a causal relationship, Dr. Epstein examined the effect of this gene on tumor cells in culture. The resulting data demonstrate a novel apoptotic and anti-proliferative role for this gene in medulloblastoma and glioblastoma cell lines.

This is the first description of a potential role for this particular gene in pediatric and adult brain tumors and other cancers.

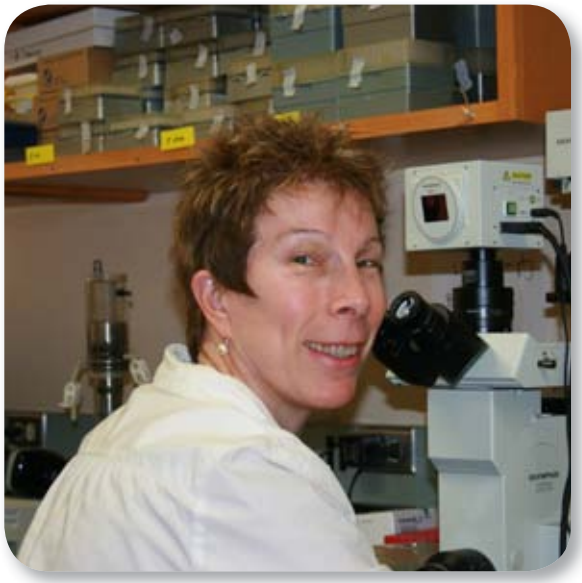
APPLICATIONS
- Brain tumor therapy, diagnosis and prognosis

ADVANTAGES
- May lead to improved therapies, prognostic and diagnostic tests

DEVELOPMENT STAGE
- In vitro proof of principle data
- Animal studies in process

IP PROTECTION
Confidential information

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531



ANAT ERDREICH-EPSTEIN, MD, PhD

ORAL FORMULATION OF FENRETINIDE WITH IMPROVED BIOAVAILABILITY

CHLA ID : 2000-008

INVENTORS
C. Patrick Reynolds, MD, PhD (Children's Hospital Los Angeles/TexasTech), Barry J. Maurer, MD (Children's Hospital Los Angeles/TexasTech)

TECHNOLOGY SUMMARY
Novel oral formulation of fenretinide that demonstrates improved bioavailability and efficacy.

BACKGROUND
Fenretinide (4-hydroxy (phenyl) retinamide) is a synthetic retinoid derivative that has been investigated for potential use in treating cancer and other diseases, such as macular degeneration. Specific types of cancer studied include bladder, breast, non-Hodgkin's lymphoma, neuroblastoma and Ewing's sarcoma.

Bioavailability of the long-established fenretinide formulation has been a limiting factor in achieving optimal therapeutic benefit.

TECHNOLOGY DESCRIPTION
This oral formulation of fenretinide has improved bioavailability.

The formulation has been tested in Phase I clinical trials in pediatric neuroblastoma and in other adult tumors. The trial has met its primary end points.

Children's Hospital is interested in collaborating with an interested partner to further the clinical development in various hyperproliferative disorders.

APPLICATIONS
- Cancer treatment (ovarian cancer, neuroblastoma, acute lymphoblastic leukemia)
- Macular degeneration
- Other hyperproliferative disorders

ADVANTAGES
- Orally administered
- Improved bioavailability
- Improved anti-tumor activity of fenretinide

DEVELOPMENT STAGE
- Phase I clinical trial in neuroblastoma and certain adult cancers

IP PROTECTION
7,780,978, 7,785,621, CN, MX, EPO

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

C. PATRICK REYNOLDS, MD, PhD

COMBINATION THERAPY FOR CANCER: ORAL FENRETINIDE AND MICROTUBULE INHIBITORS

CHLA ID : 2006-003

INVENTORS
C. Patrick Reynolds, MD, PhD (Children's Hospital Los Angeles/TexasTech), Barry J. Maurer, MD (Children's Hospital Los Angeles/TexasTech)

TECHNOLOGY SUMMARY
Combines fenretinide with microtubule inhibitors to increase its therapeutic effect as an anti-cancer drug.

BACKGROUND
Fenretinide (4-hydroxy (phenyl) retinamide) is a synthetic retinoid derivative that has been investigated for potential use in treating cancer and other diseases, such as macular degeneration. Specific types of cancer studied include bladder, breast, non-Hodgkin's lymphoma, neuroblastoma and Ewing's sarcoma.

