

**Institutional Development Award (IDeA) Program
CENTERS OF BIOMEDICAL RESEARCH EXCELLENCE (COBRE)**

Directory of Active Awards by State and Program

August 2010

IDeA – Eligible States:

Alaska (1)	Kansas (6)	Montana (4)	North Dakota (3)	South Dakota (2)
Arkansas (2)	Kentucky (8)	Nebraska (5)	Oklahoma (7)	Vermont (3)
Delaware (4)	Louisiana (9)	Nevada (2)	Puerto Rico (0)	West Virginia (3)
Hawaii (3)	Maine (2)	New Hampshire (2)	Rhode Island (6)	Wyoming (1)
Idaho (1)	Mississippi (2)	New Mexico (3)	South Carolina (5)	

Alaska

Center for Alaska Native Health Research University of Alaska – P20 RR016430

Principal Investigator

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Thematic Scientific Focus

Health disparities experienced by Alaska Natives, focusing on obesity, diabetes, and cardiovascular disease, investigated from a genetic, dietary, and cultural-behavioral perspective

Research Projects

- Yup'ik perceptions of body weight and diabetes: cultural pathways to prevention
- Developing a novel set of diet pattern biomarkers, based on stable isotope ratios
- Contaminants and nutrients in Alaskan subsistence foods: striking a balance
- Yup'ik experiences of stress and coping: intervention via cultural understanding

Research Resources

- Epidemiology and biostatistics core
- Biological specimens and genetic core
- Nutrition and physical activity core
- Culture and intervention core

Index Terms

health disparities, diabetes, nutrition, obesity, epidemiology, bioinformatics, genetics, stress, Alaska Native, Yup'ik, contaminants, stable isotopes

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Arkansas

Center for Protein Structure and Function University of Arkansas at Fayetteville – P20 RR015569

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Thematic Scientific Focus

Structure and function of biomedically important proteins, including bacterial, viral, and membrane-associated proteins, with emphasis on structure-based drug discovery and design

Research Projects

- Protein interactions with the extracellular matrix
- Protein interactions in carcinogenesis and cancer
- Protein targeting
- Fibroblast growth factor signaling complex
- Membrane Proteins

Research Resources

- NMR core – 500 MHz and 700 MHz NMR spectrometers with cryoprobes; 300 MHz solid-state NMR spectrometer for membrane proteins
- X-ray crystallography core – two Rigaku diffractometers with Saturn92 CCD detectors; robotic protein crystallization facility
- Mass spectrometry core – IonSpec 9.4 Tesla FTMS Fourier transform mass spectrometer equipped with MALDI and ESI sources; five other mass spectrometers
- Large-scale protein production facility – four Applikon bioreactors and ancillary equipment; Applied Biosystems protein sequencer, and peptide synthesizer; Beckman analytical and preparative ultracentrifuges
- High-throughput synthesis core – Bruker Avance 300 MHz NMR; CEM Explorer automated microwave synthesis workstation; eight Radley 12-vessel parallel synthesizers, and associated supporting instrumentation

Index Terms

NMR, structural biology, mass spectrometry, X-ray crystallography, drug design, protein targeting

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Center for Translational Neuroscience
University of Arkansas for Medical Sciences – P20 RR020146

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Thematic Scientific Focus

Establishment of a broad-based translational neuroscience research center

Research Projects

- Novel treatment for Alzheimer's disease
- Amphetamine withdrawal paradigm in humans
- Preventing the long-term consequences of neonatal pain
- The role of leptin in obesity and sleep
- Changing thought and action in tobacco dependence with transcranial magnetic stimulation (TMS)

Research Resources

- Telemedicine core facility – Pediatrics Physician Learning and Collaborative Education (PedsPLACE) program, and Emergency Department Physician Learning and Collaborative Education (EDsPLACE) program
- Electrophysiology core facility – human-P50 evoked potential, psychomotor vigilance, frontal lobe blood flow; animal-patch clamp, population and evoked potential recordings
- Transcranial magnetic stimulation core facility
- Image analysis core facility – confocal microscope, zoom microscope
- Molecular biology core facility – RT-PCR, Maxwell, Luminex

Index Terms

neurodegenerative disorders, drug abuse, sleep and obesity, chronic pain.

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Delaware

Center for Pediatric Research

Alfred I. duPont Hospital for Children – P20 RR020173

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Thematic Scientific Focus

Establish a translational research center to study pediatric disorders, create corresponding therapies, and develop new and better methods of prevention

Research Projects

- Developmental mechanisms of undescended testis
- Molecular mechanisms in Pelizaeus Merzbacher disease
- Peripheral nervous system in cerebral palsy
- Extracellular matrix remodeling in cardiovascular diseases
- Mechanisms of cell death in spinal muscular atrophy
- Oxygen and barotrauma effects on human airway epithelium
- Mechanistic biomarkers of endocrine disruption
- The medial olivocochlear bundle and speech-in-noise deficits
- Prognostic synovial biomarkers in juvenile rheumatoid arthritis
- Method to alter splicing of disease-associated RNAs

Research Resources

- Bioinformatics core – includes full-time biomedical statistician to assist with complex analyses
 - Clinical research services – support and oversight for research studies involving human subjects and clinical trials
 - Cell science core – services and resources for preparative and analytical studies for cell biology, protein biochemistry and molecular biology
 - Biomolecular core

Index Terms

pediatric diseases, neurological disorders, cell death, cardiovascular diseases

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COBRE for Women in Science & Engineering on Osteoarthritis
University of Delaware – P20 RR016458

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Thematic Scientific Focus

Mechanisms, prevention, and treatment of osteoarthritis, focusing on cartilage healing and the biomechanics of the human knee

Research Projects

- Perlecan and heparanase in cartilage growth and healing
- Solute transport in the subchondral bone plate of osteoarthritic joints
- Risk factors for progression of osteoarthritis of the knee
- Joint loading and the progression of osteoarthritis following TKA
- Knee stiffness, proprioception and instability affect knee control in OA

Research Resources

- Mentoring core
- Confocal microscopy and cytomechanics core
- Computational modeling core
- Clinical diagnostic and treatment facilities – surgical facilities; advanced equipment for testing and measuring material properties of tissues, muscle activation patterns, muscle performance, and limb motion
- Gait laboratories – six-camera systems with multiple force plates and EMG data acquisition capability; functional electrical stimulation equipment; biomechanical modeling; robotic-assisted training systems

Index Terms

biomechanics, orthopedics, physical therapy, magnetic resonance imaging, electromyography, tissue engineering, gait analysis

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COBRE on Membrane Protein Production and Characterization

University of Delaware – P20 RR015588

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Thematic Scientific Focus

To express, solubilize, purify and crystallize membrane proteins, to determine their structures, and to characterize their functions at the molecular level and in larger biological systems

Research Projects

- Determinants of GPCR expression in *E. coli* and yeast and of solubilization and stability
- Structure and function of platelet activating factor acetylhydrolase type II
- The role of JAM-A in cancer metastasis and spermatogenesis
- Characterization of plasmodesmal channel protein
- Solid-state NMR methods for structural studies of phospholipase C
- Non-additive interaction models for lipids and integral membrane proteins
- Spatial self-organization of plasma membrane proteins
- Functional characterization of compatible solute transporters of *Vibrio parahaemolyticus*
- Lanosterol biosynthesis in the membrane environment
- Structural and functional studies of the transmembrane selenoprotein K and its role in oxidative defense
- Elucidating the role of mitochondrial transport proteins in hepatocytes and adipocytes
- Modulation by SCN2B of prostate cancer cell migration on peripheral nerves

Research Resources

- Protein production and purification core
- Biophysical characterization core
- Protein X-ray crystallography facilities
- Bioimaging core – multiphoton confocal microscopes; electron and scanning probe microscopy; laser capture microdissection system

Index Terms

membrane proteins, G protein-coupled receptors, protein stability, surfactants, molecular biology, membrane biophysics, ion channels, molecular modeling, molecular simulations, bioinformatics, multiscale modeling, 2,3-oxidosqualene cyclase, integral membrane enzymes, monotopic proteins, solid-state NMR spectroscopy, total internal reflection microscopy, cholesterol synthesis, hypercholesterolemia, atherosclerosis, molecular genetics, reproductive genetics, electrophysiology, cancer, breast cancer, metastasis, JAM-A, cell migration, cell invasion, tight junctions, spermatogenesis, male fertility, sperm motility, cardiovascular disease, X-ray diffraction, crystallography, chemical warfare agents, NMR spectroscopy, solid-state NMR, magic-angle spinning NMR, lipid metabolism, LDL, interfacial enzyme kinetics, platelet activating factor acetylhydrolase, plasmodesmal channel protein

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Molecular Design of Advanced Biomaterials
University of Delaware – P20 RR017716

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Thematic Scientific Focus:

Development of biomaterials for regeneration of liver and vocal-fold tissues, and for drug-lead identification and payload delivery, with a focus on control of the conformational properties and the biological specificity of the molecular-scale building blocks as a means to achieve desired macroscopic properties

Research Projects:

- Molecular-level design of peptide-based antagonists and biomaterials
- Experimental and computational methodologies for biomaterials characterization
- Synthesis and assembly of bio-responsive copolymer vesicles for payload transport
- Elastic polymers with defined molecular architecture and tunable biological functions for vocal-fold tissue engineering
- β -hairpin gels for liver regeneration

Research Resources:

- Materials testing and analysis core
- Electron microscopy core
- Tissue culture core
- X-ray crystallography core
- Mass spectrometry core
- Optical microscopy core
- Surface analysis core
- Mass spectrometry core
- Networked computational facility – Linux computer cluster for molecular modeling; Beowulf-type cluster
- Protein production and purification core
- Peptide/protein NMR core – 600 MHz NMR spectrometer with cryoprobe; 300 MHz solid-state NMR spectrometer for membrane proteins; ^{19}F probe, solid-state bioprobe

Index Terms:

biomaterials, proteins, peptide folding, triggered folding, gelation, molecular architecture, unnatural amino acids, elastomeric polymers, peptide engineering, materials science, chemical engineering, chemistry, biochemistry, molecular modeling, NMR, peptide antagonist, biomaterials characterization, organic synthesis, vesicles, bio-responsive polymer, vocal fold, surfaces, regenerative medicine, tissue engineering

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Hawaii

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Thematic Scientific Focus

Molecular and cellular mechanisms underlying human cardiovascular diseases, with emphasis on animal model systems

Research Projects

- Integrins and apoptosis in the heart
- Selenoproteins in the heart
- Endothelial gene expression in cardiovascular stress
- Cardiac mast cells in heart failure
- Cardiac effects of jellyfish toxins
- Molecular signaling in the diabetic heart

Research Resources

- Genomics core – expression profiling; high-throughput real-time PCR
- Histology and microscopy core – specialized immunohistochemistry services; confocal microscopy
- Mouse phenotyping core – high frequency echocardiography, murine surgery including myocardial infarction by cryoablation and coronary ligation

Index Terms

cardiovascular disease, receptor-mediated signaling, endothelin, hypoxia-inducible factor-1, selenoprotein, caveolin, gene expression, mast cells, microbubbles

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Institute for Biogenesis Research
University of Hawaii – P20 RR024206

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Thematic Scientific Focus

Fertility and early development of mammals, with emphasis on mouse and human

Research Projects

- Sex determination of primordial germ cells
- Function of Y chromosome genes in fertilization
- Cellular and molecular mechanisms of blastocyst development
- The importance of UDP-glucuronosyltransferase enzymes in pregnancy and embryogenesis
- Transposase mediated transgenesis and gene therapy

Research Resources

- Transgenic mouse core – production of transgenic mice using novel ICSI technology combined with transgenesis

Index Terms

infertility; germ cell, zygote and blastocyst development; sperm, oocyte, embryo

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**Pacific Center for Emerging Infectious Diseases Research
University of Hawaii at Manoa – P20 RR018727**

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Thematic Scientific Focus

The emergence and spread of newly recognized infectious diseases with special attention paid to those diseases that disproportionately affect under-served ethnic minorities and disadvantaged or marginalized communities in Hawaii and the Asia-Pacific region

Research Projects

- Stem region of envelope proteins of dengue virus and re-emerging flaviviruses
- Molecular mechanisms of West Nile virus neuroinvasion
- Role of miRNAs in dengue immunopathogenesis
- Spatiotemporal expression of *Burkholderia pseudomallei* genes

Research Resources

- COBRE bioinformatics core
- BSL-3/ABSL-3 biocontainment core
- Molecular and cellular immunology core: FACS flow cytometry; cell sorting; ELISPOT and Luminex technology

