Institutional Development Award (IDeA) Program
CENTERS OF BIOMEDICAL RESEARCH EXCELLENCE (COBRE)
Directory of Active Awards by State and Program
July, 2008

IDeA-Eligible States:

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

Alaska

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

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Thematic Scientific Focus:
Health disparities experienced by Alaska Natives, focusing on obesity, nutrition, 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, nutrition, obesity, epidemiology, bioinformatics, genetics, stress

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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
- Structure-based drug discovery
- Protein targeting
- Principles of protein folding and design
- 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 Rigagku 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 sequenator, 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

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

Principal Investigator:
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Thematic Scientific Focus:
Establishment of a broad-based translational neuroscience research center

Research Projects:
- Comprehensive assessment of motion sickness and neurovestibular disorders
- Chronic low back pain and depression
- Pain: early experience and pre-attentional mechanisms
- Palliative strategies for spinal cord injury
- Cytoplasmic polyadenylation-mediated control of mRNA translation in neurogenesis and neuropathology

Research Resources:
- Community-based research and education core facility
- Electrophysiology core – psychomotor vigilance task instrumentation; transcranial magnetic stimulation system
- Image analysis core – confocal microscope; fluorescent and light microscopic systems
- Molecular biology core
- Transcranial magnetic stimulation core facility

Index Terms:
neurological disorders, chronic pain, spinal cord injury, neurogenesis, neuropathology

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Delaware

Center for Pediatric Research
Alfred I. duPont Hospital for Children – P20 RR020173

Principal Investigator:
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http://www.nemours.org/research/biomedical/center/ped-research.html

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

Research Resources:
- 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

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

Principal Investigator:
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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:
- Healing of cartilage after experimentally induced osteoarthritis
- The osteoarthritic knee: a biomechanical analysis
- Effect of in-shoe wedges on knee osteoarthritis
- Correction of genu varum deformity by an opening wedge osteotomy

Research Resources:
- Magnetic resonance imaging 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

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
- Structural analysis of Sprinter
- Towards solid-state NMR structures of GPCRs
- 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*
- Magic angle spinning solid-state NMR methods for structural studies of membrane proteins
- Lanosterol biosynthesis in the membrane environment

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

Design of Hierarchical Recognition Motifs
University of Delaware – P20 RR017716

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Thematic Scientific Focus:
Development of molecular recognition elements for structural control in macromolecules, encompassing atomic-level interactions among small molecules, proteins, and multi-protein assemblies

Research Projects:
- Small molecule alpha-helix mimics
- Peptide-based biomaterials with environ-sensitive morphologies
- Strained molecules for synthesis of unnatural amino acids
- Artificial glycoproteins for applications in materials and biology
- Determinants of stability and assembly of integral membrane proteins
- Protein assemblies and metalloproteins

Research Resources:
- Protein production and purification core
- Peptide/protein NMR core – 600 MHz NMR spectrometer with cryoprobe; 300 MHz solid-state NMR spectrometer for membrane proteins
- X-ray crystallography core
- Mass spectrometry core
- Networked computational facility – Linux computer cluster for molecular modeling

Index Terms:
proteins, recognition motifs, molecular topology, unnatural amino acids, protein engineering, materials science, chemical engineering, biomaterials

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Hawaii

COBRE Center for Cardiovascular Research
University of Hawaii – P20 RR016453

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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
- Caveolin-1 in cardiac remodeling
- Endothelial gene expression in cardiovascular stress
- Evaluation of the interaction of microbubbles and biofilms in endocarditis
- Effects of hypoxia-inducible factor-1 in the heart
- Role of endothelin in cardiac remodeling
- Cardiac mast cells in heart failure
- Cardiac effects of jellyfish toxins

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

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:
- Molecular epidemiology and natural history of human papillomavirus in men
- Immunopathogenesis of dengue virus infection
- Group A Streptococci in relation to acute rheumatic fever in Hawaii

Research Resources:
- Technical support core – FACS flow cytometry; cell sorting; real-time PCR analysis; DNA sequencing; Affymetrix gene chip DNA microarray analysis; metabolomics; bioinformatics
- BSL-3 containment facility

Index Terms:
infectious diseases, emerging diseases, health disparities, epidemiology, evolution, group A streptococci, dengue virus, human papillomavirus

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Idaho

Center for Research on Processes in Evolution
University of Idaho – P20 RR016448

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Thematic Scientific Focus:
Role of mutagenic processes on the tempo and trajectory of adaptive evolution, emphasizing the evolutionary history of functional domains in microbial proteins, structural genes, and genomes

