Barnes-Jewish Hospital Foundation / Washington University Institute of Clinical & Translational Sciences
2011 Clinical & Translational Research Funding Program Awardees

Funding Source	Type of Grant	Principal Investigator	Project Period	Proposal Title	Description
ICTS	Planning	Jose A. Pineda, MD, MSc	6/1/11 - 5/31/12	Measuring Cerebral Blood Flow in Pediatric Cardiac Arrest: A Feasibility Study	Children who survive cardiac arrest (CA) frequently experience unfavorable outcome. Abnormal cerebral blood flow (CBF) is important in the pathophysiology and recovery after CA, but its significance has not been well studied in children. We aim at optimizing Arterial Spin Labeling [an MRI method originally developed to measure CBF in adults] for use in pediatric studies of CBF abnormalities after CA.
BJHF	Planning	Rumi K. Price, PhD, MPE	6/1/11 - 5/31/12	Planning for the StrongMind Stigma Reduction in the National Guard	The objective of this Planning Grant proposal is to assess the feasibility of implementing a mental health stigma reduction program for Missouri National Guard soldiers, and their family members and significant others, prior to soldiers' departures to conflict regions. We incorporate Motivational Interviewing techniques to a group setting. Results will provide pilot data for the planned StrongMind study for full implementation and an open trial.
BJHF	Planning	Enola K. Proctor, PhD	6/1/11 - 5/31/12	Building a Team and Agenda for Research on Sustainability of Evidence-Based Care	To advance methodology for studying the sustainability of evidence-based care once implemented in routine care, a new transdisciplinary team is conducting pilot work on four methodological challenges: measurement, study design, data sources, and data analysis. Data collection on treatments ends at grant termination, so the team is identifying ways to mine existing data on sustainability and developing external grant proposals to advance research methods on this translational medicine challenge.
ICTS	Research	Paul M. Allen, PhD	6/1/11 - 5/31/13	Prognostic T Cell Receptor Repertoire Analysis in HSCT and GvHD	Hematopoetic stem cell transplantation (HSCT) is a curative therapy for several hemaologic conditions, but is limited by graft versus host disease (GvHD) and opportunistic infections (OI). Currently, there exists no predictive biomarker for GvHD nor are there adequate biomarkers to assess qualitative T cell reconstitution and risk of OI. We propose to utilize flow cytometric analysis of the T cell receptor repertoire to investigate GvHD and T cell development in HSCT with the goal of developing novel predictive biomarkers.
ICTS	Research	Avraham Beigelman, MD	6/1/11 - 5/31/14	Pilot Study: Azithromycin to Prevent Asthma Following RSV Bronchiolitis	Severe respiratory syncytial virus (RSV) bronchiolitis is frequently followed by recurrent wheezing and asthma. The outcome of asthma has been linked to the severity of the acute bronchiolitis. This project is a proof-of-concept pilot study evaluating the efficacy of azithromycin in attenuating airway inflammation and preventing recurrent wheezing post-severe RSV bronchiolitis.
BJHF	Research	Ellen F. Binder, MD	6/1/11 - 5/31/13	Neural Activation and Connectivity in Response to Exercise and Cognitive Training	The goal of this pilot study is to evaluate whether healthy, sedentary older adults have increased activation of specific brain areas, in response to exercise and cognitive training, in comparison to a control group, and whether observed brain network changes are related to psychometric test performance.
BJHF	Research	Meghan C. Campbell, PhD	6/1/11 - 5/31/14	Resting State Functional Connectivity in Parkinson Disease Dementia	For this pilot study, we propose to collect resting-state functional connectivity magnetic resonance imaging (rs-fcMRI) data as a potential in vivo biomarker of Parkinson disease (PD) dementia. Rs-fcMRI provides insight into functional relationships among various brain regions and may be a sensitive biomarker reflecting the integrity of functional brain networks relevant for cognitive processing and onset of PD dementia.
ICTS	Research	Erin R. Foster, OTD, MSCI, OTR/L	6/1/11 - 5/31/13	Rehabilitation of Everyday Memory Impairment in Parkinson Disease: A Pilot Study	Prospective memory impairment is associated with reduced quality of life among individuals with PD; however, existing interventions do not address it. This project will address this gap by determining if (1) a targeted intervention strategy improves PD participants' laboratory prospective memory performance and (2) whether PD participants can apply the strategy to real-world tasks to improve everyday prospective memory.
ICTS	Research	Jane M. Garbutt, MBChB, FRCP	6/1/11 - 5/31/12	Community Input to Reduce Disparities in Outcomes for Children with Asthma	We will conduct group and individual interviews with about 70 parents and 30 healthcare providers who care for children who have been hospitalized for asthma care and are from high-risk urban, minority groups. Our goal is to learn their beliefs, attitudes and concerns regarding asthma and its management and to learn from their experience. This information will inform the development, implementation and evaluation of a new program for asthma care.
BJHF	Research	Dennis E. Hallahan, MD	6/1/11 - 5/31/13	Targeted Delivery of Cancer Chemotherapy to Radiation-Inducible Receptors	We will study the temporal and spacial distribution of cancer specific peptide ligands by use of radiolabeling and PET imaging. We will accrue patients with poor prognosis cancers who are treated with radiotherapy and image peptide binding to unresectable cancers of the esophagus, breast, Lung, Pancreas, and Glioblastoma.