Index Terms

emerging and re-emerging infectious diseases, molecular pathogenesis, dengue virus, West Nile virus, Burkholderia, translational research

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Idaho

Initiative for Bioinformatics and Evolutionary Studies (IBEST)

University of Idaho – P20 RR016448

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Thematic Scientific Focus

Investigate the importance and consequences of critical mutagenic processes, identify patterns of change that emerge during the course of evolution, develop and test models to understand these patterns, and devise means to analyze large genetic data sets

Research Projects

- Evolution of antibiotic resistance plasmid host range
- Spatial structure and adaptive evolution of viruses
- Molecular dissection of adaptive evolution
- Interdisciplinary study of viral host switching
- Evolution of antibiotic resistance in biofilms
- Mechanisms of pathogenicity in an emerging fungal pathogen

Research Resources

- Bioinformatics core
- DNA sequence analysis core

Index Terms

evolutionary biology, molecular biology, computational, biology, statistics, genomics, microbial ecology

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Kansas

Center for Cancer Experimental Therapeutics University of Kansas, Lawrence – P20 RR015563

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Thematic Scientific Focus

Cancer-related research at the interface between chemistry and biology, focusing on identifying novel bioactive compounds for use as basic biomedical research tools and new therapeutic agents

Research Projects

- Identification of *in vivo* Pak1 protein kinase inhibitors
- Nanocarrier-based intralymphatic imaging and therapy for melanoma
- Design of 2-Methoxyestradiol pro-drug and evaluation of its anti-cancer potential
- Nanoelectric chip for kinase profiling
- Nanoparticle-based dual gene therapy for lung adenocarcinoma

Research Resources

- High-throughput screening and target identification core – robotic bioassay system for screening chemical libraries; custom chemical and biomolecular structure databases
- Medicinal chemistry core – combinatorial organic chemistry; custom synthesis and purification of small-molecule libraries of enzyme inhibitors

Index Terms

medicinal chemistry, combinatorial chemistry, bioassays, molecular library screening, drug design, cancer, oncology, cell biology, molecular biology, retrovirus, high-throughput screening

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Center for Epithelial Function in Health and Disease
Kansas State University College of Veterinary Medicine – P20 RR017686

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Thematic Scientific Focus

Epithelial function in health and disease, emphasizing epithelial cell physiology and pathophysiology to create a strong foundation for translational research

Research Projects

- Roles of CFTR in thyroid epithelial cell iodide secretion
- The function of *Anopheles* serpins during malaria parasite invasion of mosquito epithelia
- Corticosteroid-modulated epithelial Na⁺ and HCO₃⁻ transport
- Dietary supplements protect retinal pigment epithelial cells from apoptosis
- Salivary gland transcriptome and peptidome analysis in *Crocota crocuta*
- Intestinal epithelial wound healing: NSAIDs and calpain inhibition
- Role of IL-1beta in colon cancer cell - macrophage interaction
- Xenobiotic transport across the mammary epithelium
- Simulation of spontaneous peptide insertion and assembly in epithelial membranes

Research Resources

- Confocal microfluorometry and microscopy – Zeiss LSM510 Meta confocal microscope, Zeiss LSM700 confocal microscope, Leica cryostat microtome, CryoJane tape-transfer system, Epson Stylus Pro 4000 printer
- Molecular biology and biochemistry – Agilent bioanalyzer, Beckman-Coulter Biomek NXp 96-well RT-PCR robotics system, Bio-Rad 96-well plate thermocyclers, Cepheid Smartcycler II, Beckman-Coulter DNA sequencer, Kodak imager for western blots, Nanodrop µl spectrophotometer and fluorometer
- Epithelial electrophysiology – AE vibrating current-density and ion-flux probe system, Axon Instruments single-cell electroporator, custom tissue dissection station, DSP dual phase lock-in amplifier, Stoelting microforge and pipet puller

Index Terms

epithelium, electrophysiology, molecular biology, gene expression, ion transport, pharmacology, cellular regulation

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COBRE in Protein Structure and Function
University of Kansas School of Pharmacy, Lawrence – P20 RR017708

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Thematic Scientific Focus

Protein structure-function relationships at the atomic and molecular level

Research Projects

- Structural characterization of the anthrax toxin protective antigen
- Mechanism of chaperone-assisted assembly of proteasome regulatory particle
- Remodeler translocation along DNA
- The role of dynamics in PEPCK mediated catalysis

Research Resources

- Protein production core – preparative scale production, purification and characterization of proteins; protein binding assays including surface plasmon resonance; protein mass spectrometry; 2-D gel electrophoresis
- Protein structure core – protein crystallization and X-ray data collection and analysis; structure solution and refinement
- Bio-NMR core – assists investigators in elucidating protein structure and/or dynamics by means of NMR at 600 and 800 MHz

Index Terms

protein structure, X-ray crystallography, NMR spectroscopy, mass spectrometry, proteomics, bioinformatics, protein interactions, anthrax toxin, multimeric protein structure, pore formation, transcriptional activation, DNA remodeling, chaperones, glycoproteins, membrane proteins, signal transduction, rational drug design, medicinal chemistry

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Molecular Regulation of Cell Development and Differentiation
University of Kansas Medical Center, Kansas City – P20 RR024214

Principal Investigator

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Thematic Scientific Focus

Basic mechanisms of cell and tissue development

Research Projects

- Organization of the nerve terminal by synaptic cleft components
- Preimplantation embryonic secreted/released proteins as embryo quality predictors
- Genetic models of congenital vascular malformations
- Transcriptional mechanisms of endothelial function and differentiation
- Germ cell development in the atrichosis mutant mouse

Research Resources

- Transgenic, gene targeting and genotyping core – creation of transgenic mice through DNA microinjection, electroporation of embryonic stem cells and blastocyst injection, genotyping of transgenic and knockout mice
- Molecular biology core – DNA sequencing, oligonucleotide synthesis, microarray chip processing and bioinformatics analysis
- High-resolution imaging core – confocal microscopy, laser capture microdissection, scanning and transmission electron microscopy, immunoelectron microscopy

Index Terms

development, differentiation, organogenesis, neurogenesis, angiogenesis, vasculogenesis

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Novel Approaches for Control of Microbial Pathogens
University of Kansas Medical Center – P20 RR016443

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Thematic Scientific Focus

Novel molecular mechanisms for inhibiting replication of pathogenic microbes, emphasizing immunopathological responses to infectious agents and host antigens

Research Projects

- Regulation of CCR7 mediated events in breast cancer cells and in T cells
- Post-transcriptional regulation of parvovirus B19 capsid gene expression
- Identification and regulation of stress response genes in Group A *Streptococcus*
- Hepatitis B virus/hepatitis delta virus infection, its relation to pathogenesis
- Modulation of NF- κ B signaling by *E. coli* protein kinases
- Mechanics of hantaviral nucleocapsid protein mediated translation initiation of viral mRNA

Research Resource

- Flow cytometry core – identification of cells of the immune system that are involved with development of specific immune responses
- Luminex core – provides a mechanism for measuring minute quantities of cytokines and chemokines produced by cultured immune cells
- Signal transduction core – provides a mechanism for identifying molecular pathways involved in production of viral proteins in infected cultures and in generating host responses
- Writing core – provides writing development seminars and individual editing services

Index Terms

pathogens, host-pathogen interaction, hepatitis, hantavirus, virology, *streptococci*, pathogenic *E. coli*

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Nuclear Receptors in Liver Health and Disease
University of Kansas Medical Center, Kansas City - P20 RR021940

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Thematic Scientific Focus

Nuclear receptors and their role in liver health and disease

Research Projects

- Autophagy protects against ethanol-induced liver injury by removal of damaged mitochondria and protein aggregates
- Role of HNF4alpha in regulation of hepatocyte proliferation
- Functional interaction of ABCB6 with cytochrome P450s
- The role of human PXR in anti-tuberculosis drug-induced liver injury

Research Resources

- Molecular biology core – basic and advanced molecular biology and molecular genetics tools to enhance investigators' research, including: DNA sequencing, real time PCR, high throughput PCR for rapid genotyping; a vector, plasmid, and bacteria bank
- Null-mouse development and husbandry core – timely and free breeders of genetically modified mice on C57BL/6 background, nuclear receptors, genes involved in liver and/or gastrointestinal health
- Histology core – instrumentation and training necessary to process tissue samples for histopathological evaluation
- Analytical core – HPLC, LC-MS/MS, and UPLC-MS/MS; UV/visible, fluorescence, and luminescence spectrophotometry

Index Terms

nuclear receptors, ligands, transporters, drug interactions, hepatic diseases, lipid metabolism

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Kentucky

Center for the Biologic Basis of Oral/Systemic Diseases University of Kentucky, College of Dentistry – P20 RR020145

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Thematic Scientific Focus

The biological principles that underlie the apparent linkage among chronic oral infections, inflammation, and systemic disease sequelae, with an emphasis on translational studies of host-parasite interactions and on clinical implications for systemic disease

Research Projects

- Chronic oral inflammation and inflammatory bowel disease
- Chronic inflammation at oral and cervico-vaginal mucosa
- Gene therapy for orofacial pain
- Ontogeny of innate immune responses at mucosal surfaces
- Physiology of the stress response in patients with TMD and fibromyalgia

Research Resources

- Biostatistics and bioinformatics core – statistical consultation on study design and data analysis
- Transgenic mouse facility
- Microarray core – complete Affymetrix gene chip system

Index Terms

oral infections, inflammation, translational research, HIV, atherosclerosis, gestational diabetes, periodontal disease

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**Center of Excellence in Diabetes and Obesity Research
University of Louisville – P20 RR024489**

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Thematic Scientific Focus

Diabetes as a cardiovascular disease; degenerative changes associated with atherosclerosis—that clinically appear as acute myocardial infarction and stroke—resulting from “diabetic” changes, such as insulin resistance, even in patients not traditionally considered diabetic

Research Projects

- Redox mechanisms of hyperglycemic injury
- Stem cells and diabetic cardiomyopathy
- Bioenergetic regulation of cardiac progenitor cells
- Foam cell formation and diabetic atherogenesis
- Resolution of diabetic vascular inflammation: role of lipid mediators

Research Resources

- Imaging and flow cytometry core – high resolution confocal microscopic image acquisition and analysis and flow cytometric cell sorting and analysis of antigen expression on cell surface
- Cardiovascular pathology core – pathological analysis of blood and cardiovascular tissues using chemical histochemical analysis; ischemia and carotid injury surgeries to quantitate infarct and proliferation
- Animal core
- Cardiovascular imaging and function core – ultrasonic imaging, blood pressure monitoring, and hemodynamic studies

Index Terms

cardiovascular, inflammation, diabetes, obesity, atherosclerosis, heart disease, vascular disease

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**Center of Research in Obesity and Cardiovascular Disease
University of Kentucky – P20 RR021954**

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Thematic Scientific Focus

Identification of mechanisms linking obesity to the development of cardiovascular diseases

Research Projects

- Thrombospondin 1 mediates macrophage infiltration into adipose tissue and promotes obesity-induced atherosclerosis
- Obesity-induced platelet activation mediates a pro-thrombotic state
- Dietary fat promotes chylomicron-dependent intestinal absorption of gut antigens to mediate obesity-induced inflammation
- Maternal consumption of a western diet promotes obesity and hypertension in offspring
- Microsomal prostaglandin E synthase-1 deficiency attenuates the development of diet-induced obesity in male mice

Research Resources

- Analytical core – mass spectroscopy (ABI4000 Q-Trap Mass Spectrometer) analysis of lipids, multiple-analyte measurements of cytokines and adipokines (Luminex)
- Physiologic core for measurements in mice – measurement of blood pressure by radiotelemetry (DSI International, 16 platforms), quantification of atherosclerosis, euglycemic hyperinsulinemic clamps, analysis of body fat using NMR (EchoMRI-100) and DEXA-IR, measurement of food intake, water intake, indirect calorimetry and physical activity (TSE LabMaster)
- Pathology core – paraffin embedding, sectioning, staining and immunohistochemistry

Index Terms

obesity, diabetes, atherosclerosis, hypertension, thrombosis, inflammation, developmental programming

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Mechanisms of plasticity and repair after SCI
University of Louisville – P20 RR015576

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Thematic Scientific Focus

Molecular and cellular mechanisms of spinal cord injury and repair, with emphasis on developing and characterizing clinically relevant animal models

Research Projects

- Heat shock proteins in spinal cord neural survival
- GSK3B as a target for pro-neuronal survival in CNS neurons
- The plasminogen activator system in spinal cord repair
- Cell intrinsic mechanisms in spinal cord plasticity
- Role of estrogen and progesterone in SCI pain