Bioavailability of the long-established fenretinide formulation has been a limiting factor in achieving optimal therapeutic benefit.

TECHNOLOGY DESCRIPTION
Proposes using fenretinide, a well-known anti-cancer agent, in combination with microtubule inhibitors. These inhibitors are another important class of anti-cancer agents.

Pre-clinical data from multiple tumor xenograft models show that fenretinide is more effective when used with microtubule inhibitors instead of as a single agent.

The combination of fenretinide and microtubule inhibitors is well-tolerated in mice. Its synergistic effect presents a novel treatment approach in oncology.

Kang MH, Wan Z, Kang YH, Sposto R, Reynolds CP (2008). Mechanism of synergy of (4-hydroxy (phenyl) retinamide) and ABT-737 in acute lymphoblastic leukemia cell lines: Mcl-1 inactivation. *J Natl Cancer Inst.* 2008 Apr 16;100(8):580-95.

APPLICATIONS
- Cancer treatment
- Macular degeneration

ADVANTAGES
- Orally administered
- Improved bioavailability
- Improved anti-tumor activity of fenretinide

DEVELOPMENT STAGE
- Pre-clinical proof of principle data

IP PROTECTION
PCT application filed PCT/US2007/011686

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

BARRY J. MAURER, MD

COMBINATION THERAPY FOR CANCER: ORAL FENRETINIDE AND KETOCONAZOLE

CHLA ID : 2007-012

INVENTORS
C. Patrick Reynolds, MD, PhD (Children's Hospital Los Angeles/TexasTech), Barry J Maurer, MD (Children's Hospital Los Angeles/TexasTech)

TECHNOLOGY SUMMARY
Combines fenretinide with metabolic degradation inhibitors of fenretinide to increase its therapeutic effect as an anti-cancer drug.

BACKGROUND
Oral fenretinide (4-hydroxy (phenyl) retinamide) is a synthetic retinoid derivative that has been investigated for potential use in the treatment of cancer and other diseases.

Sub-optimal bioavailability of traditional fenretinide formulations has been a limitation for achieving high efficacy.

TECHNOLOGY DESCRIPTION
Uses metabolic degradation inhibitors of fenretinide to increase the plasma and tissue levels of fenretinide.

The preliminary data show that ketoconazole, a fenretinide degradation inhibitor, has singular effect in increasing fenretinide's bioavailability and efficacy.

Our pre-clinical data in multiple tumor xenograft models demonstrate the usefulness of this combination as an effective way to improve fenretinide's therapeutic potential as an anti-cancer agent.

APPLICATIONS
- Cancer treatment

ADVANTAGES
- Orally administered
- Improved bioavailability
- Improved anti-tumor activity of fenretinide

DEVELOPMENT STAGE
- Pre-clinical proof of principle data

IP PROTECTION
PCT application filed PCT/US2008/011207

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

ADIPOCYTE-SECRETED FACTOR ATTRACTS LEUKEMIA CELLS

CHLA ID : 2009-014

INVENTORS
Steven D. Mittelman, MD (Children's Hospital Los Angeles), Rocky Pramanik, PhD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
Novel cancer cell chemo-attractant, secreted by adipocytes, as a therapeutic target for treating obese cancer patients.

BACKGROUND
Obesity is associated with increased cancer incidence and mortality. Our researchers have found that obesity in children is associated with a 50 percent increased recurrence of acute lymphoblastic leukemia (ALL) in high-risk patients. They have developed and shown the mechanisms of this association in novel in vivo and in vitro preclinical models.

Obesity increases relapse after monotherapy in obese mice injected with syngeneic ALL cells. This occurs even though the drug is dosed proportionally to body weight, equalizing blood and tissue drug levels.

Co-culture of adipocytes with ALL cells significantly impairs the anti-leukemia efficacy of monotherapy, as well as three other chemotherapies. This protection is independent of cell-cell contact, and it is observed with human leukemia cell lines as well. Adipocytes prevent chemotherapy-induced apoptosis (Adipocytes impair leukemia treatment in mice. *Cancer Res.* 2009 Oct 1; 69(19):7867-74. Epub 2009 Sep 22.).

These findings highlight the role of adipocytes in fostering leukemia chemotherapy resistance. They also highlight the need to further investigate the increased rate of relapse in obese children and adults with leukemia.