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ICTS	Research	Aaron Hamvas, MD	6/1/11 - 5/31/13	Prevalence of Surfactant Dysfunction Mutations in Idiopathic Pulmonary Fibrosis	Childhood interstitial lung diseases and adult idiopathic pulmonary fibrosis (IPF) may represent varying manifestations of mutations in surfactant-associated genes. We will use next-generation sequencing to determine the prevalence of surfactant dysfunction mutations in adults with IPF. These data will provide the basis for a program project proposal to understand the contribution of these mutations to respiratory disease across the age spectrum.
ICTS	Research	Paul T. Kotzbauer, MD, PhD	6/1/11 - 5/31/13	Development of Radiotracers for Alpha-synuclein Accumulation in Parkinson Disease	Accumulation of misfolded alpha-synuclein in Lewy bodies is the pathological hallmark of Parkinson Disease (PD) and is implicated in disease pathogenesis. The goal of this project is to develop a Positron Emission Tomography probe to detect misfolded alpha-synuclein accumulation in the brain, which would improve the diagnosis and evaluation of therapeutic approaches in PD.
BJHF	Research	Jin-Moo Lee, MD, PhD	6/1/11 - 5/31/13	Genetics of Brain Repair	The brain has a remarkable ability to adapt to injuries, evidenced by some recovery of function in the weeks to months following brain injury. In this study, we aim to determine if specific genes involved in brain remodeling and plasticity, may influence recovery following stroke.
BJHF	Research	Jonas Marschall, MD	6/1/11 - 5/31/13	Biomarkers of Bacterial Biofilms in Patients with Urinary Catheters	We propose to use small molecule metabolites secreted by bacteria as biomarkers of clinical urinary tract infection. We will expand upon our present set of candidate biomarkers using differential mass spectrometric analysis of culture supernatants. We will then monitor catheterized patients to compare biomarker profiles with urine culture findings and clinical symptomatology.
BJHF	Research	Jeremiah J. Morrissey, PhD	6/1/11 - 5/31/13	Specific Non-Invasive Diagnosis of Kidney Cancer	We have shown that aquaporin-1 and adipophilin are significantly increased in urine of patients with kidney cancer. These are the first ever sensitive and specific urine biomarkers for detecting kidney cancer. Here we seek to establish the ability of these markers in urine and blood to diagnose kidney cancer; differentiate kidney cancers from others of the urinary tract or common non-cancerous kidney diseases, closely monitor for recurrence, and monitor effectiveness of chemotherapy in patients with metastatic disease.
ICTS	Research	Joshua Shimony, MD, PhD	6/1/11 - 10/31/13	Classification of Optic Pathway Gliomas Using Advanced MRI Techniques	Optic pathway gliomas (OPG) are a common tumor in children with Neurofibromatosis I, which can lead to loss of vision and pose significant clinical management issues. The goal of our project is to use advanced MRI imaging methods (diffusion tensor imaging and functional MRI) as predictive biomarkers that monitor progression of disease and can help in guiding therapy to minimize vision loss.
ICTS	Research	Fumihiko Urano, MD, PhD	6/1/11 - 5/31/13	Translating Mechanisms for a Genetic Neurodegenerative Disease to New Therapies	Wolfram syndrome (WS) is a rare childhood disease characterized by insulin dependent diabetes mellitus and neurological dysfunctions. The strategy is to use a yearly clinic to observe patients in a longitudinal fashion beginning early in the disease process to discover biomarkers for monitoring disease progression. This information will position us for clinical trials of agents to treat WS, Type 2 diabetes and other neurodegenerative diseases.
ICTS	Research	Geoffrey L. Uy, MD	6/1/11 - 5/31/13	Disrupting the Marrow Microenvironment with G-CSF in Acute Lymphoblastic Leukemia	This project will test the ability of G-CSF to alter the bone marrow microenvironment by suppressing osteoblasts and decreasing expression of key cytokines/chemokines which support the growth and proliferation of B-cell acute lymphoblastic leukemia. We predict that G-CSF will enhance the effect of chemotherapy and will conduct a pilot study combining G-CSF priming with chemotherapy in adult patients with relapsed or refractory B-ALL.
ICTS	Research	Matthew J. Walter, MD	6/1/11 - 5/31/13	Dysregulation of the DNA Damage Response in Leukemia	By exploiting the differences in DNA repair activities between cancer cells and normal cells, clinicians may be able to choose specific agents that preferentially result in death of cancer cells while sparing the normal surrounding cells. We will test whether this paradigm of synthetic lethality, in which dysfunction in one repair pathway sensitizes cells to a chemical inhibitor of an alternative pathway, can be used to treat leukemia.

Barnes-Jewish Hospital Foundation / Washington University Institute of Clinical & Translational Sciences
2010 Clinical & Translational Research Funding Program Awardees

Funding Source	Type of Grant	Principal Investigator	Project Period	Proposal Title	Description
ICTS	Planning	Robert W. Gereau, PhD	6/1/10 - 5/31/11	Planning a Clinical Study on the Analgesic Efficacy of Fenobam	Fenobam is a selective antagonist of metabotropic glutamate receptor subtype 5 (mGlu5). Fenobam is well-tolerated and has been tested in clinical trials for anxiety and Fragile X Syndrome. Our work demonstrated an important role of mGlu5 pre-clinical pain models. This project supports the planning of two clinical studies in healthy volunteers testing whether fenobam can reverse hypersensitivity in a validated human surrogate pain model.