Research Resources

- Cell culture and molecular biology core – neuronal stem cell culture; FACS analysis; production of viral vectors for gene transfer experiments
- Animal surgery core – gene transfer manipulations; stem cell transplantation; nerve grafting; neuroanatomy analysis
- Animal behavior and electrophysiology core – gait analysis; electropotential recordings *in vivo* and in tissue slices and single cells
- Microscopy core – immunohistochemistry; confocal and light microscopes; transmission and scanning electron microscopes

Index Terms

neurobiology, cell culture, molecular biology, surgery, behavior, electrophysiology, microscopy, apoptosis, immunology, signaling, central nervous system, spinal cord injury, stem cells

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COBRE in the Molecular Basis of Human Disease
University of Kentucky College of Medicine – P20 RR020171

Principal Investigator

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Thematic Scientific Focus

The molecular basis of human disease, with an emphasis on examining the role of altered gene expression and protein processing on promoting the diseased state

Research Projects

- Structural studies of neuropilin signaling
- The connection between Lafora disease and other polyglucosan body diseases
- Negative regulation of the yeast MRP, Ycf1p, and human MRPs by CKII
- Mechanisms of peripheral regulatory T cell generation
- Molecular mechanism of mammalian autophagy

Research Resources

- Protein analytical core
- Imaging core – epifluorescence microscopes
- Proteomics core – SELDI-TOF protein profiling system, Q-TOF mass spectrometer with both MALDI and LC/ESI source capabilities, MALDI TOF TOF mass spectrometer
- Organic synthesis core
- Viral production core

Index Terms

transcriptional regulation, cancer genes, signal transduction, diabetes, prostate cancer

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COBRE in Molecular Targets
University of Louisville – P20 RR018733

Principal Investigator

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University of Louisville

James Graham Brown Cancer Center

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http://www.browncancercenter.org/news/news_ind.aspx?id=325

Thematic Scientific Focus

Identification of novel molecular targets for cancer therapy using the techniques of modern structural biology

Research Projects

- The programmed cell death pathway arising from the endoplasmic reticulum
- Control of tumor growth by Ras-related proteins
- Roles of IKKa in skin development and dysplasia
- Structure-activity analysis of tissue-specific carcinogens
- Very small embryonic-like (VSEL) stem cells and brain regeneration in a murine model of sleep apnea

Research Resources

- Microsequence array facility – Affymetrix gene chip instrumentation
- Molecular modeling facility – state-of-the-art modeling projections from structural data obtained through X-ray crystallographic or NMR analysis
- Computational resources – Silicon Graphics array; time on the institution's IBM SP2 supercomputer
- NMR and protein purification facility – 650 MHz and 800 MHz NMR instruments; comprehensive protein expression laboratory that includes an analytical ultracentrifuge
- Biophysics facility – state-of-the-art capabilities in calorimetry, electronic spectroscopy, rapid kinetics and hydrodynamics determinations; provides training in biophysical methods and data analysis; is integrated with the molecular modeling and structural biology cores at the Brown Cancer Center to enhance drug discovery efforts

Index Terms

neoplastic transformation, cancer, molecular targets, signaling pathways, cytokines, growth factors, kinases

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COBRE in Women's Health
University of Kentucky – P20 RR015592

Principal Investigator

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Thematic Scientific Focus

Roles of female reproductive hormones in manifestations of health and disease in women and in animal model systems

Research Projects

- Estradiol and testosterone regulation of cardiac injury
- Hormone-mediated regulation of ovarian and uterine function
- Transcriptional regulation of hormone action
- Hormonal Interaction on the neuroendocrine axis
- Actions of estradiol and progesterone on behavior: clinical neuropharmacology

Research Resources

- Magnetic resonance imaging core
- Behavioral core
- Animal core
- DNA microarray core
- Bioinformatics and biostatistics core

Index Terms

women's health, estrogen, reproduction, cell biology, molecular biology, behavior, steroids, HIV, neurodegenerative diseases, cognition, aging, cancer, ovary, brain

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Molecular Determinants of Developmental Defects
University of Louisville Birth Defects Center – P20 RR017702

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<http://louisville.edu/birthdefectscenter/cobre.html>

Thematic Scientific Focus

Molecular and cellular mechanisms controlling normal embryonic development and etiology of birth defects

Research Projects

- Regulation of neural crest cell migration by SDF1 CXCR4 signaling
- TGF β signaling during mouse secondary palate elevation and fusion
- Pre- and postnatal tobacco smoke exposure: effects on neurocognitive development
- Intermittent hypoxia mediated oligodendrocyte defects in a murine model of gestational sleep apnea
- FGF signaling and zinc finger proteins in gonad development and reproduction
- Phagocytosis and the MERTK family of receptor tyrosine kinase
- Biomarkers of neurotoxicity associated with fetal tobacco smoke exposure

Research Resources

- DNA and microarray cores – DNA sequencing; mutation and SNP detection; gene expression profiling
- Laser capture microdissection
- Protein mass spectrometry core – protein purification and sequencing; MALDI-TOF and ESI mass spectrometers
- Animal care and transgenic mouse cores
- Biostatistics core

Index Terms

birth defects, developmental biology, embryogenesis, gene expression, signal transduction, craniofacial disorders, neural tube defects, neural crest cells, cardiovascular defects, neurocognitive development, fetal metabolism, oogenesis, stem cells, gestational sleep apnea

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Louisiana

Center for Experimental Infectious Disease Research Louisiana State University – P20 RR020159

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Thematic Scientific Focus

The immunological and pathogenetic basis of infectious diseases

Research Projects

- Enhancement of dengue virus transmission due to mosquito salivary proteins
- Regulation of innate immunity to human metapneumovirus infection
- *M. Tuberculosis* SigH and its regulon in the immunopathology of tuberculosis
- Importance of antigen-specific immunoglobulin responses in controlling SIV/HIV infection

Research Resources

- Molecular immunopathology core – DNA sequencing; library construction; protein production and purification; FACS analysis; confocal and laser capture microscopy; transmission and scanning electron microscopy; live imaging microscopy; real time PCR analysis; protein multiplex analysis; anatomical, clinical and molecular pathology; custom antibody production; statistical consultation and training

Index Terms

infectious diseases, non-human primate models, retrovirus, SIV, dengue virus, mosquito salivary proteins, innate immunity, human metapneumovirus

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Center for Molecular and Tumor Virology
Louisiana State University Health Sciences Center – P20 RR018724

Principal Investigator

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Thematic Scientific Focus

The molecular mechanisms by which viral gene products alter the cell and orchestrate events leading to disease

Research Projects

- Axonal degeneration can trigger demyelinating disease
- Immune correlates of BK virus persistence and reactivation
- Mechanism by which the EHV-1 IR2 protein inhibits viral gene expression and replication
- Defining the bone marrow as a reservoir for gammaherpesvirus latency
- Role of platelets in cytomegalovirus-induced inflammation

Research Resources

- Administrative core
- Molecular analyses core
- Bioinformatics core

Index Terms

virology, infectious agents, molecular pathogenesis, viral oncology

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Center of Excellence in Oral and Craniofacial Biology
Louisiana State University School of Dentistry – P20 RR020160

Principal Investigator

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Thematic Scientific Focus

Oral infectious diseases, including projects that focus on oral health anomalies, including oral opportunistic infections in the HIV patient, periodontal disease, and dental caries

Research Projects

- Role of vacuole expansion in the oral pathogen *Candida albicans*
- Mechanisms behind CX3CL1-driven monocyte recruitment during periodontitis
- Novel amelogenin-based biomimetic remineralization dental materials for early caries treatment

Research Resources

- Biomedical equipment core – equipment and expertise to carry out periodontal protocols
- Statistical core – support in the areas of study design, sample size estimation/statistical power analyses, statistical methodology and database management

Index Terms

oral health, oral infectious diseases, periodontal disease, HIV

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Mentoring a Cancer Genetics Program
Tulane University Health Sciences Center – P20 RR020152

Principal Investigator

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Thematic Scientific Focus:

To develop a center in cancer genetics and gene regulation with an emphasis on understanding how genetic instability contributes to the initiation and progression of cancer

Research Projects:

- The role of L1 elements in cancer origins and progression
- The role of TNFR1 in protection from colitis-associated carcinoma
- Uncovering the mechanisms of osteosarcoma metastasis suppression by MTBP
- Somatic variations of the human DNA polymerase genes polB, poln and polk and prostate cancer
- The role of cytokine receptor interleukin-17RC in initiation of prostate cancer
- Glyceollins as novel targeted therapeutics for the treatment of metastatic triple negative breast cancer

Research Resources:

- Cell assay core – a series of devices for gene function, expression and mutagenesis assays, including new instrumentation for high-throughput microscopy and the BD Pathway 855 which is designed to carry out fluorescent image analysis on cells in 96-well plates in real time

Index Terms:

cancer genetics, gene instability, gene regulation, tumors, leukemia, cell cycle, angiogenesis

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Mentoring in Cardiovascular Biology

Louisiana State University Health Sciences Center – P20 RR018766

Principal Investigator

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Thematic Scientific Focus

The molecular and physiological basis of cardiovascular function, with particular emphasis on vascular biology and cell signaling as related to vascular disease

Research Projects

- mTOR signaling in vascular smooth muscle cells and diabetic vascular disease
- Intracellular trafficking of alpha 2c-adrenergic receptors in Raynaud's phenomenon
- Rho/ROCK signaling, inflammation and endothelial permeability in vascular smooth muscle cells
- Protective role of GAPDH against OxLDL-induced atherogenic effects in cultured cells and in an animal model of atherosclerosis
- Role of brain Gi2 sub-unit proteins in neural regulation of cardiovascular function and salt-sensitive hypertension

Research Resources

- Cell and molecular analysis core – cell culture and molecular biology services; real time PCR analysis; 2-D gel electrophoresis, mass spectroscopy, *in vivo* (L-band) and *in vitro* (X-band) EPR spectroscopy; HPLC
- Imaging and histology core – tissue processing, staining and pathology analysis; a wide array of microscopic techniques for both fixed and live cell samples
- Cardiac and vascular function core – telemetry, *in vivo* ultrasound imaging, cardiac and pulmonary function services

Index Terms

cardiovascular disease, atherosclerosis, MAP kinase signaling, ischemic heart damage, oxidative stress, cell trafficking, G protein-coupled receptors, sympathetic nervous system

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Mentoring Neuroscience in Louisiana
Louisiana State University Health Sciences Center – P20 RR016816

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Thematic Scientific Focus

Cellular and molecular basis of neurological plasticity and survival in the contexts of stroke, neuronal trauma, and neurodegenerative diseases

Research Projects

- System A transporters in glutamatergic neurotransmission
- Mechanisms of acetylcholine plasticity in hypothalamus
- Secreted phospholipases A2 participate in neuron survival
- Cyclooxygenases in neuronal synaptic plasticity

Research Resources

- Molecular neurobiology core – data imaging and quantitation systems; custom DNA microarray production and analysis; transgenic mouse maintenance and genotyping
- Neurochemistry core – characterization of lipid messengers structure and metabolism by TLC, HPLC, GLC, LC-MS/MS
- Imaging core – two-photon laser scanning microscope, laser scanning confocal microscope, upright electrophysiology microscope with high-speed CCD camera

Index Terms

neuroscience, stroke, neurological trauma, neurodegenerative diseases, imaging, molecular biology, cell biology

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Mentoring Obesity & Diabetes Research in Louisiana
Pennington Biomedical Research Center – P20 RR021945

Principal Investigator:

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Thematic Scientific Focus:

Molecular and cellular mechanisms controlling adipocyte differentiation and expansion during the development of obesity and diabetes

Research Projects:

- Role of galanin-expressing leptin receptor neurons in leptin action
- The role of protein malnutrition on circadian physiology of C57BL/6J mouse dams and their offspring
- Characterization of ubiquitin and ubiquitin-like modification of PPAR- γ in adipocytes
- Mechanisms of aging-induced leptin resistance and obesity

Research Resources:

- Cell biology and bioimaging core – provides access to state of the art imaging, analytical, and histological equipment as well as technical expertise and assistance to researchers at the PBRC, LSU's main campus, and outside the LSU university system
- Genomics core – seeks to achieve high quality research data production through education of core facility users, optimal use of qPCR and RNA/DNA quality and quantity instrumentation, and quality Sanger sequencing, next-generation sequencing, robotics, and microarray services; services are provided to internal and external researchers

Index Terms:

insulin resistance, diabetes, obesity, metabolic syndrome, adipose tissue, adipogenesis