Given the growing prevalence of obesity worldwide, these effects are likely to have increasing importance to cancer treatment.

TECHNOLOGY DESCRIPTION
Discovered a factor secreted by adipocytes that attracts acute lymphoblastic leukemia (ALL) cells and shelters them from chemotherapeutic drugs.

APPLICATIONS
- Cancer treatment in obese patients

ADVANTAGES
- Novel therapeutic intervention approach for improved ALL treatment

DEVELOPMENT STAGE
- In vitro and in vivo proof of principle data

IP PROTECTION
Confidential information

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

STEVEN D. MITTELMAN, MD

CHLA ID : 2007-014

RNAi THERAPY FOR BRAIN TUMORS

INVENTORS
Hae-Ri Song, MD (Children's Hospital Los Angeles); David Anderson, PhD (California Institute of Technology); Benjamin Deneen, PhD (California Institute of Technology)

TECHNOLOGY SUMMARY
Novel RNAi-based therapy targets a nuclear protein to treat gliomas.

BACKGROUND
Gliomas, tumors derived from glial cells of the central nervous system (CNS), account for approximately 30 percent of all primary brain tumors in adults. The median survival rate is about 12 months. Gliomas are usually treated by surgery, chemotherapy, radiotherapy and/or fractionated stereotype radio surgery.

Recent advances in molecular genetics have revealed many genetic mutations and associated signaling pathways that play a causative role in the generation of gliomas.

These advances have provided numerous candidate pathways that can be utilized in developing rational therapy rooted in the biology of the disease. It remains to be seen whether such approaches will come to fruition. There is a continued need for glioma therapies. This invention targets that unmet need.

TECHNOLOGY DESCRIPTION
This therapy targets the Nuclear Factor I (NFI) family that is expressed in all grades of human astrocytomas, the most deadly form of gliomas, and has been shown to have a causative role in the disease. NFIA inhibitors are proposed as therapeutic compositions to treat gliomas based on the elucidation of NFIA's role in gliomas formation. The inventors propose a molecular medicine approach to inhibit NFIA using interfering RNA (RNAi). The RNAi construct has been prepared to specifically target the protein's expression in gliomas, knockdown its expression and reduce glioma formation. Preliminary data in cell lines and animal studies is suggestive of a protective effect by this construct. Further research is in progress.

DEVELOPMENT STAGE
- Pre-clinical proof of principle

IP PROTECTION
Issued U.S. patent 7,951,785

APPLICATIONS
- Brain tumor treatment (gliomas and astrocytomas)

ADVANTAGES
- High specificity to the molecular target

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

CLINICAL RADIOLOGY SOFTWARE FOR MR UROGRAPHY

CHLA ID : 2010-002

INVENTORS

Rex Moats, PhD (Children's Hospital Los Angeles); Yang Tang (Children's Hospital Los Angeles); Priyank Sharma (Children's Hospital Los Angeles); Hollie Jackson, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY

Post-processing Magnetic Resonance (MR) image analysis software for clinical MR urography that analyzes both anatomical and functional parameters of the kidney.

BACKGROUND

Imaging the urinary tract in children with MR urography has many advantages. This imaging can be done with one exam and without using ionizing radiation. This is the current preferred method for children. The functional analysis of the MR urography scan requires external post-processing image analysis software. This software has three major limitations in pediatric radiology: complexity, a need for specialized personnel to run the software and the length of time needed to carry out the analyses.

The ideal functional MR urography analysis software would be simple, user-friendly, fast and easily operated by the average radiologist. This invention provides an optimized functional analysis software that can be used in pediatric and adult patients.

TECHNOLOGY DESCRIPTION

Provides an interactive 3-D image analysis tool for MR urography. Uses computational analysis to quantitatively analyze MRI kidney data to assess functional, physiological and anatomical parameters. These parameters include renal transit time, urinary excretion, renal blood flow, glomerular filtration rate, plasma flow or volume etc. The parameters can be analyzed and visualized in various intuitive ways to help in diagnosis. The software uses a cluster-based method to analyze and segment the 4-D MRI kidney data on a pixel-by-pixel basis.

The software automatically groups dynamic MRI kidney data into clusters that contain pixels with similar functional activities. The software then uses these clusters, anatomical knowledge and logistic model to automatically segment the kidney for further evaluation.