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ICTS	Planning	Deborah Kiel, PhD	6/1/10 - 5/31/11	Weight Management by Advanced Practice Nurses: Formation of a PBRN	The study will survey Advanced Practice Nurses (APNs) and their patients to identify APN's unique contribution to managing overweight/obesity and inform the development of an intervention to improve care. Subject recruitment for the study and dissemination of study findings will be used to recruit APNs into a new, regional practice-based research network of APNs, thereby developing capacity for community-based nursing research in our community.
BJHF	Planning	Timothy Miller, MD, PhD	6/1/10 - 5/31/11	Does SMN Copy Number Influence Survival in Amyotrophic Lateral Sclerosis?	Amyotrophic lateral sclerosis (ALS) is an adult-onset, fatal, neurodegenerative disorder caused by loss of motor neurons. This study will determine whether *Survival Motor Neuron (SMN)* gene copies influence survival in ALS using a set of 480 DNA samples from a group of well-characterized ALS patients. This study has the potential to define a new prognostic factor of survival and a new therapeutic target for patients with ALS.
ICTS	Planning	Jacqueline E. Payton, MD, PhD FCAP	6/1/10 - 5/31/11	Epigenomic Signatures in Normal and Malignant Myelopoiesis	In contrast to the immutability of *genomic* mutations associated with Acute Myeloid Leukemia, *epigenomic* modifications, the superstructure of the genome, are reversible and therefore may be more amenable to targeted therapeutics. We hypothesize that consistent, coordinated changes in genome-wide chromatin modification patterns occur during normal myelopoiesis, and that key targetable components of these signatures are dysregulated in AML.
BJHF	Planning	Catherine M. Roe, PhD	6/1/10 - 5/31/11	O*Net Occupational Dimension Scales in Alzheimer's Disease Research	Greater occupational complexity is associated with lower risk of Alzheimer's disease (AD). We will estimate the sample size needed for research using the Occupation Information Network (O*NET) occupational complexity scales in an existing sample representative of those used in AD research, and explore whether individual O*NET characteristics discriminate between individuals with and without dementia among those with substantial AD pathology.
BJHF	Planning	Nina D. Wagner-Johnston, MD	6/1/10 - 5/31/11	Clonal Ig DNA in Plasma from Patients with Diffuse Large B-cell Lymphoma	In many cancers, DNA is released from tumor cells into the blood, and generally represents products of cell death. I am evaluating a potential tumor marker in the blood which is specific for lymphoma. Immunoglobulins (Ig) are proteins made by mature B cells which are often rearranged in lymphomas. My project aims to evaluate plasma from patients with newly diagnosed diffuse large B-cell lymphoma for clonal Ig DNA rearrangements.
BJHF	Research	Thomas C. Bailey, MD	6/1/10 - 5/31/12	Early Warning System for Clinical Deterioration on General Medical Wards	Our goal is to develop a two-tiered monitoring system to improve the care of patients on medical wards at Barnes-Jewish Hospital. We intend to 1) develop and test an automated early warning system (EWS) to identify patients who may be at risk for clinical deterioration, and 2) further develop and test a low-cost portable wireless pulse oximeter for patients identified by the EWS that will provide real-time event detection in these high-risk patients.
ICTS	Research	Robert H. Baloh, MD, PhD	6/1/10 - 5/31/12	Locus-Selection and Deep Sequencing to Identify Neuromuscular Disease Genes	We will use genomic DNA-capture technology coupled with next generation sequencing to identify the causative gene mutations in two large families where we have already used linkage analysis to identify the genomic interval which contains the disease gene. This methodology represents a paradigm shift in human genomic research that will enable us to rapidly expand the number of new disease-causing genes that can be identified at the Washington University Neuromuscular Disease Center.
BJHF	Research	Tammie L. S. Benzinger, MD, PhD	6/1/10 - 5/31/12	QBOLD MR Measurements of Oxygen Extraction Fraction in Patients with Brain Tumors	Brain oxygen extraction fraction (OEF) will be evaluated in brain tumors using MR qBOLD, a technique developed at Washington University. Validation between MR qBOLD and PET will be performed. MR qBOLD will be done pre- and post-treatment and followed serially. Data suggests MR measurements of OEF provide a unique measure of in vivo physiology in brain tumors. Validation with PET is necessary before this technique can be used clinically.