Research Projects:
- Predictability of viral evolution
- Evolution of antibiotic resistance plasmids
- Evolution of protein flexibility
- Computational and mathematical analysis of biomedical data

Research Resources:
- Molecular biology core – DNA cloning and sequencing; protein expression and purification; computer workstations and software for molecular modeling
- Bioinformatics core – Three Beowulf Supercomputers: 54 node with 54 processors; 134 node with 268 processors; and 50 node with 100 processors
- Structural biology core – 600 MHz NMR spectrometer; cell-culture systems for preparative-scale protein labeling with stable isotopes

Index Terms:
evolutionary biology, molecular biology, structural biology, microbial ecology, computational biology, statistics, genomics, proteomics

Molecular and Cellular Basis of Host-Pathogen Interaction
University of Idaho – P20 RR015587

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Thematic Scientific Focus:
Molecular and cellular basis of host-pathogen interactions, emphasizing microbial pathogenesis

Research Projects:
- Potassium sensing by the obligate intracellular parasite *Toxoplasma gondii*
- The impact of lipid metabolism on staphylococcal mastitis
- Human cytomegalovirus interactions with cellular p53
- Investigation of the *Y. pestis* immune evasion response to human neutrophils
- Maintenance of hyphal polarity by DopA protein and its role in *Aspergillus* pathogenesis
- Role of Hsp90 in polarized cell morphogenesis in *S. cerevisiae* and *C. albicans*
- Transcriptional attenuation of the type I interferon response by rhinovirus

Research Resources:
- Molecular biology core – DNA cloning and sequencing; protein expression and purification; computer workstations and software for molecular modeling
- Bioinformatics core – 64-node Beowulf cluster supercomputer
- Structural biology core – 600 MHz NMR spectrometer; cell-culture systems for preparative-scale protein labeling with stable isotopes
- BSL-3 facility – certified and registered by the Centers for Disease Control and Prevention
- Cell separation core – FACSCalibur flow cytometer, Becton Dickinson FACSAria flow cytometer/cell sorter, PALM microbeam laser microdissection system with epifluourescent capability

Index Terms:
molecular biology, cell biology, pathogens, *E. coli*, antiviral, immunology, *Staphylococcus,* gangrene, colitis, microbiology, virology, sexually transmitted diseases, HIV, trauma, antibiotic resistance, *Clostridium, Yersinia pestis, Toxoplasma*, mastitis, immunocompromised, invasive Aspergillosis, neutrophil, rhinovirus, human cytomegalovirus

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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
- Nanoencapsulated signal transduction inhibitors for breast cancer
- MyoGEF in cancer cell migration and mouse embryogenesis
- Phosphatidylcholine biosynthesis and anticancer agent miltefosine

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

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

Principal Investigator:
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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:
- Transepithelial ion transport and its regulation
- Renal, reproductive, mammary and intestinal epithelia
- Molecular basis of migration pathology in intestinal epithelia caused by non-steroidal anti-inflammatory drugs
- Molecular basis of protein and vesicle traffic in epithelia
- Interactions between pathogens and arthropod midgut epithelial cells
- Canine urogenital beta-defensins, a novel family of epithelium-derived antimicrobial peptides

Research Resources:
- Confocal microfluorometry – Zeiss LSM510 Meta, microfluorometry of fast Ca2+ signals in cultured and native epithelial tissues; subcellular visualization and co-localization of fluorescently labeled molecules; Leica CM3050 S cryostat; Zeiss/PALM laser catapulting dissection microscope
- Molecular biology core – DNA sequencing; quantitative RT-PCR; DNA microarrays and related equipment for gene expression profiling; protein analysis support (mass spec)
- Epithelial electrophysiology core – tools for noninvasive current and nonradioactive ion flux measurements, including self-referencing ion-selective electrodes, vibrating current-density probes

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

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:
- Interactions of *Salmonella* needle and tip proteins
- Mechanism and role of a novel Chlamydial transcriptional regulator CHXR
- 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, transcriptional activation, DNA remodeling, chaperones, glycoproteins, membrane proteins, signal transduction, rational drug design, medicinal chemistry

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

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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