DEVELOPMENT STAGE

- Ready for clinical validation
- User interface needs to be built

IP PROTECTION

PCT application filed PCT/US2011/036797

CONTACT

Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

REX MOATS, PhD

DIAGNOSTIC TARGET FOR EWING'S FAMILY TUMORS

CHLA ID : 2008-014

INVENTORS
Timothy Triche, MD, PhD (Children's Hospital Los Angeles), Daniel Wei (Children's Hospital Los Angeles), Michele Wing, PhD (Children's Hospital Los Angeles), Elizabeth Lawlor, MD, PhD (Children's Hospital Los Angeles/ University of Michigan)

TECHNOLOGY SUMMARY
Novel non-coding RNA transcript to diagnose Ewing's Family of Tumors.

BACKGROUND
Ewing's Family of Tumors (EFTs) is the second most common primary malignant bone tumor in adolescents and children. Due to the severity of the disease, misdiagnosis leads to poor outcomes.

EFTs are caused by chromosomal translocation. Eighty-five percent of cases are due to the translocation of EWS-FL1 between chromosomes 11 and 22. FISH (Fluorescent in situ hybridization) is a reliable diagnostic for EWS-FL1 translocation. However, other variant translocation types cannot be reliably diagnosed with this approach.

It would be valuable for clinicians to have one diagnostic marker that identifies all types of EFTs.

TECHNOLOGY DESCRIPTION
This diagnostic tool is based on an RNA transcript. The transcript was identified using microarray gene expression profiling. This gene expression is associated with and highly specific for EFTs.

In its largest form, the RNA transcript is referred to as AK057037, or simply AK. The AK transcript is a relatively large transcript that shows high levels of expression in EFTs, but not in other common childhood tumors or healthy tissue. It is therefore highly and significantly associated with EFT.

AK is highly expressed regardless of translocation type (EWS-FLI1 or EWS-ERG). It is therefore an excellent diagnostic marker for EFTs.

AK also may serve as a prognostic marker for EFTs. Its prognostic use can provide information related to the effectiveness of a chosen cancer treatment modality.

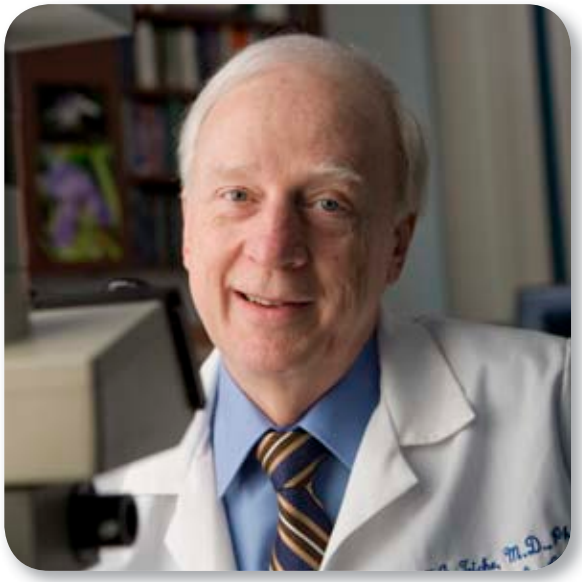
APPLICATIONS
- Diagnosis of Ewing's Family of Tumors

ADVANTAGES
- Provides a single biomarker for all EFTs
- Simple and inexpensive detection using PCR

DEVELOPMENT STAGE
- Clinical validation in progress

IP PROTECTION
None

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531



TIMOTHY TRICHE, MD, PhD

DIAGNOSTIC KIT FOR FUNCTIONAL DISORDERS

CHLA ID : 2007-014

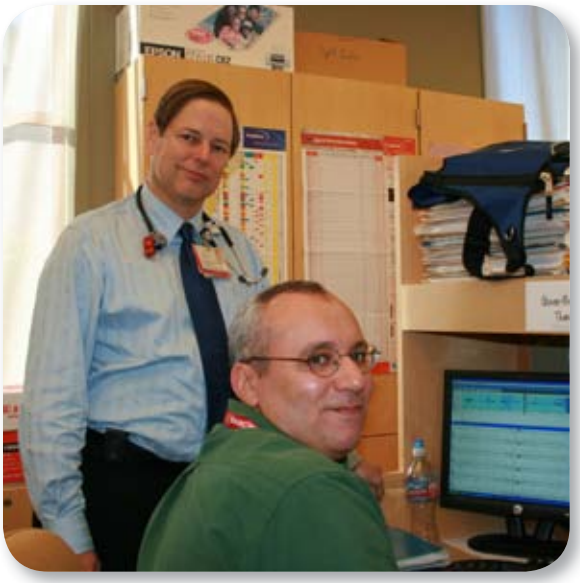
INVENTORS
Richard Boles, MD (Children's Hospital Los Angeles), Essam Zaki, PhD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
A simple PCR-based diagnostic test for functional disorders.