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BJHF	Research	Delphine L. Chen, MD	6/1/10 - 5/31/12	PET Imaging of Endotoxin-Induced iNOS Activation in Healthy Volunteers	Neutrophilic inflammation contributes to the development of a number of airway diseases, including acute respiratory distress syndrome (ARDS), cystic fibrosis, chronic obstructive pulmonary disease, certain sub-types of asthma, and bronchiolitis obliterans in lung transplants. Inflammatory stimuli such as endotoxin can initiate the recruitment of neutrophils to the lungs that can ultimately lead to lung tissue injury as a result of increased oxidant production. Inducible nitric oxide synthase (iNOS) activation in response to endotoxin contributes to the development of lung inflammation. However, the role of iNOS in contributing to the development of lung inflammation in humans still requires further study. Methods that investigators could use to measure the activity of iNOS in humans would be a highly useful in furthering our understanding of the role of iNOS in human inflammatory lung disease. [^{18}F](+/-)NOS is a tracer that binds specifically to the iNOS isoform in vivo. This tracer was recently approved through an exploratory IND for initial evaluation in humans. The main goal of this study is to assess the ability of [^{18}F](+/-)NOS to quantify iNOS activation in healthy volunteers receiving endotoxin intrabronchially. The ultimate goal is to establish [^{18}F](+/-)NOS as a reliable biomarker of iNOS in humans for future clinical research investigations to determine the efficacy of therapies for treating inflammatory lung diseases.
ICTS	Research	Kyunghee Choi, PhD	6/1/10 - 5/31/12	Efficient Generation and Application of Cardiac Progenitors for ES and iPS Cells	Hematopoietic, vascular and cardiac cells can be derived from Flk-1 expressing mesoderm. While an Ets transcription factor ER71 is critical for hematopoietic and vascular commitment, it is a negative regulator of cardiac development. This proposal is to investigate if pure cardiac progenitors, compatible for cell-based therapy for cardiac injuries, can be efficiently and robustly generated from ES and iPS cells by inhibiting ER71 expression.
ICTS	Research	Allan Doctor, MD	6/1/10 - 5/31/12	Role of Red Blood Cells in Diabetic Vascular Pathobiology	We seek to elucidate the role of red blood cells (RBCs) in diabetic vasculopathy. RBCs are regulate vessel tone through redox-based control of nitric oxide (NO) in plasma. We hypothesize HbA1C disrupts regulation of RBC antioxidant systems by altering Hb interaction with regulatory proteins. Our Aims are: 1. Determine the influence of HbA1C on RBC reducing equivalent recycling. 2. Determine the influence of HbA1C on coupling between O2 gradients, NO flux through RBC suspensions and RBC derived vasoactivity.
BJHF	Research	David S. Gierada, MD	6/1/10 - 5/31/12	Computer-Aided Diagnosis of Lung Nodules Using CT and Clinical Data	This overall goal is to improve the noninvasive diagnosis of the solitary pulmonary nodule. Previous studies using 2D CT computer-aided diagnosis methods have been promising but have not fully exploited the capabilities of the technology or the predictive value of clinical information. We hypothesize that using high resolution 3D CT image data, combined with patient clinical information, will more accurately predict the likelihood of malignancy.
ICTS	Research	Allison A. King, MD	6/1/10 - 5/31/12	Neuroprotection Feasibility Trial in Infants with Sickle Cell Disease	Approximately one-third of the children with SCD will have overt strokes or silent cerebral infarcts (SCI). For children with overt strokes the biggest risk factor is elevated transcranial doppler (TCD) measurement in the middle cerebral artery. The only means of preventing a stroke in this case is with indefinite monthly blood transfusion therapy. We have recently demonstrated that low hemoglobin F percent is a modifiable risk factor for SCI. Hydroxyurea (HU), an agent associated with increasing percent of hemoglobin F and decreasing (TCD) measurement, is a reasonable option for primary prevention of both elevated TCD measurements and SCI. Our immediate goal is to perform, through the CTSAs of two institutions (Johns Hopkins University and Washington University), a feasibility trial using HU to prevent elevated TCD measurements and SCI. The results of this proposal, may lead to a more definitive multi-center NIH funded trial.
ICTS	Core	Steven Kymes, PhD	6/1/10 - 5/31/12	Establishment of a Center for Economic Evaluation in Medicine	Economic evaluation systematically compares the cost and benefit of alternative courses of action. In the context of health care, we are evaluating disease prevention and treatment to provide information to those making decisions concerning the allocation of health care resources. It encompasses areas of inquiry that include burden of illness studies, cost-benefit analysis and cost-effectiveness analysis.
ICTS	Research	Brian R. Lindman, MD	6/1/10 - 5/31/12	Medical Therapy for Aortic Stenosis: Role of PDE5 Inhibition	Aortic stenosis (AS) is a common heart valve disease that has been considered a “surgical disease” without effective medical therapy. The nitric oxide (NO)—guanosine 3',5'-cyclic monophosphate (cGMP) pathway affects tissue calcification, cardiac hypertrophy, and pulmonary vasodilation. This study will explore the hypothesis that upregulation of NO-cGMP signaling via phosphodiesterase type 5 (PDE5) inhibition will improve outcomes in AS.

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ICTS	Core	Jeanne M. Nerbonne, PhD	6/1/10 - 5/31/12	Translational Cardiovascular Tissue Core	The Translational Cardiovascular Tissue Core is being developed as a centralized facility for the acquisition, s-rage and distribution of human cardiovascular tissues. Acquired phenotypic (electrophysiological, structural, molecular, biochemical) and genotypic (genomic and somatic) data collected will be integrated with archived (tissue and blood) samples and clinical information in a database that is queryable and accessible - the basic, translational and clinical cardiovascular research communities.
BJHF	Research	Linda R. Peterson, MD	6/1/10 - 5/31/12	Reversal of Obesity Cardiomyopathy: An Interdisciplinary Study	We hypothesize that 1) obese humans with diastolic heart failure who lose weight will improve their heart fat deposition and 2) this fat deposition change will predict improved diastolic function. To study this, we will enroll subjects with class II obesity and diastolic heart failure, before and 3-months after surgery-induced weight loss. We will use state-of-the-art methods (MRI and echocardiography) in order to measure our endpoints.
BJHF	Research	Aseem Sharma, MD	6/1/10 - 5/31/12	Spectrum of Perfusion Abnormalities in Developmental Venous Anomalies	Developmental venous anomalies (DVAs) are variations of normal venous drainage pathway in the brain. Though mostly asymptomatic, these can be associated with hemorrhage or become symptomatic. Utilizing perfusion weighted MRI, a non-invasive means to characterize brain perfusion, this study aims to provide insight into the changes in brain perfusion around different types of DVAs.
ICTS	Research	Thaddeus S. Stappenbeck, MD, PhD	6/1/10 - 5/31/12	Role of Paneth Cell ATG16L1 in Crohn's Disease	Alterations in the function of the autophagy gene ATG16L1 is associated with abnormal Paneth cells in mice and Crohn's disease patients (Nature 456:259-265). An interaction has been proposed between ATG16L1 and NOD2, another gene with risk alleles for CD. Our goals are to determine the role of NOD2 in Paneth cells relative to ATG16L1 and determine if the Paneth cell abnormities are reversible in remission in response to specific therapies.
BJHF	Research	Susan L. Stark, PhD, MSOT	6/1/10 - 5/31/12	Effectiveness of a Fall Prevention Program	Falls are responsible for significant morbidity and mortality among community dwelling older adults. The results of the proposed innovative study will provide new evidence about the effectiveness of intensive tailored home interventions to reduce falls. This study has the potential to decrease the health care costs associated with falls and to provide evidence for guiding public health policy for older adults who have fallen.
ICTS	Research	Seth A. Strope, MD, MPH	6/1/10 - 5/31/12	Increasing Efficiency of Surveillance Imaging for Urinary Tract Cancer Survivors	With the intent of decreasing mortality, surgically treated urinary tract cancer patients undergo surveillance imaging to detect recurrence at a potentially curable stage. Little data exists to guide the use of this imaging. Current practice focuses on finding recurrent disease; yet, the impact of such imaging on mortality is unknown. We explore factors underlying utilization of imaging studies, and the impact of imaging on mortality outcomes. We hope to provide evidence informing tailored follow up imaging after surgery.
BJHF	Research	Jason C. Woods, PhD	6/1/10 - 5/31/12	Multidisciplinary Approach to Imaging and Understanding BOS in Lung Transplant	3He MR imaging will be used to identify and monitor ventilation defects, which likely result from bronchiolitis obliterans syndrome (BOS) lesions, in a subset of transplant recipients at high risk of early BOS. Bronchoscopically-obtained biopsies of those identified lesions and putatively normal regions will validate imaging findings, allow development of more precise markers, and allow progression studies in patients at high risk for BOS.