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:
- Structure-function relationship of antibiotic targets MurA and EPSP synthase
- Bacterial cell division proteins as targets for antimicrobials
- Antimicrobials targeted to M protein of Streptococci
- Purification and crystal structure of a novel baculovirus RNA polymerase subunit
- Pseudomonas Type 3 effector protein AvrPto in pathogenesis: host defense
- Immunogenicity of HIV DNA vaccines and cytokines in mice
- Roles of p30 in HTLV-1 latency
- HCV NS5B polymerase mutations: biology/pharmacology
- Development of peptidyl nucleosides as novel antifungals
- Lyme borreliosis and babesial coinfection
- CAEV/SHIV chimera for studies on bystander death of CD4+ T cells in goats
- Biodegradable nanoparticles for AIDS gene therapy replication of noroviruses in cell culture
- Regulation of CCR7 mediated adhesion of T cells through LFA-1
- The Gads adaptor protein in T cell-mediated prevention of viral pathogenesis
- Faculty Recruitment Enhancement Projects:
  - HHV-8 envelope glycoprotein gB as a target for novel therapeutic agents
  - Structure-function analysis of *Borrelia* vsp and vlp surface lipoproteins
  - Synthesis of novel C-5' modified nucleoside analogs
  - Gene therapy of TB granulomas in mice
  - Breaking HTVL-1 latency: p30-RNA interaction as a novel therapeutic target
  - Characterization of the novel *Enterococcus faecalis* protein EBSG in lipoteichoic acid structure and function
  - Siderophore production and import in *Pseudomonas aeruginosa*
  - Hepatitis C virus in NS5B polymerase
  - Genetics of capsular polysaccharide production in *Enterococcus faecalis*
  - Effect of hemifluorinated surfactants on membrane insertion/folding of diphtheria toxin T domain
  - Regulation of CCR7-mediated adhesion of T cells through LFA-1
  - The Gads adaptor protein in T cell-mediated prevention of viral pathogenesis
  - Early gene expression curing T cell activation
  - Cytotoxic necrotizing factor 1 in *E. Coli* Meningitis
  - High resolution structure of herpesvirus

- Characterization of immune T cells induced by a unique HIV
- DNA vaccine role of CNF1 in *E. coli* meningitis
- Post-transcriptional regulation of parvovirus B19 capsid gene expression
- Identification and Regulation of Stress Response Genes in Group A *Streptococcus*

Research Resources:

- X-ray crystallography core – protein crystallization and structure determination; high-throughput screening of small-molecule libraries; molecular modeling; structure-based drug design
- Fermentation and screening core – preparative scale production and purification of native and engineered proteins
- Flow cytometery 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, microbial infection, molecular structure, protein X-ray crystallography, mechanism-based enzyme inhibitors, drug development, cell mediated immune responses, development of the immune system

Nuclear Receptors in Liver Health and Disease
University of Kansas, Lawrence - P20 RR021940

Principal Investigator:
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Thematic Scientific Focus:
Nuclear receptors and their role in liver health and disease

Research Projects:
- The role of organic anion transporting polypeptides (OATPs) in nuclear receptor activation
- Mechanisms by which farnesoid-x-receptor (FXR) alters hepatic lipid metabolism and decreases fatty liver development
- Role of SHP (small heterodimer partner) in fatty liver
- Physiological function of nuclear receptors in cholestatic liver diseases
- Identification and functional characterization of SNPs (single nucleotide polymorphisms) in RXRα (retinoid-x-receptor α) gene

Research Resources:
- Molecular biology core – DNA Sequencing; real time PCR including reagents; high throughput PCR for rapid genotyping; a vector, plasmid, and bacteria bank
- Null-mouse development and husbandry core
- Phenotyping/pathology core –serum chemistries and immunohistochemistry
- Analytical core – HPLC, LC-MS/MS, FPLC, and multi-mode 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:
- Oral infections and HIV recrudescence
- Cox-2 and 12/15-LO in atherosclerosis
- Impact on gestational diabetes
- Dietary regulation of local and systemic inflammatory responses
- Viral/bacterial infections in chronic disease
- Smoking: effect of genotype on periodontitis

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

Central Nervous System Injury and Repair
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:
- Methylprednisolone and spinal cord injury: a new approach to an old therapy
- Reconstructing locomotor circuitry after spinal cord injury
- Human olfactory epithelium as a source of stem cells for CNS repair
- Cellular mechanisms of neuronal vulnerability to intermittent hypoxia
- Signaling pathways in neuronal apoptosis

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

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

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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:
- Studies of RILP and RILP-binding protein Dynactin P150 glued and huntingtin
- Structural studies of neuropilin signaling
- Deciphering the role of AMP-activated protein kinase (AMPK) in Lafora disease and Wolff-Parkinson-White syndrome
- Negative regulation of the yeast MRP, Ycf1p, and Human MRPs by CKII
- Mechanisms of peripheral regulatory T cell generation