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Mentoring Translational Researchers in Louisiana
Louisiana State University Health Sciences Center – P20 RR021970

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Thematic Scientific Focus

To understand the immunobiology of disease; specifically, investigations focus on elucidating and subsequently controlling the mechanisms that lead to chronic inflammation and tissue damage during disease

Research Projects

- Prosaposin, a promoter of prostate carcinogenesis and a novel therapeutic target
- L-arginine availability regulates proliferation of malignant T cells
- Genetic profiles of gastric lesions in patients with gastritis and mice infected with *Helicobacter pylori*
- Identification of protective and pathogenic human B cell epitopes in dengue virus
- HSV-2 subversion of the innate immune response by targeting cell-intrinsic pathways

Research Resources

- Immunology and cell analysis core – flow cytometry, cell sorting and cell separation services
- Microarray and sequencing core – low cost sequencing and GeneChip preparation and analysis services
- Biostatistics core – data analysis and project and publication statistical design
- Faculty development core – provides ongoing faculty development curriculum on research, administration, communication, education, and leadership, and cultural competence
- Genomics / Illumina core - provides support in sequencing reagents for experimental use, and planning and conducting larger scale experiments with patient samples including SNP analysis, methylation analysis, and high through-put sequencing
- Grants and development core – identifies and prepares funding applications and streamlines the grant submission process, establishes a repository for peripheral and regulatory documents, and assists the PIs with building relationships with funding agency representatives

Index Terms

inflammation, host defense, immune response, T cells

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Tulane COBRE in Hypertension and Renal Biology
Tulane University School of Medicine – P20 RR017659

Principal Investigator

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Thematic Scientific Focus

Factors contributing to development of hypertension and subsequent consequences on renal and cardiovascular function

Research Projects

- Citrate transport in the proximal tubule
- Endothelial dysfunction, adipocytokines, inflammation, and chronic kidney disease
- Macronutrient composition of diet and risk factors for cardiovascular disease
- Mechanism of resistance artery structural remodeling in hypertension
- Transcriptional control of ureteric bud growth and branching
- Distal nephron renin and prorenin receptor in angiotensin II-dependant hypertension

Research Resources

- Molecular, imaging and analytical core – provides major support to COBRE and other Tulane investigators and includes: RIA, ELISA, gel documentation system, real-time PCR system, Licor's Odyssey system, Stratagene, Qiagen BioRobot system, Dako Cytomation's AutostainerPlus, Fluostar Optima Microplate Radar, PTI Ratiomaster, Next Advance Inc.'s Bullet Blender BLUE, Nexcelom Cellometer Automated Cell Counter, EVOS fl Fluorescence Microscope, Fisher Scientific's accuSpin Micro17R Microcentrifuge, and Thermo Scientific's NanoDrop 2000
- Transgenic and gene-targeted animal core – breeding colonies of rat and mouse transgenic strains used by investigators in the Hypertension and Renal Center

Index Terms

hypertension, blood pressure, renal, angiotensin, cardiovascular disease, kidney disease

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Maine

COBRE in Stem Cell Biology and Regenerative Medicine Maine Medical Center Research Institute – P20 RR018789

Principal Investigator

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Thematic Scientific Focus

Discovery of novel regulators of stem and progenitor cell survival, proliferation and development with clinical relevance to tissue repair (including cell-cell, cytokine receptor, transcription factor and (epi)genetic signals)

Research Projects

- Slug as a key regulator of hematopoietic stem cell survival
- Mechanisms of *de novo* human blood vessel formation
- Roles of Podocalyxin during the onset and progression of acute myeloid leukemia
- Molecular mechanisms of adipogenic conversion of skeletal muscle stem cells: crosstalk between Myostatin and Wnt signaling
- Lymphoma suppression: DNA break repair in stem cells and their microenvironment
- Map3k7: An intersection between inflammatory and regenerative signaling in kidney injury

Research Resources

- Progenitor cell analysis core – flow cytometry (and Vi-Cell) analyses; fluorimetric and luminometric analyses; fluorescent microscopy
- Histopathology core – tissue fixation, processing, embedding, sectioning, staining and coverslipping of paraffin or frozen tissue sections; (from H&E's to specific tissue stains for collagen, amyloid, bone, cartilage, vessels, kidney basement membranes, and hematopoietic cells); immunohistochemical staining for general antibody sets
- Bioinformatics and genomics core – robotic DNA and RNA isolation, quantitative (RT) PCR, and project-specific *in-silico* array analyses
- FACS and ES Cell Core – FACS and preparative AUTOMACS isolation of primary cell populations; basic murine and human ES cell services

Index Terms

stem cell biology, cytokine signal transduction, hematopoiesis, leukemogenesis, kidney development/regeneration, genomic instability, R-spondin/Wnt

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COBRE in Vascular Biology
Maine Medical Center Research Institute – P20 RR015555

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Thematic Scientific Focus

Cell and molecular mechanisms regulating development and homeostasis of the vascular system including vascular remodeling, angiogenesis, and disease mechanisms

Research Projects

- Mechanisms of dyslipidemia in cardiac muscle prior to onset of atherosclerosis
- Control of vascular fibrosis and collagen deposition by novel regulator, CTHRC-1
- The contribution of smooth muscle cells to the pathology of gastrointestinal stromal tumors
- Smad-independent TGF-beta signaling mechanisms in angiogenesis
- Mechanism of non-classical release of the angiogenesis regulator, IL1-alpha
- Role of insulin-like growth factor binding proteins (IGFBPs) in angiogenesis

Research Resources

- Structural biology core – capillary-based automated DNA sequencing; peptide and protein sequencing; protein mass spectrometry with MALDI-TOF and quadrupole tandem mass spectrometers; confocal microscope
- Molecular genetics core – transgenic mouse and gene knock-out mouse production; small animal MRI; Micro CT, and fluorescence-based small animal imaging platforms; a VIVO 770 small animal ultrasound instrument for monitoring blood flow and heart function in mice
- Viral vector core – large scale preparation of adenovirus, lentivirus and retrovirus for *in vitro* and small animal studies

Index Terms

structural biology, molecular biology, molecular genetics, angiogenesis, signaling, vascular biology, cancer, inflammation, endothelial cell, vascular smooth muscle cell, atherosclerosis, restenosis, FGF, Notch, TGF-beta, IGF, IGFBPs tumor growth, integrins, cryptic epitopes

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Mississippi

Center for Psychiatric Neuroscience University of Mississippi Medical Center – P20 RR017701

Principal Investigator

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Thematic Scientific Focus

Interdisciplinary neuroscience research to elucidate the interactions of neurons and glia and their relationship to behavior, pharmacological mechanisms of potential psychotherapeutic drugs, and the genetic bases and pathophysiological processes of depression

Research Projects

- Vascular and cellular pathology in depression
- Cortical glutamate synapse in depression
- Molecular and cellular integrity of the serotonin system in depression
- Serotonin-related transcription factors in animal stress models related to depression

Research Resources

- Human brain collection core – post-mortem brain specimens from psychiatrically characterized subjects and matched normal control subjects
- Animal core – animal brain collection focused on behavioral studies related to depression and its treatment and rodent behavioral core to assess the effects of chronic stress paradigms modeling human depressive behaviors
- Imaging core – sophisticated imaging systems with the ability to estimate, in three- dimensional space, numbers of cells, terminals, or synapses and to analyze the density of receptor binding and the level of specific proteins
- Molecular biology core – biotechnologically advanced amplification, visualization, detection and analysis systems to study the expression, structure, function, and localization of a variety of neural substrates

Index Terms

psychiatric neuroscience, depression, alcohol psychoactive substance use disorders, schizophrenia, antidepressant medications, chronic stress, neurotrophic factors, angiogenic factors, serotonin, glutamate, transcription factors, genomics

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Center of Research Excellence in Natural Products Neuroscience
University of Mississippi – P20 RR021929

Principal Investigator

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Thematic Scientific Focus

Identification and characterization of psychoactive properties of natural products

Research Projects

- Natural product-derived HIF-1 inhibitors for neuroblastoma
- Mechanism of antidepressant action of cannabinoids
- Rational design of novel natural product-derived cannabinoid ligands
- Vehicles to enhance nose to brain bioavailability of drugs

Research Resources

- Chemistry core – isolation, structure elucidation, analysis
- Pharmacology core – *in vitro* functional assays, *in vivo* and behavioral evaluations
- Community outreach series

Index Terms

natural products, dietary supplements, drug discovery, drug development, drug delivery, drug abuse, cancer, opioid, cannabinoid

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Montana

Center for the Analysis of Cellular Mechanisms and Systems Biology Montana State University – P20 RR024237

Principal Investigator

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Thematic Scientific Focus

Provide advanced infrastructure for development of improved understanding of cellular mechanisms and an integrative approach to systems biology, with focus on host-pathogen interactions; develop improved methods to determine changes in protein post-translational modifications and changes in enzyme activities that control cellular mechanisms

Research Projects

- Systems biology of host-pathogen interactions
- Proteomic approach to assess the role of PLAGL2 in the host inflammatory response
- Proteomic profiling of *Candida albicans* responses to nitrosative and oxidative stress
- Global analysis of the host cell response to *Toxoplasma gondii* infection in astrocytes

Research Resources

- Mass spectrometry, metabolomics, and proteomics core facility – electron transfer dissociation and microfluidic chipLC interfaces; two high resolution Qtof mass spectrometers; two ion trap mass spectrometers, MALDI Tof and MALDI Tof/tof mass spectrometers, and ultra high pressure liquid chromatography system; three color laser-excited fluorescent gel scanner; hyperspectral fluorescent gel imager; targeted protein electro-elution and microfluidic digestion system; solution NMR spectrometer with SampleJet automatic sampler with metabolomics software
- DNA microarray facility
- Proteomics reagent synthesis core

Index Terms

systems biology, signaling networks, biological mechanisms, proteomics, protein post-translational modifications, proteomic detection reagents, fluorescence multiplexing, differential analysis of enzyme activity, metabolomics, quantitative metabolic flux analysis, hyperspectral imaging, protein electro-elution, microfluidic digestion, inflammation, nitrosative stress, oxidative stress, *Toxoplasma gondii*, *Candida albicans*, astrocytes, macrophages, neutrophils, innate immunity, reactive oxygen species, ROS

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Center for Environmental Health Sciences
University of Montana, Missoula – P20 RR017670

Principal Investigator

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Thematic Scientific Focus

Effects of environmental agents in causing or exacerbating human diseases; focus areas include: chronic inflammation, respiratory and immunotoxicology, neurotoxicology, molecular and genetic toxicology, epidemiology and exposure assessment

Research Projects

- Mechanisms of woodsmoke-induced immune suppression
- Role of innate immunity in ozone-induced asthma exacerbations
- The role of pulmonary subpopulations and Th2 immunity in Balb/c silicosis model
- Gestational exposures, epigenetics and respiratory health
- Consequences of aryl hydrocarbon receptor activation in Crohn's disease

Research Resources

- Molecular biology core – microarray, proteomics, QPCR, epigenetic analyses, viral vector generation
- Inhalation and pulmonary physiology core – whole body animal exposures (e.g., ozone, woodsmoke, particulate matter, methamphetamine), various instillation methods for animal exposures, small animal surgery, whole body and direct measurements of lung resistance and dynamic compliance
- Molecular histology and fluorescence imaging core – fixed and live cell imaging (Olympus FV1000 scanning confocal); pathology and fluorescence imaging; automated histology services
- Flow cytometry core – flow cytometry (FACSAria), cell sorting, automated fixed cell and tissue analyses (iCys), AutoMacs cell sorting, multiplex analytical resources

Index Terms

environmental health, toxicology, immunology, neurotoxicology, exposure assessment, epidemiology, epigenetics, chronic inflammation, aging, woodsmoke, particulates, nanomaterials, respiratory diseases

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Center for Immunotherapies to Zoonotic Diseases
Montana State University – P20 RR020185

Principal Investigator

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Thematic Scientific Focus

The pathogenesis of zoonotic and emerging infectious diseases and the development of novel therapeutic treatments for these diseases

Research Projects

- Role of the SaeR/S regulatory system in invasive staphylococcal disease
- Mechanisms of *Aspergillus fumigatus* hypoxia adaptation and virulence
- Bone marrow failure and immune responses to pulmonary fungal infections

Research Resources

- Cellular analysis core – technical expertise and state-of-the-art instrumentation for the analysis of biological samples using flow cytometry, confocal fluorescence microscopy, and immunohistochemistry
- Animal models core – technical support to investigators utilizing animal models of infectious disease pathogenesis, resources and expertise to assist investigators in developing new animal models, and access to BSL-3 and ABSL-2 animal research facilities
- Bioinformatics core – technical expertise, equipment, and software for bioinformatic research and support to investigators implementing bioinformatics tools in their research