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BJHF	Planning	Peter Crawford, MD, PhD	6/1/09 - 5/31/10	Nutrient-metabolite Responses and Arythmic Outcomes in Cardiomyopathy Patients	The major goal of this project is to establish whether ketone body utilization is augmented in the hearts of cardiomyopathy patients, and if metabolic responses to meals of varying carbohydrate and lipid content can be used as signatures to predict arrhythmic outcomes in cardiomyopathy patients.
BJHF	Planning	Michael Elliott, PhD	6/1/09 - 5/31/10	Environmental Moderators of Diabetes, Self-Management Education	This project examines the relationship between environmental factors and the effectiveness of a diabetes management education program using a socio-ecologic framework. How the physical activity and nutrition environments are perceived by a high-needs population living with diabetes, and how the effectiveness of a diabetes self management program as measured by HbA1c levels is mediated by environmental factors are being assessed.

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ICTS	Planning	Louise Flick, MSN, MPE, RN	6/1/09 - 11/30/10	Patterns of Prenatal Tobacco Use and Psychiatric Disorders	This planning project is the first of 3 stages before submitting a National Children's Study (NCS) adjunct study proposal. This adjunct study will be a prospective cohort study of prenatal tobacco use persistence, the role of psychiatric disorders and effects on health. In the current project we revise and test the CDIS for use in pregnancy, submit a proposal for a preliminary study and develop the design of the adjunct study.
ICTS	Planning	Judith Lieu, MD	6/1/09 - 12/31/10	Research Network for Studies of Children with Unilateral Hearing Loss	Children with unilateral hearing loss (UHL) have hearing loss in one ear only. Children with UHL have worse oral language skills than siblings with normal hearing and more educational problems. No clinical trials have tested the effectiveness of interventions in these children. Our Aims are to develop research networks to facilitate community-based studies of children of all ages with UHL, and to pilot test interventions in "real-world" settings.
BJHF	Planning	Timothy Miller, MD, PhD	6/1/09 - 5/31/10	Measuring SOD1 in the Cerebral Spinal Fluid of ALS Patients	Mutations in superoxide dismutase 1 (SOD1) gene cause a proportion of amyotrophic lateral sclerosis. Evidence suggests that lowering SOD1 levels in patients with SOD1 mediated ALS would be protective. We have developed an antisense oligonucleotide based strategy for lowing SOD1 protein and are planning a Phase I trial based on this technology in late 2009. In order to follow the effect of the antissense oligos, we will measure SOD1 levels in the CSF in patients. Little is known about SOD1 CSF levels in ALS patients, in general. In order to better understand changes in SOD1 levels in the CSF in the upcoming Phase I trial, we will examine CSF SOD1 protein levels in 100 ALS patients, 50 healthy controls, and 42 disease controls.
ICTS	Planning	Gregory Storch, MD	6/1/09 - 5/31/10	Causes of Fever in Children 2-36 Months of Age	This study will use advanced molecular diagnosis to analyze the viral causes of fever in children 2-36 months seen in the St. Louis Children's Hospital Emergency Room. Well children who are having outpatient surgery will be used as controls. The results may lead to the development of a rapid diagnostic test to help determine the cause of fever in children with febrile illnesses. This could be helpful in limiting unnecessary antibiotic use.
BJHF	Planning	Craig Zaidman, MD	6/1/09 - 5/31/10	Radiologic Predictors of Functional Outcome in Newborn Brachial Plexus Injury	Neonatal brachial plexus palsy (NBPP) affects nearly 1% of all newborns. Most of these injuries represent a transient neurapraxia, and heal well without surgery. The challenge is selecting those infants for whom surgery is appropriate. Currently we rely on serial clinical examinations, with the clinical exam at age three months being crucial. The rationale for this projects is to demonstrate that neuroimaging using ultrasound, conventional MRI, and DTMRI will detect signs of brachial plexus injury that correlate with a poor functional recovery oat age three months in infants with NBPP.
BJHF	Research	Hilary Babcock, MD, MPH	6/1/09 - 5/31/11	Osteomyelitis in Diabetic Foot Infections: Impact of Bone Biomarkers	Foot infections, including osteomyelitis, are common in diabetic patients and can lead to amputation. Few markers of response to treatment exist to guide clinical management. This project will evaluate several markers of bone turnover and their relationship to clinical treatment outcomes in osteomyelitis. These markers could lead to better treatment and prevention strategies and improve clinical outcomes in patients with this common infection.
BJHF	Research	Monica Bessler, MD, PhD	6/1/09 - 5/31/11	Running the Stop in Bone Marrow Failure	Inherited bone marrow failure syndromes (IBMFS) are genetic disorders characterized by inadequate production blood cells. In 10-15% of patients the causative mutation is a premature STOP-codon leading to a truncated protein. PTC124, a new investigational drug promotes ribosomal read-through of premature STOP-codons, is bioavailable orally and well tolerated. We propose to test whether PTC124 rescues hematopoiesis in an in vitro culture assay and in certain patients with IBMFS due to a premature STOP-codon.
BJHF	Research	Anne Cross, MD	6/1/09 - 5/31/11	Directional Diffusivity as a Window into the Pathology of MS. Substudy of CSF	Among the distinct clinical syndromes observed as part of the pathology of multiple sclerosis (MS) are spinal cord disease and cortical demyelination. Each syndrome has unique candidate cerebrospinal fluid (CSF) biomarkers hypothesized to provide information vital to disease pathogenesis, prognosis, and treatment. In this project, neurofilament heavy chain levels are correlated with diffusion tensor imaging (DTI) in transverse myelitis. Additionally, CSF visinin-like protein (VILIP-1) is evaluated in MS.
ICTS	Research	Michael Diamond, MD, PhD	6/1/09 - 5/31/11	Structural Immunology of Hepatitis C Virus and Generation of Epitope Diagnostics	Hepatitis C virus (HCV) infects ~4% of the world's population leading to chronic liver disease. Despite this, little remains known as to how antibodies neutralize HCV. Here, we propose to develop novel methodologies to define the functional and structural correlates of antibody-mediated neutralization of HCV infection, with the long-term goal of developing clinically useful diagnostic assays serum antibodies from patients infected with HCV.