Research Resources:
- Tissue culture and protein production core – tissue culture hoods and incubators for mammalian cell culture; fermenters, bioreactors, cell cracking equipment, and chromatography instrumentation for production of recombinant proteins
- Imaging core – three epifluorescence microscopes (Nikon Eclipse 600, Zeiss Axiovert 100 and 200M) with digital image capture capability (Spot CE and Orca ER digital cameras with Metaview and Open Lab software)
- Proteomics core – quantitative and qualitative protein profiling and identification analysis, as well as post-translational modification and sequence analysis through a combination of 2D gel, mass spectrometry and Edman sequencing analysis services; equipped with Bio-Rad IPG and SDS-PAGE apparatus for 2D gel analysis, a Typhoon phosphorimager/scanner system for detection and quantitation of fluorescent protein dyes, a Ciphergen SELDI-TOF protein profiling system, an ABI QSTAR II Q-TOF mass spectrometer with both MALDI and LC/ESI source capabilities, an ABI MALDI TOF TOF mass spectrometer, Waters HPLC systems and multiple PCs for data acquisition and analysis including a site license for PDQuest software and a five station site license for Ciphergen software
- Chemistry core – synthetic capabilities for the preparation of a variety of organic compounds to support research projects

Index Terms:
transcriptional regulation, cancer genes, signal transduction, diabetes, prostate cancer

COBRE in Molecular Targets
University of Louisville – P20 RR018733

Principal Investigator:
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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

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

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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
- Estradiol and LH-mediated regulation of ovarian function
- Transcriptional regulation of hormone action
- Interactions of estradiol and antidepressants in hippocampal neurogenesis
- Actions of estradiol and progesterone on behavior: clinical neuropharmacology

Research Resources:
- Magnetic resonance imaging core
- Transgenic mouse 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

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

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http://www.louisville.edu/hsc/birthdefectscenter/cobre/index.htm

Thematic Scientific Focus:
Molecular and cellular mechanisms controlling normal embryonic development and etiology of birth defects

Research Projects:
- Role of patched 1 and suppressor of fused in the ovary
- Regulation of neural crest cell migration by SDF1-CXCR4 signaling
- Role of TGF-ß modulators in vertebral development
- Molecular mechanisms of neural tube closure defects
- Pre- and postnatal tobacco smoke exposure: effects on neurocognitive development
- Infant age at the time of cleft palate repair: effects on language development

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, cardiovascular defects; neurocognitive development; oogenesis

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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:
- Pathogenesis of *Borrelia burgdorferi*
- Pathogenesis of Rickettsia species
- *M. Tuberculosis* SigH and its regulon in the immunopathology of tuberculosis
- Host response in HIV-1 & microsporidia coinfection

Research Resources:
Molecular biology and immunology core – providing DNA sequencing; library construction; microarray analysis; FACS analysis; confocal microscopy; live imaging microscopy; realtime PCR analysis; protein multiplex analysis
Non-human primate and laboratory core

Index Terms:
infectious diseases, non-human primate models, retrovirus, SIV, RSV, pathogenesis, host response

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:
- Persistent norovirus infection of lymphoid tissue impairs protective immunity
- 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

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

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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:
- Development of new adhesive fluoride-releasing monomers
- Effect of aging on periodontal disease
- Role of vacuole expansion in the oral pathogen *Candida albicans*
- Mechanisms behind CX3CL1-driven monocyte recruitment during periodontitis

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

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

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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:
- Phosphorylation in solid muscle tumor alveolar rhabdomyosarcoma
- Innovative therapies for T(4;11) leukemia
- ATR kinase and UV-induced cell cycle checkpoints
- Genetic instability, environmental activation of mobile elements
- Environmental cues, mesenchymal stem cells, tumor angiogenesis

Research Resources:
- Cell assay core – employs a series of devices for gene function, expression and mutagenesis assays

Index Terms:
cancer genetics, gene instability, gene regulation, tumors, leukemia, cell cycle, angiogenesis

Mentoring in Cardiovascular Biology
Louisiana State University Health Sciences Center – P20 RR018766

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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:
- Brain-targeted ACE2 over-expression and blood pressure regulation
- 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

Research Resources:
- Cell and molecular analysis core – cell culture and molecular biology services; real time PCR analysis; 2-D gel electrophoresis, mass spectroscopy
- Imaging and histology core – tissue processing, staining and pathology analysis
- 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

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

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

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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
- Commitment of adult stem cells into the adipocyte lineage
- Characterization of ubiquitin and ubiquitin-like modification of PPAR in Human Adipose-Derived Adult Stem (ADAS) Cells
- Mechanisms of aging-induced leptin resistance and obesity