Index Terms

zoonotic diseases, infectious agents, emerging infectious diseases, *Toxoplasma gondii*, *Streptococcus pyogenes*, Dengue virus, *Coxiella burnetii*, *Aspergillus fumigatus*, pulmonary aspergillosis, prions, *Staphylococcus aureus*, bacterial pathogenesis, fungal pathogenesis, innate immunity, genomics, vaccine development, complementary and alternative medicine

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Center for Structural and Functional Neuroscience
University of Montana – P20 RR015583

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Thematic Scientific Focus

Protein structure and function in the central nervous system, focusing on transport, membrane protein dynamics, mechanisms of neurodegeneration, and synaptic transmission

Research Projects

- Cholinergic modulation of hippocampal interneuron subtypes

Research Resources

- Core laboratory for neuromolecular production
- Biospectroscopy core
- Molecular histology and fluorescence imaging core
- Molecular computational core
- Molecular biology and viral vector core

Index Terms

anxiety, central nervous system, depression, hearing, molecular modeling, neurological diseases, neurophysiology, neuroscience, prion diseases, protein function, protein structure, proteomics, spectroscopy, neurochemistry

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Nebraska

Center for the Molecular Biology of Neurosensory Systems University of Nebraska Medical Center – P20 RR018788

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Thematic Scientific Focus

The molecular mechanisms that underlie neurosensory disorders, and the optimal means of intervention

Research Projects

- Functional characterization of Nr2e3 in the developing and adult photoreceptor cells
- The role of the E2F2 modulation of Rb1 in cochlear hair cells and supporting cells to mediate hair cell regeneration
- Mechanisms of retinal degeneration in Usher syndrome type IIa
- Molecular analysis of the Lmx1a (DreherJ) mutant inner ear
- Characterization of a microRNA misexpression model of age related deafness
- Neuroprotective strategies for degenerative balance disorders

Research Resources

- Mouse genome engineering core – expertise in the construction of transgenic and knockout mice, including conditional knockout and knockdown
- Molecular phenotyping/histology core – specialized morphological and histological analysis of neurosensory development; immunohistochemistry, molecular phenotyping services
- DNA microarray core – services to determine global gene expression patterns, transcriptional profiling and DNA-protein interactions

Index Terms

neurosensory disorders, inner ear development, retinal development, tissue differentiation, balance control, otoconia, induced pluripotent stem cells, central nervous system, peripheral nervous system, epidermal growth factor receptor, nerve repair

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Nebraska Center for Cellular Signaling
University of Nebraska Medical Center – P20 RR018759

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http://www.unmc.edu/dentistry/nebraska_center_cellular_signaling.htm

Thematic Scientific Focus

Elucidation of cellular signaling transduction mechanisms with particular emphasis on cell motility, growth regulation, apoptosis, metastasis, invasion, and cell adhesion receptors, including receptor tyrosine kinases

Research Projects

- The mechanism of aberrant DNA methylation in mouse lymphomagenesis
- Regulation of Aurora-A kinase signaling modules by mitotic scaffold protein AurAIPs
- Endocytic regulation of raft-associated GRI-anchored protein trafficking
- KIBRA, Aurora-A and the Hippo signaling

Research Resources

- Microscopy core – electron and confocal laser scanning
- Histology core
- Molecular biology core
- Monoclonal antibody core
- Tissue culture core
- Flow cytometry core – Becton Dickinson FACStarPlus flow cytometer operating under Lysis II; Ortho Cytofluorograph System 50H flow cytometer operating under Cytomation software; Meridian ACAS 570 Confocal Laser Scanning Cytometer
- Microarray core
- Biostatistics core
- Human tissue bank
- Protein structure core facilities
- Animal facility
- Transgenic mouse facility
- Live cell imaging core

Index Terms

signal transduction, DNA repair, cell survival, mitosis, cancer

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Nebraska Center for Nanomedicine
University of Nebraska Medical Center – P20RR021937

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Thematic Scientific Focus

Development of nanomaterial-based therapeutic modalities to improve outcomes for cancer, neurodegenerative, and cardiovascular diseases, by delivering drugs to focal areas of central nervous system disease or directly to tumors; seeking nanotechnologies to improve diagnostic measures and disease monitoring to maximize clinical benefits and limit untoward side effects

Research Projects

- Nanoformulations of redox enzymes for treatment of ischemic stroke
- A nanozyme antioxidant therapy for the treatment of angiotension II-dependant hypertension
- Anti-viral peptide nanocomplexes (APN) for treatment of HIV/HCV co-infection
- Targeted nanocarrier for siRNA delivery to tumor vasculature

Research Resources

- Bioimaging core – Kodak multi-spectrum FX *in vivo* imaging system, Bruker Avance magnetic resonance imaging (MRI) and spectroscopy (MRS) system (7T/21 cm, Bruker, Karlsruhe, Germany), and a Bruker Pharmascan (7T/16 cm) MRI/MRS system equipped with resonance research
- Nanomaterials core
- Microscopy core
- Histology core
- Molecular biology core
- Monoclonal antibody core
- Tissue culture core
- Flow cytometry core
- Biostatistics core
- Protein structure core facilities
- Animal facility
- Transgenic mouse facility
- Live cell imaging core

Index Terms

drug delivery, nanomedicine, drug targeting, pharmaceutical sciences, nanotechnology, polymer therapeutics

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Nebraska Center for Virology
University of Nebraska - Lincoln – P20 RR015635

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Thematic Scientific Focus

Fundamental mechanisms and regulation of the replicative cycle of human, animal, and plant viruses, and host responses involved in disease pathogenesis

Research Projects

- Longitudinal analysis of HIV-1 clade C fitness
- Novel rodent model for human immunodeficiency viral infection
- Characterization of HIV-1 preintegration complex assembly and nuclear transport

Research Resources

- DNA microarray core – human and mouse oligonucleotide arrays; robotic arrayer; confocal laser microarray scanner
- Microscopy core – upright and inverted confocal microscopes; laser capture microdissection system; transmission and scanning electron microscopes
- Proteomics and genomics core – LC/MS, ESI and MALDI mass spectrometers for protein identification and quantification
- Flow cytometry core – BSL-3 containment level fluorescence-activated cell sorter for analyzing virus-infected cells

Index Terms

virus, pathogens, bioinformatics, microscopy, structural biology, HIV, neurodegenerative diseases, apoptosis, herpes, inflammatory disease, signaling, immunology, neuropharmacology, electrophysiology, stress, trauma, antiviral, prion diseases

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Redox Biology Center
University of Nebraska, Lincoln – P20 RR017675

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Thematic Scientific Focus

Biological oxidation-reduction reactions that regulate normal cellular functions, including those that may influence the pathophysiology of human diseases linked to oxidative stress

Research Projects

- Structure/function relationships of eukaryotic DJ-1-like proteins
- Role of mitochondrial-produced reactive oxygen species in neurogenic hypertension
- Mechanistic insights into cadmium detoxification
- Role of reactive oxygen species in the genetic resistance to autoimmunity
- Redox coordinated extracellular matrix remodeling in cancer
- Thiol-dependent redox processes and thiol-based signaling
- Structure/function relationships in enzymes involved in glutathione synthesis and recovery
- Oxidative stress responses in pathogenic *pseudomonas* species
- Redox homeostasis in tuberculosis latency
- Reactive carbonyl species and cerebral microvascular diseases
- NMR metabolomics core for redox biology
- Redox regulation of neuronal cell death
- Roles of OST3/6 thiol oxidoreductases in N-linked protein glycosylation and ER redox homeostasis

Research Resources

- Metabolomics and macromolecular analysis core – tandem mass spectrometers equipped with ESI (microspray and nanospray) and APCI sources; HPLC systems for LC-MS or LC-MS/MS analysis of complex analytes mixtures; MS-based methods are available for identification and mapping of post-translational modification of proteins; facilities for analyzing low molecular weight metabolites, proteins and protein modifications and +/- protein-protein interactions
- Microscopy core – upright and inverted confocal microscopes; laser capture microdissection system; transmission and scanning electron microscopes

Index Terms

redox biology, biochemistry, oxidative stress, metalloenzymes, redox signaling, aging

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Nevada

Chloride Channel Function and Role in Cardiovascular Disease University Of Nevada, Reno – P20 RR015581

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Thematic Scientific Focus

Role of chloride channels in normal cardiac function and disease

Research Projects

- Molecular physiology and regulation of volume sensitive chloride channels
- Signal transduction pathways regulated by cell volume
- Characterization and genomic studies of cardiovascular chloride
- Chloride channel function in animal models of cardiac disease

Research Resources

- Targeted and transgenic mouse core – animal breeding and maintenance facility; ES cell culture and gene targeting services (null, tissue-specific, and inducible knock-out gene constructs); microinjection expertise and equipment for blastocyst and pronuclear injections; strain cryopreservation and rederivation via IVF and embryo transfer; mouse genotyping
- Imaging core – immuno- and enzyme histochemical staining techniques for protein localization in tissues and cells, including subcellular co-localization and reorganization; upright histology microscope, transmission electron microscope, inverted fluorescent microscope, confocal microscope, digital camera imaging system, cryostat
- Molecular and genomics core – expression vector constructs; promoter mapping; custom BAC and YAC analyses

Index Terms

transgenic animals, molecular biology, genomics, imaging, cardiovascular disease, electrophysiology, genetics, cystic fibrosis, myotonia, kidney disease, cardiac arrhythmia, congestive heart failure

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Smooth Muscle Plasticity: A COBRE
University of Nevada School of Medicine – P20RR018751

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Thematic Scientific Focus

The causes and consequences of the ability of smooth muscles to change phenotype to conform to changing stimuli or microenvironments

Research Projects

- Correlation between structural and motor defects in diabetic gastroparesis
- Phosolamban and CaM kinase II in stomach smooth muscle plasticity
- An *in vitro* model system for determining regulatory mechanisms for smooth muscle mechanics
- Smooth muscle hypertrophy regulated by microRNAs and their target genes
- Stretch dependent potassium channel regulation in overactive bladder

Research Resources

- Molecular expression and transgenic core – critical technique support to projects that require the use of challenging molecular and cellular biology techniques and transgenic mice; includes breeding and genotyping of transgenic mice, Generation of new TG mouse lines, Small RNA cloning and sequencing, real time quantitative RT-PCR, and cytometry
- Protein expression and cell morphology core – expertise in protein expression (Western analysis) and cell morphological techniques (histochemistry, immunohistochemistry, confocal and electron microscopy with immunocytochemistry)
- Dynamic imaging facility – dynamic imaging and analysis services to the COBRE program; equipment and expertise to carry out Ca²⁺/video imaging experiments and assist in the analysis of any type of imaging data; two dedicated Ca²⁺ imaging rooms, each with a complete setup for acquiring Ca²⁺ movies combined with either electrophysiology and/or tension recordings

Index Terms

smooth muscle biology, smooth muscle plasticity, integrins, calmodulin, smooth muscle proteomics, stretch-activated potassium channels, bowel obstructions

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New Hampshire

Cellular and Molecular Mechanisms of Lung Disease **Dartmouth Medical School – P20 RR018787**

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Thematic Scientific Focus

The molecular and cellular mechanisms that underlie the initiation, pathogenesis, progression and treatment of lung disease

Research Projects

- Aurora A kinase and lung cancer
- Phospholipase C (PlcH) in *P. aeruginosa* virulence
- Humanizing alginate depolymerase: new strategies for de-immunizing enzyme therapies
- Biodiesel and petroleum diesel: exposure profiles and public health consequences

Research Resources

- Proteomics and Bioinformatics core – a complete array of protein analysis and bioinformatics services

Index Terms

lung cancer, Aurora A kinase, cystic fibrosis, *Pseudomonas aeruginosa*, cystic fibrosis transmembrane conductance regulator, biofilm, biodiesel, protein engineering

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**Center for Molecular, Cellular, and Translational Immunological Research
Dartmouth Medical School – P20 RR016437**

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Thematic Scientific Focus

Modulation of immunity in various disease states, via non-specific and antigen-specific immune response pathways, to find new ways to influence immune responses to combat tumors and bacterial and viral infections, or to suppress inflammation and autoimmunity

Research Projects

- The impact of IRF-3-dependent mechanisms on the replication and virulence of HSV
- NKG2D Expression on CD8+ T cells within the transplanted cells predicts clinical outcomes
- Mechanisms of immune protection from TB: The DARDAR Trial
- Peripheral blood mononuclear cell (PBMC) gene expression in metastatic renal cell carcinoma