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BJHF	Research	Gammon Earhart, PhD	6/1/09 - 5/31/11	Role of Occulomotor Control in Parkinsonian Gait: Mechanisms and Treatment	This project explores the relationship between impaired eye movement control and impaired walking in individuals with Parkinson disease (PD). We will examine the potential for the use of visual cues to facilitate eye movements during walking, thereby improving walking performance. The long-term objective of the work is to develop novel rehabilitative strategies to ameliorate gait deficits in PD. Such approaches could lead to enhanced functional mobility, reduced fall risk, and improved quality of life for people with PD.
ICTS	Core	Matthew Ellis, MB, PhD, FRCP	6/1/09 - 5/31/11	Human and Mouse Linked Evaluation of Cancer Core Facility	This core sets out to bridge the knowledge gap between breast cancer genome structure and function with new mouse xenografting techniques called HIM for "Human in Mouse". We term this project "HAMLET" for "Human And Mouse-Linked Evaluation of Tumors" to emphasize the features of the core which includes annotation of the clinical history associated with the original tumor and comprehensive comparison to the mouse graft to determine whether genomic and proteomic features were stable during the transplantation process.
BJHF	Research	Jack Engsberg, PhD	6/1/09 - 5/31/11	Developing Virtual Environment Authoring Tools for Creating Therapy Interventions	Purpose is to develop and test a virtual environment (VE) therapeutic programming tool for persons with stroke. The impact will be to change practice by creating a more effective and motivating home-based therapy service. Aim 1: Develop VE programming components to create therapy training interventions. Aim 2: Determine feasibility of conducting a 6-week VE training intervention to improve reaching, upper extremity function, and participation.
ICTS	Core	Victoria Fraser, MD	6/1/09 - 5/31/11	Clinical Research Core Facility for Administrative Claims Data	The core provides large administrative data sets on secured server space (CMS, Medicaid, etc.), server based statistical software, regular data backup, data management, programming, and data analysis & assistance with IRBs and grant applications for those using administrative claims data. Investigators & trainees interested in health services, outcomes, comparative effectiveness research, and economic evaluation will be able to utilize the core for their research more efficiently than if they had to purchase and manage these complex files on their own.
ICTS	Research	Jane Garbutt, MBChB, FRCP	6/1/09 - 5/31/11	Community Care for Croup	This randomized clinical trial to compare the effectiveness of prednisone 2mg/kg/day for 3 days vs. dexamethasone 0.6mg/kg for 1 day for treatment of 200 children with mild or moderate croup will be conducted in a practice-based research network of community pediatricians in the St. Louis area. Outcomes include additional health care for croup, duration of symptoms, nights of disturbed sleep, parental stress, missed work days, and adverse events.
BJHF	Research	Robert Gropler, MD	6/1/09 - 5/31/11	An Inter-disciplinary Approach to the study of NAFLD	Nonalcoholic fatty liver disease (NAFLD) has become an important public health problem in many industrialized countries because of its high prevalence, potential progression to severe liver disease, and association with cardiometabolic abnormalities, including diabetes, the metabolic syndrome, dilated cardiomyopathy and coronary heart disease. The mechanisms responsible for the pathogenesis of steatosis are poorly understood. This proposal involves a multidisciplinary group of investigators who have the range of expertise to address the metabolic mechanisms responsible for NAFLD in humans for the first time.
BJHF	Research	Robert Grubb, MD	6/1/09 - 5/31/11	Multicontrast MRI for Improved Tumor Localization in Prostate Cancer	Accurate noninvasive localization of prostate cancer is necessary for optimal outcomes for focal ablation of tumors. Patients undergo MRI with multiple MRI sequences prior to curative treatment (radical prostatectomy or brachytherapy). The surgically removed prostate undergoes full pathologic analysis and ex vivo diffusion MRI, which facilitates coregistration of histology and in vivo MRI images. This linkage will be a key to validating the accuracy of MRI for identification of tumors within the prostate.
ICTS	Research	Daniel S. Ory, MD	8/21/09 - 2/29/12	HDL Lipid Biomarkers for Atherosclerotic Disease in Type 2 Diabetes	The goal of our proposal is to test the hypothesis that alterations in the lipids associated with HDL may explain the increased risk of atherosclerosis among subjects with type 2 diabetes (DM), and will provide novel biomarkers for type 2 DM to facilitate early detection and risk stratification for atherosclerotic disease. This hypothesis will be tested by identification of HDL-associated lipid biomarkers for atherosclerotic disease in DM, and correlation of candidate HDL lipid biomarkers with measures of HDL function.
ICTS	Core	Enola Proctor, PhD	6/1/09 - 5/31/11	Dissemination and Implementation Research Core	The Dissemination and Implementation Research Core provides methodological expertise to advance translational research to move efficacious health practices from clinical knowledge into routine, real-world use. The DIRC will develop tools for studying the dissemination and implementation (D&I) of health care discoveries. Per the NIH CTSA PA, the DIRC will focus on T2 research--research to inform the adoption of best practices in the community.