Research Resources:
- Cell biology and bioimaging core – (http://labs.pbrc.edu/cellbiology/index.htm) Zeiss 510 META multiphoton confocal microscope, Zeiss Axioskop 40L microscope, Zeiss Axiovert 40 CFL microscope, Everest Imaging System built around a Zeiss Axioplan 2 microscope, Nikon TE2000 inverted microscope for live cell imaging, Molecular Devices FlexStation fluorometric plate reader, BD FACSCalibur flow cytometer (2 laser, 4 color)
- Genomics Core – (http://gcf.pbrc.edu) Applied Biosystems 3700 Genetic Analyzer, Applied Biosystems 3100 Genetic Analyzer, Packard Biosciences Scan Array System, Applied Biosystems 7700 & 7900 Real Time PCR Systems, Biomek FX robotic liquid handling workstation, GeneMachine OmniGrid Microarrayer

Index Terms:
insulin resistance, diabetes, obesity, metabolic syndrome, adipose tissue, adipogenesis

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:
- Tolerance mechanisms in head and neck cancer and approaches to overcome them
- Overcoming tumor tolerance through *in vivo* generated dendritic cells
- Alterations in T cell signal transduction caused by chronic inflammation in steroid-resistant idiopathic nephrotic syndrome
- Dendritic cells and immune response in corneal tissue
- Manipulation of lymphocyte homeostasis for enhancing anti-tumor immunity

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

Index Terms:
inflammation, host defense, immune response, T cells

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

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Thematic Scientific Focus:
Factors contributing to development of hypertension and subsequent consequences on renal and cardiovascular function

Research Projects:
- Angiotensin in distal nephron ontogeny
- Citrate transport in the proximal tubule
- Endothelial dysfunction, adipocytokines, inflammation, and chronic kidney disease
- Heme oxygenase in angiotensin II hypertension
- 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
- Tubular renin-angiotensin system in hypertension

Research Resources:
- Molecular, imaging & 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, and PTI Ratiomaster
- Transgenic and gene-targeted animal core – maintains 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

Center for Regenerative Medicine
Maine Medical Center Research Institute – P20 RR018789

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http://www.mmcri.org/cmm/stemCOBRE.html

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

Research Projects:
- Regenerative properties of nephrogenic mesenchyme
- EphB4 regulation of hematopoietic vs endothelial progenitor cell fate
- Genome instability and stem cell function in lymphomyeloid neoplasia
- pMesogenin and cristin/R-spondin regulation of mesodermal differentiation
- Role of WNT signaling in the preimplantation embryo
- Slug factor regulation of hematopoietic progenitor cell survival, and leukemogenesis

Research Resources:
- Progenitor cell isolation and analysis core – supports FACS and preparative MACS isolation of primary cell populations, flow cytometric (and Vicell) analyses; basic murine and human ES cell services
- Bioinformatics and genomics core – supports robotic DNA and RNA isolation, quantitative (RT) PCR, and project specific in silico array analyses
- Histopathology core – provides stained tissue sections via fixation, processing, embedding, sectioning, staining and coverslipping of paraffin or frozen tissue sections; staining ranges from H&E's to specific tissue stains for collagen, amyloid, bone, cartilage, vessels, kidney basement membranes, and hematopoietic cells; the core also offers immunohistochemical staining for general antibody sets

Index Terms:
stem and progenitor cell biology, cytokine signal transduction, nephron mesenchyme, endothelial, EphB4, R-spondin, mesoderm, genomic instability, hematopoiesis, leukemogenesis, Wnt signaling

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

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http://www.mmcri.org/cmm/vascularCOBRE.html

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
- 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

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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 – an animal brain collection focused on behavioral studies related to depression and its treatment
- 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

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

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www.olemiss.edu/cobre

Thematic Scientific Focus:
Identification and characterization of psychoactive properties of natural products

Research Projects:
- Mitragynine based opioid ligands
- THC pro-drugs for oral transmucosal delivery
- Isolation and characterization of minor constituents of *Cannabis*
- Natural product-derived HIF-1 inhibitors for neuroblastoma
- Antidepressant leads from marine derived natural products

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

Pesticide Toxicity to the Nervous and Endocrine Systems
Mississippi State University College of Veterinary Medicine – P20 RR017661

Principal Investigator:
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Thematic Scientific Focus:
Environmental health, focusing on toxicological effects of pesticides on mammalian nervous and endocrine systems and links between pesticide exposures and cancer incidence

Research Projects:
- Effect of organophosphate insecticides on brain development
- Epidemiology and exposure assessment of pesticides
- Molecular dynamics simulations of organophosphate inhibition of cholinesterase
- Pesticide metabolism by human enzymes
- Effects of dieldrin exposure on atrazine disposition
- Dieldrin-induced effects on esterase levels and expression