Research Resources

- Immunology monitoring lab core – custom production of biologic and immunogenic reagents; cytokine and chemokine analysis
- Transgenic mice core – general animal husbandry; custom production of transgenic DNA constructs and mice; mouse breeding and genotyping; strain preservation and rederivation
- Informatics support core – support to COBRE members for the use of existing proteomics and genomics facilities at Dartmouth
- DartMouse support core – genome-wide SNP-chip analyses to support mouse speed congenic breeding, genetic background assessment, and QTL linkage analysis

Index Terms

cancer, inflammation, immunology, infection

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New Mexico

Center for Evolutionary and Theoretical Immunology University of New Mexico – P20 RR018754

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Thematic Scientific Focus:

Dedicated to studying the origins, evolution and diversification of immune systems and to understand from a theoretical point of view the principles that underlie defense systems

Research Projects:

- Schistosomiasis in snails: understanding the immunological basis of long-term production of human-infective cercariae
- Modeling of host immune responses and antiviral therapy against hepatitis C virus infection: *in vivo* and *in vitro*
- *Schistosoma mansoni* defense genes: identification and exploitation in the development of new therapeutics
- Predicting viral dynamics, immune response and epidemic spread of multi-host pathogens

Research Resources:

- Molecular biology facility – two ABI 3100 DNA sequencers, ABI 377 DNA sequencer, Agilent bioanalyzer 2100, NanoDrop ND-1000 spectrophotometer, Kodak Gel Logic 200 and Image Station 440 digital imaging systems, ABI 7000 Q-PCR, MJ Research Tetrad thermocycler, Zeiss Discovery and Axioscop microscopes
- Controlled environment facility – two Conviron E8 reach-in environmental chambers and one Conviron C1006 controlled environment room; a fully equipped tissue culture room

Index Terms:

evolutionary immunobiology, theoretical immunology, innate immunity, immunology, RNAi, comparative immunology, evolution, host-pathogen interaction

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Center on Neural Mechanisms of Schizophrenia
University of New Mexico – P20 RR021938

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Thematic Scientific Focus

Integrative, multimodal neuroimaging research focused on the study of neural mechanisms that underlie impaired cognition in schizophrenia

Research Projects

- Multimodal imaging of the sensory gating deficit in schizophrenia
- Auditory and visual integration in schizophrenia using MEG, EEG and fMRI
- Fronto-temporal coherence: a test of the disconnection hypothesis in schizophrenia
- Fronto-subcortical disconnection underlying neurocognitive dysfunction in schizophrenia

Research Resources

- Siemens Sonata Maestro 1.5 Tesla MRI system – standard transmit and receive RF coils, as well as receive-only surface coils; capable of BOLD EPI, diffusion tensor imaging, perfusion and diffusion imaging, and spectroscopy
- Siemens TIM Trio 3T system – including 32 RF channels x 102 coil elements, multinuclear support, and clinical features (extremity coil, shoulder array coil, spectrus injector)
- Elekta Neuromag 306-channel MEG system – planar gradiometers and magnetometers, 128 channel EEG system fully integrated with the MEG data acquisition and housed in a three-layer (two mumetal, one aluminum) magnetically-shielded room (Vacuumschmelze)
- BioSemi ActiveTwo 128 channel high-density EEG system – double-walled sound and RF attenuated audiometric booth, infrared visual patient monitoring, mock MRI with EEG recording capability
- Extensive computer support for image processing and spectroscopic analysis

Index Terms

magnetoencephalography, magnetic resonance, schizophrenia, neural integration, diffusion tensor imaging, magnetic resonance spectroscopy, functional magnetic resonance imaging, cognitive dysfunction

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Integrative Program in CNS Pathophysiology Research
University Of New Mexico – P20 RR015636

Principal Investigator

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Thematic Scientific Focus

Integrative, multimodal neuroimaging research focused on the pathophysiology of ischemic stroke, hemorrhagic stroke, traumatic brain injury, and epilepsy

Research Projects

- Astrocyte activation and neuronal hyper-excitability
- Nuclear matrix metalloproteinases (MMPs) activation in neurons at early reperfusion time and mechanisms of neuron death after stroke
- HIF-1 α in vasculotrophic support of neural stem cells following cerebral ischemia
- Normobaric hyperoxia (NBO) treatment extends the time window of tPA thrombolysis for ischemic stroke

Research Resources

- Magnetic resonance imaging core – Bruker 4.7T actively shielded scanner with 40 cm bore for non-invasive large and small animal studies
- Electron paramagnetic resonance core – Bruker EPR spectrometer and *in vivo* imager for analytical studies and *in vivo* non-invasive imaging of tissue oxygenation and oxidative stress
- Optical imaging core – two-photon scanning laser microscope, photodiode array, DIC infrared microscopy; *in vivo* and *in vitro* imaging of membrane potentials and intracellular calcium
- Cellular and molecular biology core – RT-PCR; microplate reader; fluorescence microscopes; immunohistochemistry for degeneration, regeneration, and inflammation studies

Index Terms

magnetoencephalography, magnetic resonance, electron paramagnetic resonance, optical imaging, cell biology, molecular biology, central nervous system injury, pathophysiology, inflammation, ischemia, intracerebral hemorrhage, electrophysiology, stroke, epilepsy

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North Dakota

Center for Visual Neuroscience
North Dakota State University – P20 RR020151

Principal Investigator

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Thematic Scientific Focus

Analyzing visual performance in normal and dysfunctional states, to develop clinically useful diagnostic tests for assessing visual performance, to understand the neural mechanisms that control eye movements under natural environmental conditions, to understand how the brain processes visual information, how neural activity is related to visual perception, and how visual processing interacts with other brain systems which underlie cognition and action

Research Projects

- Attention and the representation of visual environments
- Inhibition and age-related changes in visual search
- Visual orienting effects of directional cues

Research Resources

- High-density electroencephalography core – EEG data acquisition and analysis systems housed in electromagnetically shielded recording chambers, gigabit intranet connectivity with a terabyte data storage array and two high-performance EEG analysis workstations
- Driving simulation core – research driving simulator (360-degree wrap-around display, fully instrumented research driving simulator with real-time motion simulation via integrated force-platform)
- High dynamic range imaging core – high dynamic range display monitor and calibrated high-resolution camera systems
- Immersive virtual reality core – head-mounted stereoscopic display with 360-degree (diagonal) field of view, hemispherical projection system
- Eyetracking core – eyetrackers, remote video eyetrackers, eyetracker integrated with the driving simulator
- Electro-optical instrumentation core – luminance meter (LS-110), SpectraColorimeter, liquid crystal tunable spectral filter, sound level meter

Index Terms

visual processing, eye control, visual neural activity, cognition

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Center for Protease Research
North Dakota State University – P20 RR015566

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Thematic Scientific Focus

Understanding the biological role played by proteases, such as matrix metalloproteinases and histone deacetylases, in cancer and other diseases such as asthma and lupus

Research Projects

- Epigenetic regulation of vasoactive intestinal peptide receptor-1 (VPACR-1) by Ikaros
- Design, synthesis, and evaluation of isozyme-specific histone deacetylase inhibitors
- Understanding the role of MMP-9 in regulation of apoptosis in prostate cancer cells
- Vasoactive intestinal peptide regulation of MMP-2 in allergic asthma
- Investigating the structural and biochemical bases of the mechanisms of autophagy and innate immunity proteins in the defense against pathogens

Research Resources

- Mass spectrometry center – Bio-TOF III high resolution mass spectrometer and Esquire 3000 MS/MS system
- Microscopy facility – confocal microscope
- Core biology facility – cell and tissue culture, bioassay
- Core synthesis facility
- NMR facility
- Molecular modeling and bioinformatics studio
- Materials characterization laboratory

Index Terms

drug design, cancer, asthma, lupus, drug delivery, arthritis, epigenetics, histone deacetylase, matrix metalloproteinase

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COBRE in Pathophysiological Signaling in Neurodegenerative Disorders
University of North Dakota School of Medicine & Health Sciences – P20 RR017699

Principal Investigator

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Thematic Scientific Focus

Enhancing and expanding the ability to elucidate causes of, and identify potential treatments for, neurological disorders such as Alzheimer's and Parkinson's diseases, traumatic brain injury and epilepsy, using molecular/genetic, pharmacological, electrophysiological, biochemical and systems biology approaches

Research Projects

- Tachykinin modulation of epilepsy
- TRPC1, calcium and Parkinson's disease
- Cholesterol, caffeine and Alzheimer's disease-like pathology in rabbit brain
- Lipid-mediated signaling and neuroinflammation
- CNTF promotes neuronal survival and axonal sprouting

Research Resources

- Mass spectrometry core – high-resolution electrospray-quadrupole/time-of-flight MS, electrospray-triple quadrupole MS, and gas chromatography-ion trap MS
- Imaging core – transmission and scanning electron microscopes, laser scanning confocal microscope, ConfoCor2 fluorescence correlation spectroscopy unit

Index Terms

neurodegeneration, Alzheimer's disease, Parkinson's disease, traumatic brain injury, epilepsy, necrosis, apoptosis, axonal degeneration and regeneration, growth factors, phospholipid metabolism

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Oklahoma

Biofilm Formation and Metabolism on Dental Surfaces

University of Oklahoma Health Sciences Center – P20 RR018741

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Thematic Scientific Focus

Microbial biofilm formation and metabolism on natural and artificial dental surfaces

Research Projects

- Microbial mediators of tissue cell behavior
- Analysis of biofilms on natural and synthetic dental surfaces
- Genetic and biochemical studies of *Streptococcus mutans* biofilm formation
- *Streptococcus mutans* sugar transport and biofilm formation

Research Resources

- Microscopy core facility – Leica TCS NT confocal microscope
- Microarray facility – GeneTAC microarray analyzer, ABI real-time PCR 7000 sequence detection system
- Genomics core and training facility – fully equipped Affymetrix GeneChip technology

Index Terms

biofilms, periodontal disease, gingivitis, dental caries, dental surfaces

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Functional Genomic/Proteomic Analysis of Bacterial/Host Interactions
University of Oklahoma Health Sciences Center – P20 RR015564

Principal Investigator

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Thematic Scientific Focus

Genome-scale analysis of bacterial pathogenesis, emphasizing functional genomic and proteomic analysis of bacteria-host interactions

Research Projects

- Receptor mediated effect of intermedilysin on human polymorphonuclear lymphocytes
- HIV-1 subtype C fitness evolution and mother-to-child transmission
- Enhancement of humoral immunity by CD1d-restricted NKT cells
- Efficacy of Bb in the treatment of experimentally induced IBK
- Bdelloplast germination and development in *bdellovibrio bacteriovorus* strain w

Research Resources

- Functional genomics cores (OUHSC and OSU) – microarray fabrication, hybridization, and scanning; microarray-based gene expression profiling; high-throughput DNA sequencing and oligonucleotide synthesis; protein 2-D gel electrophoresis and N-terminal amino acid sequencing; protein fractionation (PF2D), mass spectroscopy
- Informatics core – computer hardware and software for primer design, image processing, and data analysis

Index Terms

genomics, proteomics, DNA microarray, bacteria, pathogens, lymphocytes, toxins, conjunctivitis

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Mentoring Diabetes Research in Oklahoma
University of Oklahoma Health Sciences Center – P20 RR024215

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Scientific Focus

To mentor and train junior investigators in diabetes research

Research Projects

- Impact of age and exercise on insulin action
- Activation of AMPK protects against diabetic vascular complications
- The role of ubiquitin in hyperglycemia-induced mesangial cell hypertrophy
- 26S Proteasome and endothelial dysfunction in diabetes

Research Resources

- Diabetes animal core – to establish tissue banks of diabetic animal models and assist promising junior investigators in diabetes animal models
- Histology and image core – to provide free service for histology and image analysis
- Biostatistics core – to provide free service for biostatistics

Index Terms

diabetes, diabetic, hyperglycemia, insulin

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Science in a Culture of Mentoring

Oklahoma Medical Research Foundation – P20 RR015577

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Thematic Scientific Focus

Molecular and cellular immunology in the context of human health and disease

Research Projects

- Effects of ERK Pathway inhibition on DNA methylation in SLE
- Development of a multivariate test of disease activity in rheumatoid arthritis
- Memapsin 2 (beta-secretase) immunization as therapy for Alzheimer's disease
- Structure/function studies of T cell rafts
- Effects of influenza infection on systemic autoimmunity