BACKGROUND
Functional disorders (migraines, depression, chronic fatigue syndrome, irritable-bowel syndrome, chronic abdominal pain, sudden infant death syndrome, cyclic vomiting syndrome, etc.) are the most common reasons for medical visits worldwide.

It has been known for centuries that individuals who suffer from one functional disorder often suffer from several of the disorders, as do their relatives. Currently, there are no tests or biomarkers for these functional disorders.

A simple, low-cost PCR-based DNA test will be useful in patients with chronic functional complaints. The test could determine whether their symptoms are functional in nature or have another cause that requires a more invasive intervention.



RICHARD BOLES, MD, AND ESSAM ZAKI, PhD

TECHNOLOGY DESCRIPTION
Preliminary data demonstrate that a small number of mitochondrial single nucleotide polymorphisms (SNPs) confer substantial risk for multiple functional disorders.

The presence of such SNPs confers odds ratios ranging from three to 17. These odds ratios are likely to increase substantially as additional disease-associated SNPs are identified.

This testing specifically can be useful in determining which patients should undergo costly and/or invasive testing for "organic" disease instead of conservative treatment of symptoms with follow-up.

For example, in a patient with chronic abdominal pain, a test result indicating a low risk for functional disorders would suggest starting with a work-up for organic disease, such as endoscopy and GI radiological series. A test result indicating a high risk would suggest starting with a trial of functional-disorder targeted therapy with re-evaluation.

APPLICATIONS
- Diagnostic test kit for functional disorders

ADVANTAGES
- Simple
- Inexpensive
- Easy to perform
- No current testing exists

DEVELOPMENT STAGE
- Data available in migraines, depression, chronic fatigue syndrome, irritable bowel syndrome, chronic abdominal pain, sudden infant death syndrome and cyclic vomiting syndrome

IP PROTECTION
PCT application filed PCT/US2008/003994

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

NOVEL RESEARCH TOOL FOR NEURON CULTURE: THE NEURON CHIP

CHLA ID : 2008-021

INVENTORS
Richard Simerly, PhD (Children's Hospital Los Angeles), Stephen Chen (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
Novel cell culture coating technology. Allows neuroscientists to sort through myriad molecular cues that impact neurons and neural circuit formation in a more high-throughput manner.

BACKGROUND
Although neurological disease is one of the most heavily researched areas in medical science worldwide, we are still in the very early stages of understanding how the brain functions.

The complexity of neurological systems and process—along with the difficulty of culturing and studying neurons and their behavior in a systematic, reproducible and rapid way—represent a bottleneck in the field.

Children's Hospital has developed a unique and patented cell culture-coating technology to help accelerate basic research in the neurosciences.

The resulting coated culture chambers—or neuron chips—allow scientists to measure the amount of branching, growth rates and signaling between neurons or between neurons and target cells with greater efficiency, specificity, rapidity and cost savings.

RICHARD SIMERLY, PhD

TECHNOLOGY DESCRIPTION
Below are images of neurons cultured with current tools (figure 1) and neurons grown using our proprietary coating technology (figure 2):

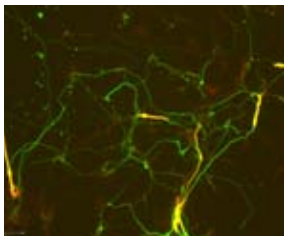


Figure 1 – Axoms extend haphazardly

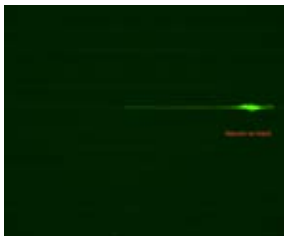


Figure 2 – Axom bundle extends in an orderly fashion, following a predetermined path (e.g., a straight line as depicted here)

Features: Linear growth means that growth rate measurement can be easily obtained and automated.