Research Resources:
- Bioanalytical core – liquid chromatography, gas chromatography, mass spectrometry
- Molecular biology/microscopy core – laser capture microdissection, stereology, PCR, gene expression

Index Terms:
environmental health, pesticide toxicity, neurotoxicity, environmental estrogens, developmental neurotoxicity, neurodegeneration, cancer, epidemiology, pesticide exposure assessment, computational chemistry, cardiovascular toxicity

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Montana

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

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Thematic Scientific Focus:
Effects of environmental agents on human health and disease, focusing on respiratory and immunotoxicology, neurotoxicology, molecular and genetic toxicology, and cardiovascular and developmental toxicology

Research Projects:
- Arsenic Toxicity causes vascular dysplasia, placental insufficiency and spontaneous abortion
- Cellular mechanisms of asbestos-induced autoimmunity
- SPARC and extracellular matrix production after amphibole exposure
- Evaluation of amphibole contamination in tree bark within Libby, Montana and transportation corridors throughout the Pacific Northwest
- Effects of Asbestos on T Cell Activation

Research Resources:
- Mass spectrometry and proteomics – LCT, QTOF, MALDI-DE, and inductively coupled plasma mass spectrometers
- Microarray – robotic arrayer, scanner, expression profiling, polymorphism detection
- Fluorescence imaging – confocal microscopes; flow cytometer and high-speed cell sorter; laser scanning cytometer with motorized stage for high-throughput scanning of microscope slide specimens; high-resolution CCD video and digital cameras
- Molecular histology – microtomes, cryostats, staining hoods, embedding equipment
- Analytical – analytical and preparative HPLC separations of peptides and nucleic acids
- Molecular computation – computer graphics workstations and software for modeling structure-function relationships, protein-ligand and protein-protein interactions
- Animal facility – includes surgical suites for rodents and large animals

Index Terms:
environmental health, toxicology, immunology, development, arsenic, lead, asbestos, woodsmoke, cardiovascular disease, oxidativestress, carcinogenesis, receptor signaling, macrophages

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

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http://cobre.montana.edu

Thematic Scientific Focus:
The pathogenesis of zoonotic diseases, and the development of immunotherapies to diseases that affect man, livestock and wildlife

Research Projects:
- Host-parasite communication in *Toxoplasma gondii*
- Metal uptake and regulation in *Streptococcus pyogenes*
- *Aspergillus fumigatus* alcohol fermentation and pathogenesis in response to hypoxia
- Role of copper in prion diseases
- The saeR/S system of *Staphylococcus aureus*: sensing and responding to innate immunity

Research Resources:
- Genomics and proteomics core – technical expertise and training for reagent development in genomics, e.g., nucleic acid isolation, genetic library construction, and probes for conventional and microarray hybridization and proteomics; computer assisted analysis of genomic and proteomic data
- Cell analysis core – flow cytometry and confocal microscopy services
- Biosafety lab core – facilities and expertise for investigators studying diseases that require either small or large animal biocontainment

Index Terms:
zoonotic diseases, infectious agents, *Toxoplasma gondii*, *Streptococcus pyogenes*, Aspergillosis, prions, *Staphylococcus aureus*, bacterial pathogenesis, fungal pathogenesis, innate immunity, genomics

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:
- Glutathione: linking DNA repair regulation and neuronal vulnerability
- Cholinergic modulation of hippocampal interneuron subtypes

Research Resources:
- Mass spectrometry and proteomics core – Micromass LCT mass spectrometer; Micromass QTOF Micro mass spectrometer; Applied Biosystems MALDI mass spectrometer; Waters capillary liquid chromatograph; Waters HPLC 2790XE; Biorad robotic spot cutter
- Core laboratory for biospectroscopy – two ultra-fast Ti:Sapphire lasers for time-resolved spectroscopy and imaging; SPEX fluorometer; Hitachi absorption spectrometer; fluorescence microscope and scan-head for multi-photon imaging
- Molecular histology and fluorescence imaging core – includes microtomes, cryostats, auto-stainer, tissue processor, and embedding center for histology; the light/epifluor microscope with DIC optics is equipped with Nuance multispectral imaging software and the BioRad confocal microscope has three lasers for imaging
- Molecular computational core – supercomputer arrays linked to 3D graphics workstations with software for modeling structure-function relationships, protein-ligand and protein-protein interactions
- Animal facility – AAALAC certified facility includes SPF facilities and surgical suites for rodents and large animals