Funding Source	Type of Grant	Principal Investigator	Project Period	Proposal Title	Description
ICTS	Research	Enola Proctor, PhD	8/21/09 - 2/29/12	Internet Based Translation-2 Research for Psychiatric Illness Using a PBRN	This project tests a web-enhanced dissemination and implementation strategy to train mental health clinicians in a trauma focused psychotherapy. Clinicians will be trained using prepackaged web material, a treatment manual, scaffolded activities, webinars, and discussion groups, and compared to a delayed treatment group. Clinicians will be from across Missouri and members of a practice-based research network of Medicaid mental health clinicians.
ICTS	Research	Brad Racette, MD	6/1/09 - 5/31/11	Neuropathology of Chronic Manganese Exposure	Parkinson disease (PD) is a common neurodegenerative disorder and metal exposure may be a risk factor. The primary goal of this grant is to compare brains of South African manganese (Mn) miners to the brains of South African gold (Au) miners to investigate the hypothesis that workers with chronic exposure to Mn will have neuropathologic findings typical of early PD, to clarify the role of environmental metal exposure in the pathogenesis of PD.
ICTS	Research	Michael Rettig, PhD	6/1/09 - 5/31/11	Characterization of CD34+ Stem Cells and T Cells Following AMD3100 Mobilization	AMD3100, an inhibitor of CXCR4, mobilizes stem cells to the peripheral blood, with minimal side effects. Mobilization of stem cells with AMD3100 as a single agent is appealing and would result in shorter mobilization times compared with G-CSF (one day vs. four) without the side effects associated with G-CSF. Here, we are optimizing the kinetics of stem cell mobilization and characterizing the different stem cell subsets mobilized by AMD3100.
ICTS	Research	Michael Tomasson, MD	6/1/09 - 5/31/11	The Role of Neurobeachin (NBEA) in Multiple Myeloma	Multiple myeloma (MM) is an incurable hematopoietic malignancy associated with destructive bone lesions and renal failure. Using array comparative genomic hybridization (aCGH), Dr. Tomasson identified NBEA, a gene on chromosome 13, to be dysregulated in MM patients. Dr. Tomasson and his collaborators will test NBEA as a biomarker and will use genomic technologies to identify additional chromosome 13 variants that contribute to poor outcomes in MM.
BJHF	Research	David Warren, MD, MPH	6/1/09 - 5/31/11	Molecular Epidemiology of S. Aureus Bacteremia and Clinical Outcomes	Staphylococcus aureus bacteremia is a common and challenging problem. Despite the high morbidity and mortality associated with S. aureus bacteremia, little is known about the interaction between host- and pathogen-specific risk factors in complicated S. aureus infections. We propose to perform molecular characterization of S. aureus isolates from a prospectively collected cohort of 370 patients with S. aureus bacteremia. The goal of this study is to determine if infection with specific S. aureus strains carries a greater risk of mortality and complicated infections, independent of host factors.
ICTS	Research	Amy Waterman, PhD	6/1/09 - 5/31/11	Improving Kidney Transplant Education to Increase Living Donation Rates	This Explore Transplant study will validate a transplant decision-making scale to assess kidney patients' interest and knowledge about living donation. We will then develop a computerized expert system to provide patient education about living donation by telephone and mail based on their decision-making assessment. We will then conduct a pilot test of the telephone Expert System with new kidney recipients in preparation for a large-scale randomized controlled education trial.

Washington University Institute of Clinical and Translational Sciences
2008 Pilot and Novel Methodologies Funding Program Awardees

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ICTS	Planning	John C. Clohisy, MD	2/1/08 - 1/31/09	Development of a Collaborative Team for the Prevention of Hip Osteoarthritis	The multidisciplinary project has two aims. First, a standard language and set of data collection tools for a young patient population with pre-arthritic hip disease will be established. Physical examination, radiographic treatment outcome measures will be analyzed for reliability and validity. A manual of operations will define and communicate patient evaluation, radiographic and clinical outcome measures. Secondly, a multicenter database for joint preservation surgery of the hip will be developed and refined.
ICTS	Planning	Todd A. Fehniger, MD, PhD	2/1/08 - 1/31/09	Isolation, Expansion, and Activation of Human Natural Killer (NK) Cells for Adoptive Immunotherapy of Cancer	The long term goal of this project is to design and implement translational clinical trials utilizing natural killer (NK) cells for the cellular immunotherapy of cancer. Here, we will develop preliminary data for a novel methodology to isolate human NK cells using GMP-ready high speed cell sorting with expansion and activation using cytokines and accessory cells. The resultant NK cell product will be functionally validated in vitro and in vivo.