Neurite growth rates are 10 times faster than in standard culture conditions, representing time and reagent savings.

Neurites no longer intersect at a point, as seen in figure 1. Instead, they connect along their lengths, leading to more synapses formed between neurites, more sensitive electrophysiological measurements, more neuron pairs to measure and the formation of axon bundles.

APPLICATIONS
- Neuron cell culture

ADVANTAGES
- Study compounds embedded in the substrate or in solution
- Axon growth is accelerated by a factor of 10 compared with standard culture methods
- Scale up for increased throughput
- Conduct live imaging and immunostaining
- Generate many neuron pairs, facilitating patch-clamp experiments

DEVELOPMENT STAGE
- Prototype-coated cover slips have been developed and used for neuron culture
- Manufacturing method has been developed

IP PROTECTION
PCT application filed WO 2010/057025

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

CHLA ID : 2003-003

MINIMAL LENTIVIRAL SYSTEM

INVENTORS
Paula Canon, PhD (Children's Hospital Los Angeles), Celina Ngiam (USC)

TECHNOLOGY SUMMARY
Lentiviral gene delivery vector with improved safety and efficiency.

BACKGROUND
Lentivirus vectors based on the human immunodeficiency virus-1 (HIV-1) are prominent vectors used for gene transfer studies. That's because these vectors have an ability to transfer and integrate genes into dividing and non-dividing cells.

Lentiviral vectors have been shown to deliver genes to neurons, lymphocytes and macrophages. Other retrovirus vectors cannot be used for these cell types. Lentivirus vectors also have been proven to be effective in transducing brain, liver and muscle cells without toxicity or immune responses.

Lentivirus systems have been widely used to integrate siRNA efficiently in a wide variety of cell lines and primary cells, both in vitro and in vivo.

TECHNOLOGY DESCRIPTION
Provides a lentivirus vector system that is safer and more efficient than other lentivirus vector systems.

Lentivirus particles are usually produced from 293T cells through transient transfection of plasmids that encode for the components of a virion.

Separating the components of the system on different plasmids reduces the chance of generating a replication-competent lentivirus (RCL). RCLs pose major safety concerns among users.

Despite separating the components, there is still substantial overlap between components in currently marketed vector systems. This can lead to RCLs. These regions of overlap are maintained in these systems because they are thought to be essential for high activity of gene transfer.

Our new lentivirus system has been engineered to remove this overlap. It enhances safety without compromising the efficacy of gene transfer. In addition, this improved minimal lentivirus vector system can accommodate large gene inserts.

APPLICATIONS
- Gene therapy
- Protein production (e.g. viral vaccine production)

ADVANTAGES
- Allows large gene inserts
- Improved safety profile without compromising efficacy
- Higher safety may lead to quicker IRB and FDA approvals for clinical use

DEVELOPMENT STAGE
- Market-ready
- Available for licensing on a non-exclusive basis

IP PROTECTION
6,620,595, PCT/US2004/040789

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

PROJECT AIM (ADULT IDENTITY MENTORING): A PROGRAM TO REDUCE SEXUAL RISK AND SUBSTANCE ABUSE RISK AMONG YOUTH

CHLA ID : 2008-012

INVENTORS
Leslie Clark PhD, MPH (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
Group-level youth development intervention to address risk trajectories, emergence of environmental risk and the debilitating effects of poverty and racism.

BACKGROUND
The intervention program is based on the "Theory of Possible Selves." The theory states that a person's motivation is determined by a balance of positive and negative ways in which people see themselves in the future.

Individuals who are able to imagine both positive and negative futures are more likely to work toward their life goals and achieve future success. Project AIM encourages at-risk youth to imagine a positive future and discuss how current risk behaviors could be a barrier to a successful adulthood.

PROGRAM DESCRIPTION
Project AIM consists of 12 50-minute sessions delivered to groups of 10 to 20 youth. The intervention is divided into four parts, using group discussions and interactive activities.

Part 1 encourages youth to explore their personal interests, social surroundings and what they want to become as an adult. Youth identify people in their lives who may be barriers to success or supporters. Young adults from the community who are on their road to success are invited to speak with youth.

In Part 2, youth envision themselves in a future career and connect current behavior with success as an adult. Activities include completing a career interest inventory, developing business cards and resumes and participating in interviews.