Index Terms:
anxiety, central nervous system, depression, hearing, molecular modeling, neurological diseases, neurophysiology, neuroscience, obsessive-compulsive disorder, prion diseases, protein function, protein structure, proteomics, spectroscopy

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Nebraska

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

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http://www.unmc.edu/dept/moleculargenetics/index.cfm?L2_ID=10&L1_ID=2&CONREF=8

Thematic Scientific Focus:
The molecular mechanisms that underlie neurosensory disorders, and the optimal means of intervention

Research Projects:
- Test the hypotheses that epidermal growth factor receptor (EGFR) signaling is required for proper development of the peripheral nervous system (PNS) and that interactions between neural and target cells regulate PNS development
- Examine the processes involved in the repair of the central and peripheral nervous systems following virus-induced damage to the myelin of the spinal cord and sciatic nerves
- Identify and characterize the genetic/biochemical pathways regulated by microphthalmia-associated transcription factor (MITF) in development of the retinal pigment epithelium (RPE) and in the stria vascularis of the inner ear; including deducing the function of MITF in cell fate determination in the RPE and stria, its response to endothelial growth factors, and its role in modulating oxidative stress
- Demonstrate the role of OC90 in bodily balancing, in limiting otoconia formation to the inner ear, and in maintaining proper otoconia concentration

Research Resources:
- Mouse genome engineering core – expertise in the construction of transgenic and knockout mice
- Histology core – specialized morphological and histological analysis of neurosensory development; phenotyping services
- DNA microarray core – services to determine global gene expression patterns, transcriptional profiling and DNA-protein interactions

Index Terms:
neurosensory disorders, central nervous system, peripheral nervous system, epidermal growth factor receptor, nerve repair, inner ear development, balance control, otoconia

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

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http://www.unmc.edu/dentistry/research/nccs/nccs.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:
- DNA damage-dependent activation of ATR signaling by RPA
- Regulation of cell survival signaling by the myotubularin phosphoinositide phosphatase
- The function of BTB-CUL3 ligases in mitosis
- Regulation of Aurora-A kinase activities by Aurora-A interacting proteins

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

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 viruses and host responses involved in disease pathogenesis

Research Projects:
- Cellular mechanisms for HIV-1-induced neuronal injury
- Neurodegeneration and neurorestitution in murine HIV-1 encephalitis
- Inhibition of apoptosis by alphaherpesvirus latency-associated transcript
- Host cell contributions to retroviral assembly
- Herpes virus and cell interactions
- RNA virus genome replication and virus assembly
- Proteomics analysis of HIV-1-infected macrophages
- Replication of human papillomaviruses

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

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
- Mammalian proline metabolism and oxidative stress
- Function and regulation of the parkinsonism-associated protein DJ-1
- Redox coordinated extracellular matrix remodeling in cancer
- The redox-mediated regulation of iron-responsive gene expression in the liver
- Thiol-dependent redox processes and thiol-based signaling
- Structure/function relationships in enzymes involved in glutathione synthesis and recovery
- Mammalian copper transport homeostasis and its defects
- Bioinformatics of oxidoreductases

Research Resources:
- Metabolomics and macromolecular analysis core – ABI 4000 Qtrap (quadrupole ion trap); Q-Star XL ASBI (quadrapole-TOF) tandem mass spectrometers equipped with ESI (microspray and nanospray) and APCI sources; nano flow LC Packings UltiMate and micro flow Shimatzu HPLC systems for LC-MS or LC-MS/MS analysis of complex analytes mixtures—gel-based or in-solution proteins are digested and analyzed using LC MS/MS; proteins are identified using in-house Mascot database search; 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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http://www.unr.edu/med/dept/pharmacology/COBRE

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

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

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http://www.physio.unr.edu/index.asp

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:
- Understand the functional roles of the a7b1-integrin in regulating vascular smooth muscle plasticity and in vascular disease
- Elucidate the physiological significance of the tissue-specific expression of the subunit isoforms (a,b,d,g) comprising the multifunctional Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII)
- Examine the physiological changes that occur during obstructive bowel disease; specifically, analyze the hypertrophic changes in the neuronal circuits and chemical coding of specific classes of enteric neurons
- Characterize stretch-dependent potassium channels (SDK) in the bladder to understand the physiological basis for filling mechanisms and pathological distension