Research Resources

- Microarray core – printing of mouse and human genome-scale arrays; high-throughput Ventana hybridization station; microarray processing and image analysis; data warehousing; bioinformatics and statistical analyses
- Signal transduction core – measurements of intracellular calcium, protein-protein interactions, enzyme activities; phosphoaminoacid analysis; spectrofluorimetry; immuno-detection and quantification of proteins and nucleic acids; chromatography; radiolabel quantification; transient transfection services
- Imaging core – transmission electron microscope; inverted fluorescence microscope; upright microscope
- Peptide synthesis core – custom synthetic peptides for biochemical studies and solid-phase peptide epitope mapping experiments
- Human monoclonal antibody core – rapid generation of human monoclonal antibodies for immunologic studies
- Clinical core – assistance with identification, characterization, enrollment and sample procurement from autoimmune disease patients and unaffected controls for junior investigator COBRE projects; assistance with human subjects training, IRB applications and design of patient-oriented research questions

Index Terms

immunology, molecular biology, vaccine, drug design, virus, signaling, inflammation, inflammatory disease, DNA microarray, imaging, proteomics, microinjection, stem cells, immunodeficiency, autoimmune disease, arthritis, genomics

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Mentoring Vision Research in Oklahoma
University of Oklahoma Health Sciences Center – P20 RR017703

Principal Investigator

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Thematic Scientific Focus

Basic visual research with an emphasis on studying the retina and retinal diseases

Research Projects

- EGFR-mediated corneal epithelial wound healing
- *In vivo* role of caveolin-1 in modulating photoreceptor function
- Sphingolipid metabolism in the retina

Research Resources

- Image acquisition and production core
- Molecular biology core
- Animal resource core – animal surgery, antibody production and electroretinography

Index Terms

visual research, retinal disease, retinal biochemistry, light-induced signal transduction, neurodegeneration, diabetes, angiogenesis, vascularization

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Molecular Mechanisms and Genetics of Autoimmunity
Oklahoma Medical Research Foundation – P20 RR020143

Principal Investigator

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Thematic Scientific Focus

The molecular and genetic basis for autoimmune diseases

Research Projects

- Understanding the role of alternative splicing in the TNFAIP3 SLE-risk alleles
- Discovery and testing of novel immunological genes
- Select SLE candidate genes in African-Americans
- Genes involved in early autoimmunity of systemic lupus erythematosus
- Study the effects of genetic susceptibility variation in the expression of B cell genes and markers

Research Resources

- Nucleic acid analysis core
- Genotyping
- Data analysis core – statistical and bioinformatic analyses

Index Terms

autoimmune disease, inflammatory rheumatic diseases, systemic lupus erythematosus, autoantibody, autoantigen

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Post-Translational Modifications in Host Defense
Oklahoma Medical Research Foundation – P20 RR018758

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Thematic Scientific Focus

The role of glycosylation in host defense

Research Projects

- How membrane tether formation stabilizes leukocyte rolling, thus enabling leukocytes to survey the endothelium for mediators of inflammation
- The role of VH4-34 immunoglobulin heavy chain gene encoded antibody immunity and the mechanisms that provide natural immunity while avoiding an autoimmune response
- The mechanisms by which TFPI interacts with membrane surfaces
- The role of O-glycosylation in development, inflammation, hemostasis, immune responses, and other biological functions *in vivo*
- The role of proteoglycans, specifically chondroitin sulfate and dermatan sulfate, biosynthesis in atherogenesis

Research Resources

- *In vitro* microscopy core – provides expertise and the equipment to perform a diversity of techniques that include brightfield histological analysis, confocal microscopy, 3D imaging, standard transmission electron microscopy and immunogold labeling, and advanced cryo-technologies (cryoimmunogold labeling, freeze substitution, high pressure freezing, and freeze fracture and deep-etching)
- Intravital microscope core – provides expertise and equipment to dissect complex physiological or pathological cell-cell or cell-matrix interactions; advanced intravital epifluorescence microscope with water immersion objectives connected to CCD color camera, video cassette recorder, and Doppler apparatus; stereo microscope for surgical preparation; advanced Dell computer for data acquisition and analysis
- MRI/MRS core – provides non-invasive *in vivo* monitoring capabilities to assess morphological, physiological, pathophysiological and metabolic processes that occur during progressive stages of the pathogenesis of most diseases

Index Terms

host defense, inflammation, antibody, autoimmune disease, immunoglobulins, glycosylation, proteoglycans, atherogenesis

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Rhode Island

Center for Cancer Research Development Rhode Island Hospital – P20 RR017695

Principal Investigator

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Thematic Scientific Focus

Overarching theme, molecular pathogenesis of gastrointestinal cancer; developmental theme, endodermal stem cells as progenitors of GI cancers arising in the liver, gastric mucosa or intestine

Research Projects

- Post-translational modification of surviving: a novel therapeutic approach for cancer
- The RKIP-STAT3 axis in colon cancer: molecular profiles for prognosis and therapeutic intervention
- Acetylation dependent STAT3 signalsome in liver cancer
- Growth regulation of liver progenitor cells

Research Resources

- Proteomics core – protein chip analyzer, HPLC mass spectrometry, Janus Automated Workstation, which is a liquid handling system that provides real-time and future adaptability in throughput, plate capacity and dynamic volume range, the Ultraflexxtreme, which is designed for the analysis of tissue sections and can perform either MALDI-Tof or MALDI-Tof-Tof analysis, protein and analysis/purification; assists investigators in choosing appropriate methods and techniques for specific research objectives; provides a means for investigators to become directly involved in protein analysis at a level not possible with commercial suppliers; provides expertise in protein bioinformatics
- Molecular pathology core – provides instrumentation and support personnel for the research efforts of both the COBRE mentors and their junior associates, as well as specialty immunohistochemical services for the Department of Pathology; facility equipped with digital tissue scanner, automated laser capture microdissection instrument, histology equipment, quantitative real-time PCR system, automated immunohistochemistry processor, microtome and cryostat, tissue arrayer, and freezer space for the tumor bank

Index Terms

cancer, hepatocarcinoma, vaccines, colon cancer, esophageal cancer, liver cancer, anti-inflammatory cytokines, *Helicobacter pylori*, gastric cancer, liver development

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Center for Genomics and Proteomics
Brown University – P20 RR015578

Principal Investigator

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Thematic Scientific Focus

Become part of a master plan to establish a center for contemporary molecular genetics research, using a multidisciplinary approach that will combine laboratory research with clinical and human genetics at affiliated hospitals

Research Projects

- Gonad-specific transcriptional cofactors
- Wnt signaling in hepatocellular carcinoma
- High-throughput proteomic analysis of signaling pathways
- Supv3L1 helicase knockout mouse
- Bayesian inferences of cis-regulatory modules and signal transduction pathways
- Crystal structure of inositol phosphates

Research Resources

- Transgenic and knockout mouse facility
- Flow cytometry core
- Confocal imaging core
- Affymetrix GeneChip and GenePix genomic arrays
- ABI real time PCR
- Stem cell core

Index Terms

transgenic animals, knockout mouse, flow cytometry, imaging, genetics, genomics, immunology, infection, molecular biology, virus, hepatitis, neuropathology, Alzheimer's disease, microvascular disease, addiction, epilepsy, stroke, signaling, liver disease

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COBRE for Perinatal Biology
Women & Infants' Hospital of Rhode Island – P20 RR018728

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Thematic Scientific Focus

The molecular basis of cardiopulmonary signal transduction and development during fetal and postnatal life

Research Projects

- Neonatal candidiasis and immune compromise during development
- Programming of trophoblast differentiation and invasion by multiple oxygen pathways
- The role of PI3 kinase in cardiac repair and remodeling
- Epigenetic alterations as markers of the intrauterine environment

Research Resources

- Molecular biology and histology core – radiographic imaging, multicolor fluorescent imaging, tissue processing and microscopy, including phase contrast, DIC, and fluorescence

Index Terms

fetal development, perinatal development, cardiac development, pulmonary development, newborn medicine, signal transduction, placental development

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COBRE for Skeletal Health and Repair
Rhode Island Hospital – P20 RR024484

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Thematic Scientific Focus

Establish a multi-disciplinary translational research center focusing on the health and disease mechanisms and repair strategy in cartilage and bone

Research Projects

- Regulation of growth plate development by nuclear/cytoplasmic factors
- Endocrine and nutritional control of long bone growth
- Mechanism of angiogenesis and chondrosarcoma
- Trauma-induced joint injury
- Cartilage tissue engineering for joint repair

Research Resources

- Bioengineering core – testing mechanical properties of tissues and cells
- Molecular biology and imaging core – including *in vivo* imaging of animals

Index Terms

cartilage, bone, growth plate, skeletal dysplasia, joint degeneration, osteoarthritis, chondrosarcoma, angiogenesis, tissue engineering

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New Approaches to Tissue Repair
Roger Williams Hospital – P20 RR018757

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Thematic Scientific Focus

Multidisciplinary approach to mechanisms and translational aspects of repair in different tissues and organs with an emphasis on stem cell biology

Research Projects

- Bone marrow derived fibroblasts and their role in tissue repair and fibrosis
- Development of bispecific antibodies to facilitate tissue repair cell recruitment
- The use of stem cells in wound healing
- Ischemic skin flap survival using AAV-FGF2 and AAV-VEGF 165
- Bone marrow subpopulations to repair human islet injury and supports its longevity

Research Resources

- High speed cell sorter, BD FACS scan and BD FACS caliber
- Fluorescent motor-driven microscopes: upright, inverted, and confocal laser-scanning capable of four-color imaging
- IVIS system for live imaging
- Microarray scanner with three lasers
- Time lapse photography system
- Imaging and Immunohistochemistry core
- Cell sorting and flow cytometry core
- Molecular biologic core
- GMP core

Index Terms

adult stem cells, hematopoietic stem cells, bone marrow, wound healing, differentiation, RNAi, pancreatic islet, cell recruitment, gene therapy

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Stem Cell Biology: New Directions in Clinical and Basic Research
Rhode Island Hospital – P20 RR025179

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Thematic Scientific Focus

Stem cell biology: modulating the stem cell phenotype

Research Projects

- Injured lung and its influence on marrow cell phenotype
- Directed stem cell hematopoiesis and differentiation
- Tyrosine phosphatase Shp2 in stem cell property maintenance

Research Resources

- Cytometry core
- Molecular core

Index Terms

stem cell biology, regenerative medicine, hematopoiesis

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South Carolina

Center for Colon Cancer Research
University of South Carolina – P20 RR017698

Principal Investigator

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Thematic Scientific Focus

Molecular, biochemical, genetic, and lifestyle factors in the diagnosis, prevention, and treatment of colorectal cancer

Research Projects

- Genetic modulation of the tumor microenvironment in the ApcMin/+ mouse
- Role of protein phosphatases in the DNA damage response
- Peptide-based borono lectins: new tools for colon cancer
- The nature and role of the microbiome in mouse models of colon cancer
- Community based colorectal cancer prevention in South Carolina
- Inflammation-related genes, diet, and colorectal cancer
- Cancer stem cells in ApcMin/+ mice

Research Resources

- Mouse core Facility
- Histology/imaging core facility
- Biometry core facility
- Tumor biorepository
- Administrative core

Index Terms

colon cancer, cell biology, DNA repair, apoptosis, inflammation, cell proliferation, chemotherapy, cell signaling, chemoprevention, nutrition, epidemiology

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COBRE in Lipidomics and Pathobiology
Medical University of South Carolina – P20 RR017677

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Thematic Scientific Focus

How bioactive lipids influence cellular regulatory pathways and how specific lipids affect these control networks, which subsequently can contribute to the pathophysiology of certain disease states

Research Projects

- Substrate supply in *de novo* sphingolipid synthesis: regulation/impact on chemotherapy
- Role of sphingolipid pathway genes in maintenance of genome stability in yeast
- Structural and function studies of quinolone signaling in *pseudomonas aeruginosa*

Research Resources

- Lipidomics core – expertise and tools to perform research in sphingolipidomics; training in various aspects of lipidology; qualitative and quantitative analysis of sphingolipid components (metabolomic profile) from different biological materials (cells, tissue, and biological fluids); HPLC-tandem mass spectrometry (LC-MS/MS)
- Animal pathobiology core – mouse knock-out and transgenic technology for gene targeting by homologous recombination and random integration, respectively through pronuclear injections; founder mice are generated by either approach and subsequently serve as an animal resource for breeding and genotyping; rabbit model for fungal pathogenesis is being established
- Protein science core – for the expression and purification of proteins using *E. coli*, baculovirus, yeast and mammalian expression systems; purified proteins are used by COBRE investigators for functional and structural studies, or for the production of monoclonal antibodies; the folded state of proteins is monitored by circular dichroism and protein-lipid interactions are measured using NMR