Part 3 engages youth in role-playing around communication and small group activities involving planning and decision-making.

In Part 4, youth think about their futures in terms of milestone goals to accomplish and potential obstacles that must be overcome.

Clark L, Miller K, Nagy S, Avery J, Roth D, Liddon N, et al. (2005). Adult identity mentoring: Reducing sexual risk for African-American seventh grade students. *Journal of Adolescent Health*, 37, 337.e1–337.e10.

APPLICATIONS
- At-risk adolescents
- At-risk young adults

ADVANTAGES
- Addresses a number of risky behaviors affecting youth

DEVELOPMENT STAGE
- In use at multiple sites nationwide

IP PROTECTION
Registered copyright

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

KIDS N FITNESS© EVIDENCE-BASED WEIGHT MANAGEMENT PROGRAM

CHLA ID : 2008-004

INVENTORS
Division of Endocrinology at Children's Hospital Los Angeles, led by Francine Kaufman, MD

TECHNOLOGY SUMMARY
Fun, interactive program around nutrition and exercise to help children and their parents improve their health.

BACKGROUND
The problem of childhood obesity in the United States is growing at an alarming rate. Sixteen to 33 percent of children and adolescents are obese.

Unhealthy weight gain has been attributed to poor eating habits and lack of exercise. Kids are spending less time exercising and more time in front of the TV or computer or video-game console, and they lack education about healthy cooking and healthy eating habits. Overweight children are much more likely to become overweight adults unless they adopt and maintain healthier patterns of eating and exercise.

Obesity's annual cost to society is estimated at nearly $100 billion. An intervention program that emphasizes exercise and nutritional education in an encouraging family-centered environment would be instrumental in treating childhood obesity and encouraging kids to adopt a healthy lifestyle.

PROGRAM DESCRIPTION
Kids N Fitness© is a lifestyle intervention program that includes exercise and nutrition education in an encouraging, supportive and family-centered environment. It's designed to provide overweight children with the skills needed to make better food choices, and to motivate them to increase physical activity.

The program sessions were designed by an expert team of clinicians, dietitians, physical therapists and other staff members of the Division of Endocrinology at Children's Hospital Los Angeles.

According to research studies following several years of implementation, the program has reversed unhealthy eating, physical inactivity and weight gain. The program is proven to impart knowledge, teach healthy eating skills and enable overall behavioral changes consistent with a healthy lifestyle.

Program material consists of curriculum, logs, charts and family workbooks. It can be offered in a variety of settings, including schools, physical therapy clinics, gyms for children and adolescents, hospitals and nutritional and exercise clinics.

APPLICATIONS
- Weight management in obese children and adolescents

ADVANTAGES
- Clinically proven and evidence-based
- Teaches healthy eating skills
- Enables healthy behavioral changes
- Helps children lose needed weight

DEVELOPMENT STAGE
- Available for non-exclusive licensing

IP PROTECTION
Registered trademark and copyright

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

FRANCINE KAUFMAN, MD

MEDICAL EMERGENCY COMMUNICATION BOOK

CHLA ID : 2008-016

INVENTORS
Micky Heinrichs, MD (Children's Hospital Los Angeles), and Philip Malouf, MD (Children's Hospital Los Angeles)

TECHNOLOGY SUMMARY
Pictorial tool for communicating with patients in a medical emergency.

BACKGROUND

TECHNOLOGY DESCRIPTION
This communication book enables easy communication with patients of varied cultural and linguistic backgrounds in a medical emergency.

Sections of the book also can assist with history-taking, treatment communication, patient admission and discharge. This pictorial resource can be helpful under a variety of situations where it is difficult to communicate with patients.

APPLICATIONS
- Hospitals
- Nursing homes
- Emergency Medical Technicians/Paramedics

ADVANTAGES
- Makes communication possible without presence of a translator

DEVELOPMENT STAGE
- Available for purchase

IP PROTECTION
Registered copyright

CONTACT
Jessica L. Rousset, Director
JRousset@chla.usc.edu
323.361.4531

NOTES

NOTES

TECHNOLOGY HIGHLIGHTS

FALL 2011

Children's Hospital LOS ANGELES

THE SABAN RESEARCH INSTITUTE

P.O. Box 54700
Los Angeles, CA 90054-0700
CHLA.org/RESEARCH