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ICTS	Planning	Aimee James, PhD, MPH	2/1/08 - 1/31/09	Program Planning for Prevention Research in Community Health Centers	We will use community-based participatory research (CBPR) to advance relationships with safety-net clinics (SNCs) in Saint Louis. We aim to use CBPR to improve protocols for research with SNCs and then conduct a pilot study to collect preliminary data. We will present our work to community groups and talk with clinic personnel about attitudes toward medical research. This work is important because an improved community-university partnership will increase our ability to translate scientific findings to the community.
ICTS	Individual	Stephanie A. Lutter, MD	2/1/08 - 1/31/10	Exploration of the Host Immune Response in Community-Acquired Methicillin Resistant *Staphylococcus aureus* Disease	Knowledge of bacterial and host factors defining the outcomes of human encounters with community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is lacking. The goals of this project are to measure the development of antibodies to toxins implicated in the pathogenesis of CA-MRSA following colonization or infection in children; and to determine whether this immunologic response correlates with protection from subsequent infections.
ICTS	Individual	Margaret A. Olsen, PhD, MPH	2/1/08 - 1/31/10	Risk Factors for Complications after Spine Surgery in the Elderly	Neurologic and orthopaedic complications after spine surgery can result in devastating morbidity, including permanent neurologic deficit. Our study will use Medicare claims data to describe the incidence and clinical outcomes of neurologic and orthopaedic complications, determine patient, surgeon, and hospital risk factors and calculate medical costs attributable to these complications. These results can be used to to improve surgical processes of care and quality of life for the elderly.
ICTS	Individual	Prabha Ranganathan, MD	2/1/08 - 7/31/10	Effects of Gene-Environment Interactions on BMD in RA	Women with rheumatoid arthritis (RA) are at high risk for osteoporosis and low bone mineral density (BMD). In this proposal, we will determine if BMD in women with RA is influenced by environmental, RA-related, and genetic risk factors in a race-specific manner. Results from these studies will provide important insights into the race-specific contributions of genetics, the environment, and inflammation toward the development of osteoporosis.
ICTS	Collaborative	Jill B. Firszt, PhD	2/1/08 - 1/31/10	Time Course of Auditory Cortex Reorganization Following Sudden Unilateral Deafness	The proposed translational studies, using functional imaging and behavioral methods, will advance understanding of plasticity and dominance of the neural pathways in deafness and guide intervention for patients with sudden onset of unilateral hearing loss. Specifically, we will document the sequential reorganization of the brain after onset of sudden unilateral deafness and develop rehabilitation strategies to ameliorate sound localization problems that occur with unilateral deafness.
ICTS	Collaborative	Ann Gronowski, PhD	2/1/08 - 1/31/10	Formation of a "Women's Health Specimen Consortium"	Our objective is to create a structure to facilitate the collection of patient specimens for women's health research. The "Women's Health Specimen Consortium" will assist researchers in: patient consent, specimen collection, specimen storage and processing, as well as the ability to select and obtain previously banked specimens via a comprehensive database of outcomes data.
ICTS	Collaborative	Aaron Hamvas, MD	2/1/08 - 7/31/09	Collaborative Group for Necrotizing Enterocolitis (NEC)	We are interested in the role of epidermal growth factor (EGF) in the development of necrotizing enterocolitis (NEC), a devastating intestinal process affecting premature infants. We will use stable isotope measurements of EGF metabolism and measurements of inflammatory markers to develop an "EGF phenotype" that can be correlated with the genotype of EGF and its receptor in premature infants 26-32 weeks gestation to understand the metabolic, inflammatory and genetic factors that contribute to NEC.
ICTS	Collaborative	Evan D. Kharasch, MD, PhD	2/1/08 - 1/31/10	Interdisciplinary Program Development in Sickle Cell Pain Research	The acute painful episodes of Sickle Cell Disease (SCD) are unpredictable, recurrent, and debilitating. Methadone is a promising and potentially advantageous alternative to morphine in the treatment of SCD pain, yet methadone disposition in SCD patients is unknown. This pilot study will determine the pharmacokinetics of intravenous methadone in adult and pediatric SCD patients and evaluate the impact of age, disease status and known polymorphisms of cytochrome P4502B6 on methadone pharmacokinetics.
ICTS	Collaborative	Henry Lai, MD	2/1/08 - 1/31/10	Protocol Development for Comparative Urine Proteomic Studies in Human	Interstitial cystitis (IC) is an inflammatory disease of the bladder. We have assembled a multidisciplinary team to discover novel diagnostic biomarkers for IC. Currently, we are optimizing the sample collection, preparation, and data analysis protocols for urine proteomics using targeted label-free, nano-LC-LTQ-OT-MS. We are determining the variation of urine proteome that are associated with technical and biological variation.
ICTS	Collaborative	Daniel C. Link, MD	2/1/08 - 1/31/10	Pilot Study of Stem Cell Mobilization by G-CSF to Treat Severe Peripheral Artery Disease (STEMPAD Trial)	To test the hypothesis that mobilization of angiogenic cells into the blood by granulocyte colony stimulating factor (G-CSF) may stimulate angiogenesis and result in a sustained improvement in blood flow in the lower extremities of patients with critical limb ischemia (CLI) secondary to atherosclerosis. Subjects with CLI will be randomized in a double-blinded fashion to treatment with G-CSF or saline for 10 days. The primary endpoint is major limb amputation at 1 year.

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ICTS	Collaborative	Chenyang Lu, PhD	2/1/08 - 1/31/10	Wireless Sensor Network Technology for Clinical Monitoring	This project is developing and evaluating novel wireless sensor network technologies for real-time patient monitoring, which will enable timely prediction of clinical deterioration of non-ICU inpatients. Each wireless sensor consists of an embedded computer, a radio interface, and a pulse oximeter. Wireless sensors attached to patients will continuously collect and transmit data to an electronic medical record system over a wireless network.
ICTS	Collaborative	Denise E. Wilfley, PhD	2/1/08 - 1/31/10	A Randomized Controlled Trial for Parents of Young Overweight Children	Our overarching objective is to develop a clinically effective and cost efficient treatment for childhood obesity, with a high potential for dissemination. Our novel treatment, *Food for Thought* , is an Internet-delivered intervention targeting parents of overweight children ages 3-6, an understudied population with the highest potential for improvement in weight status and long-term health benefits. 62 parents will participate in a randomized controlled trial of the program.
ICTS	Collaborative	Dmitriy A. Yablonskiy, PhD	2/1/08 - 1/31/10	Gradient Echo Plural Contrast Imaging - Novel MRI Technique for Evaluating Multiple Sclerosis	The complexity of the underlying mechanisms of Multiple Sclerosis require new clinical markers for more accurate diagnosis and treatment of this debilitating disease and to aid in the evaluation of new therapies. GEPCI (Gradient Echo Plural Contrast Imaging) approach recently introduced by our group has a great potential towards this objective. The goal of this project is to introduce GEPCI as a clinical tool for diagnostic of MS.