Index Terms

lipids, angiogenesis, tumor progression, neuroblastoma, diabetes, fungal pathogenesis, cancer, chemotherapy, systems biology, crystallography

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**Center of Biomaterials for Tissue Regeneration (SCBIOMAT)
Clemson University – P20 RR021949**

Principal Investigator

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Thematic Scientific Focus

Interactions among cells and biomaterials and their implications for tissue regeneration

Research Projects

- Stem cell-myocyte electrical coupling via a laser-patterned cell bridge
- Biomaterials for guided neural regeneration
- BMP-4 as a novel angiogenic factor and its potential use in tissue engineering
- Enabling technology for brain tissue regeneration after stroke

Research Resources

- Material characterization and testing core
- Histology and imaging core
- Stem cell and genetic engineering core

Index Terms

biomaterials, tissue engineering, stem cell biology, developmental biology, tissue regeneration, regenerative medicine

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South Carolina COBRE for Developmentally Based Cardiovascular Diseases
Medical University of South Carolina – P20 RR016434

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Thematic Scientific Focus

Mechanisms of cardiovascular disease, including cell proliferation and remodeling, apoptosis, cellular transdifferentiation, and vasculogenesis

Research Projects

- Transcriptional control of cardiac growth
- Role of hyaluronan in congenital heart defects and atherosclerosis
- Hematopoietic stem cells in cardiovascular regenerative medicine
- Molecular development and pathophysiology of the atrio-ventricular conduction system
- The role of ADAMS 17 as a central regulator of angiogenesis
- Role of microRNA-155 in macrophage function and atherosclerosis
- Matrix metalloproteinase cleavage of versican in cardiac outlet remodeling
- Developmental basis of mitral valve prolapse

Research Resources

- Gene function and molecular tool kit
- Morphology, imaging and instrumentation core
- Proteogenomics core

Index Terms

cardiovascular disease, proteomics, genomics, apoptosis, cell biology, DNA microarray

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South Carolina COBRE for Oral Health
Medical University of South Carolina – P20 RR017696

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Thematic Scientific Focus

Oral and craniofacial health

Research Projects

- Role of the hexosamine biosynthetic pathway and posttranslational O-GlcNAc glycosylation in complications of diabetes pertaining to oral health
- Fluid and solute transport in human temporomandibular joint disc
- The function of SPARC in the regulation of collagen deposition in the periodontal ligament
- The relationship between periodontal diseases and Type 2 diabetes mellitus in the Gullah population and the effects of mechanical periodontal therapy and systemic antibiotics on the glycemic control and on the active matrix metalloproteinase-8 (aMMP-8) level in the gingival crevicular fluid (GCF) of these patients
- KSHV regulation of innate cytokine responses and T cell activation
- Molecular mechanisms of mRNA Stability in human saliva

Research Resources

- Biostatistics core – collaboration in study design; sample size estimation and power analyses; statistical methodology, especially for clustered data; data management, including web-based systems; manuscript and proposal preparation; bioinformatics, particularly for genomic and proteomic data analysis
- Clinical resources core – coordination of clinical research projects at the MUSC GCRC Research Center and at off-site locations; provision of calibrated dental examiners for oral exams; coordination of research methodologies available in the MUSC Center for Oral Health Research core laboratory which recently has added a new core for oral histology and image analysis

Index Terms

oral health, periodontal disease, cytokines, diabetes, oral cancer, health disparities, periodontal ligament, proteomics

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South Dakota

COBRE on Neural Mechanisms of Adaptive Behavior University of South Dakota – P20 RR015567

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Thematic Scientific Focus

Structural reorganization in neural pathways resulting in adaptive behavioral responses to novel sensorimotor experiences; employing physiological, pharmacological, anatomical, molecular, and behavioral experimental approaches

Research Projects

- Synaptic mechanisms underlying *in vitro* classical conditioning
- Adaptation of respiratory pattern generator to hypoxia
- Steroid and monoamine effects on sex, stress and seizures
- Mechanisms underlying focal cranial cervical dystonia
- Cellular mechanisms of bi-directional synaptic plasticity to learning
- Synaptic localization of NMDA receptor subunits in a PCP model of schizophrenia
- Neural mechanisms underlying adaptive coping and socially-induced anxiety
- Corticotropin releasing factor, stress and cocaine addiction
- Effect of glucocorticoids on mammalian toll-like 1 expression in the hippocampus

Research Resources

- Biological imaging core – Olympus FluoView 1000 laser scanning confocal microscope; Zeiss Axio Imager M1 upright and Axiovert 200 MOT inverted fluorescent microscope with Apotome confocal slider; BioRad VersaDoc 5000 imaging system
- Proteomics/genomics core – Applied Biosystems real-time PCR; MALDI-TOF; Axon GenePix Scanner
- Behavioral core – Noldus Ethovision video tracking system; ObserverXT data analysis system; watermaze, elevated plus maze, eight-arm radial maze

Index Terms

microscopy, conditioning, learning, memory, neurogenesis, stress, seizures, steroids, physiology, pharmacology, anatomy, behavior, molecular biology

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Mechanisms of Cardiovascular Remodeling

University of South Dakota School of Medicine – P20 RR017662

Principal Investigator

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Thematic Scientific Focus

Multi-disciplinary, highly integrated, approach toward understanding cardiovascular disease

Research Projects

- α 1-adrenergic receptor signaling and cardiac remodeling
- Role of lipoproteins in the transport and action of oxylipins
- Mechanisms of doxorubicin induced heart failure
- Myotonic dystrophy protein kinase in myocyte development
- Inhibitory effect of ω -3 PUFAs on cardiac fibrosis

Research Resources

- Physiology testing core
- Cell culture core
- Molecular biology core
- Cell imaging core

Index Terms

cardiovascular disease, heart failure, remodeling, signal transduction, α 1-adrenergic receptors, cardiotoxicity, myotonic dystrophy, molecular biology, autophagy, apoptosis, angiogenesis, lipoproteins, thyroid hormones

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Vermont

Neuroscience Center of Biological Research Excellence University of Vermont – P20 RR016435

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Thematic Scientific Focus

The molecular basis of neurological functions

Research Projects

- Spatial regulation of protein kinase A signaling during growth cone guidance
- Expression of the AMPA receptor subunit GluR2 in chick lumbar motoneurons
- Adult bone marrow stem cells for CNS repair
- Role of dipeptidyl peptidase IV (DPPIV) in peripheral neurogenesis and neuroblastomas

Research Resources

- Imaging and physiology core – fast scanning laser confocal microscope; dedicated multiphoton confocal microscope; total-internal reflection fluorescence microscope with patch-clamp capability; deconvolution microscope; ratiometric imaging system; imaging workstation with EMCCD camera; fluorescent stereo-microscope; and fixed-stage slice imaging and physiology rig with vibratome for live slice preparation
- Cellular and molecular biology core – Zeiss PALM microlaser dissection system; SELDI-TOF mass spectrometer for biomarker analysis; two quantitative real-time PCR systems; infrared imaging system for multicolor Western blotting; array printer for printing antibody/protein/RNA/DNA arrays; Qiagility isolation and pipetting robots; Nanodrop spectrophotometer; ChemiDoc gel documentation system; Qiacube RNA/DNA isolation system; RNA/DNA/protein analysis system; neuroanatomical analysis system for 3D measurements, neuron tracing and morphometrics; fluorescent inverted, upright and stereo microscopes; full histological capability including cryostat, vibratome, microtome, paraffin embedding station and a staining station with hood

Index Terms

neuroscience, cell biology, molecular biology, learning, signaling, brain, vascular biology

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Translational Research in Lung Biology and Disease
University of Vermont & State Agricultural College – P20 RR015557

Principal Investigator

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Thematic Scientific Focus

The translation of basic laboratory research into clinical applications to fight lung disease; current research projects encompass basic cell biology, translational applications, animal models and clinical trials; providing a rich research experience while creating a stimulating research environment for promising new investigators in the fields of cell biology, immunology, physiology, animal models and patient-oriented research

Research Projects

- Therapeutic effects of fish oil (Omega-3 fatty acids EPA & DHA) in patients with acute lung injury
- The mechanistic basis of the relationship between obesity and asthma: the therapeutic effect of gastric bypass
- Role of the IL-13/PAI-1 signaling axis in pathogenesis of asthma, using a mouse model of asthma
- Th2/CD4 T cell mediated lymphocyte dysfunction caused by the absence of CFTR: relevance to cystic fibrosis and asthma

Research Resources

- Transgenic/knockout animal core
- Biomedical engineering core

Index Terms

lungs, asthma, cystic fibrosis, obesity, biomedical engineering, pulmonary physiology, transgenic/knockout animals, oxidant lung injury, inflammation, Immunology, clinical trials

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Vermont Center for Immunology and Infectious Diseases
University of Vermont – P20 RR021905

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Thematic Scientific Focus

The immune response to infectious agents and their mechanism of pathogenicity

Research Projects

- Molecular determinants of iNKT cell activation by CD1 and its ligands
- Innate immune response to *Cryptosporidium parvum*
- Molecular mechanism of *Entamoeba histolytica* phagocytosis
- Subversion of host cell signaling by *Toxoplasma gondii*
- Defensins in plant innate immunity
- Microbial ecology of the cystic fibrosis lung

Research Resources

- Microarray and bioinformatics core – Affymetrix GeneChip 2500 system that includes Hybridization Station 640, Fluidics Station 400 and Scanner 2500; Agilent bioanalyzer 2100 is also available for RNA analysis
- Bioinformatics core – Unix system administrator and two programmers
- Proteomics core – MALDI-TOF mass spectrometry, two-dimensional gel scanner/extractor for differential expression profiling

Index Terms

innate and adaptive immunity, NKT cells, T cells, microbial pathogenesis, parasites

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West Virginia

COBRE for Signal Transduction and Cancer West Virginia University – P20 RR016440

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Thematic Scientific Focus

Molecular changes in cell signaling proteins that occur in cancer; the relationship between specific signal transduction pathways and regulation of gene expression as it relates to tumor metastasis and invasion

Research Projects

- NRAGE regulation of anoikis
- Epigenetics of breast cancer
- Role of cortactin in head and neck cancer
- VE-cadherin trafficking and angiogenesis
- Cas/AurA in tumor progression

Research Resources

- Flow cytometry core
- Biostatistics core
- Imaging
- Protein purification

Index Terms

cell biology, molecular biology, cancer, signaling, angiogenesis, invasion

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COBRE in Sensory Neuroscience
West Virginia University – P20 RR015574

Principal Investigator

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Thematic Scientific Focus

Neuroscience, focused on the topics of development and plasticity of sensory systems; development of treatments for human neurological diseases using both animal and human subjects

Research Projects

- Development of neocortex
- fMRI of auditory attention to complex environmental sounds

Research Resources

- Histology core
- Non-linear optical imaging core
- Transgenic animal core
- Genomics core
- Center for Advanced Imaging

Index Terms

neuroscience, neurons, genetics, imaging, sensory disorders, hearing, balance, signaling, molecular degeneration

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Transcription Factors in Cancer
Marshall University – P20 RR020180

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www.marshall.edu/cncc

Thematic Scientific Focus

The role of dietary nutrients in the prevention, progression and treatment of cancer

Research Projects

- Antineoplastic activity of capsaicin in human small cell lung cancer
- Omega 3 fatty acids to inhibit NF-kB in indolent B-cell malignancies: a phase I clinical trial
- Coordinated epigenetic regulation of gene expression by sulforaphane in prostate cancer cells
- Dietary fatty acid induced changes in hematopoiesis and impact on CML progression

Research Resources

- Genomic core – microarray profiling; single mRNA measurement abundance by real-time PCR; DNA sequencing and sequence analysis

Index Terms

dietary constituents, nutrition, cancer

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Wyoming

Neuroscience Center
University of Wyoming – P20 RR015640

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Thematic Scientific Focus

Cellular mechanisms underlying activity dependent changes in central nervous system circuitry and function

Research Projects

- Activity dependent processing in the fly eye and biologically inspired machine vision
- Daylight regulation of pars tuberalis tachykinin-induced prolactin secretion
- Activity dependent refinement of inhibitory networks in the barrel cortex
- Activity dependent mechanisms of neuropathic pain

Research Resources

- Macromolecular analysis facility – nitric oxide analyzer; MALDI-TOF mass spectrometry
- Microscopy imaging facility

Index Terms

neuroscience, neuroplasticity, nociception, somatosensory, neuroendocrine, computational, bioengineering, confocal microscopy, ultrastructure, proteomics

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