Research Resources:
- Molecular expression and transgenic core – coordinates the procurement and maintenance of mouse transgenic lines; provides adenoviral gene transfer vectors and protein transduction reagents; assesses mRNA and protein expression for all projects by RT-PCR and western blotting
- Cell proteomics interface facility – provides computational expertise in analyzing protein structures and experimental expertise in the isolation, purification and subsequent analysis of proteins, including mass spectrometry
- Dynamic imaging facility – provides expertise in fluorescent imaging; employs a high speed fluorescent imaging system and a ratio metric (Fura 2-AM) imaging system for use with pressurized blood vessels and isolated cells

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

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

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http://www.dartmouth.edu/dms/cobre/

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:
- Mechanisms of immunopathology in influenza pneumonia
- Scavenger receptor function in chaperone-elicited adaptive immune responses
- Vascular Leukocytes: Basic Immunobiology and Functional Plasticity
- Role of the chromatin regulator, MLL, in T cell development

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

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:
- The maintenance of fetal maternal tolerance in marsupials
- The spontaneous rate of gene duplication and deletion
- Mathematical modeling of signal transduction by a TIR receptor
- Computational quantitative modeling of RNA interference
- Modeling of immune responses in infectious diseases
- Diverse recognition capability: an invertebrate model
- Expression profiling of defense and stress related genes of *Schistosoma mansoni*

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
- Mass Spectrometry Facility – Micromass LCT TOFof for exact mass measurements ; Two Finnigan TSQ instruments, one for GC separation; Ciphergen SELDI-TOF; AB 4700 MALDI TOF-TOF, with MS/MS capabilities, with 2D-LC and spotting robot; AB Q-Star electrospray ionization mass spectrometer

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

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

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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:
- Mechanisms of ischemic brain injury mediated by free radicals
- Mechanisms of delayed cell death following injury to the central nervous system
- Characterization of intracerebral hemorrhage in a piglet brain model system
- Generators of human frontal lobe epilepsy

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 reactive oxygen species
- Magneto- and electroencephalography core – high-resolution MEG systems (microSQUID and 64-channel EEG systems) for non-invasive monitoring of brain electrophysiological activities
- Optical imaging core – 2-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

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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 laboratory – supports functional neuroimaging approaches to the scientific themes of the center projects; twin state-of-the-art 168-channel EEG data acquisition and analysis systems housed in electromagnetically-shielded recording chambers; gigabit intranet connectivity with a terabyte data storage array and several high-performance EEG analysis workstations
- DriveSafety DS-600c research driving simulator – 300 degree wrap-around display, fully instrumented research driving simulator with real-time motion simulation via integrated force-platform.

Index Terms:
visual processing, eye control, visual neural activity, cognition

Center for Protease Research
North Dakota State University – P20 RR015566

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Thematic Scientific Focus:
Novel strategies for targeting human diseases through protease inhibition, starting with *in vitro* cellular interactions and continuing through stages of lead product synthesis to drug design and delivery

Research Projects:
- Synthesis of inhibitors of matrix metalloproteinases, serine proteases, urokinase and plasmin
- Targeting and delivery of matrix metalloproteinase inhibitors
- Biopharmaceuticals: computational methods and quantitative structure-time-activity relationships

Research Resources:
- Mass spectral facility – Bio-TOF III high resolution mass spectrometer and Esquire 3000 MS/MS system
- Microscopy facility – confocal microscope

Index Terms:
drug design, cancer, drug delivery, arthritis, multiple sclerosis, osteoporosis, Alzheimer's disease

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

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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 – Hitachi transmission and scanning electron microscopes; Olympus FluoView 300 laser scanning confocal microscope; Zeiss 510 Meta confocal microscope (seven fluorescent channels, one DIC channel); ConfoCor2 fluorescence correlation spectroscopy unit; Axiovert200 microscope with AxioCam HRM digital camera; computer workstation and software for image data processing and analysis

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:
- Further develop an understanding of how clinically relevant biofilm forming bacteria influence the behavior and metabolism of host tissue cells
- Investigate the effect of dental restorative treatments on biofilm accumulation
- Analyze the differences on global gene expression of *Streptococcus mutans* exposed to different dietary sugars to gather information on how gene expression patterns vary under sessile or planktonic conditions
- Identify the processes needed for attachment and biofilm formation in *Actinobacillus actinomycetemcomitans* and evaluate their impact on pathogenesis and persistence in the oral cavity

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

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

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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
- Bdellocyst 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

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
- Genetic and environmental contributions to diabetes in Oklahoma American Indians
- Regulation of oxidative stress and inflammation in diabetic retinopathy
- The role of ubiquitin in hyperglycemia-induced mesangial cell hypertrophy

Research Resources:
Administrative core – to coordinate COBRE activities and budget
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

Mentoring Immunology in Oklahoma: A Biomedical Program
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
- Neutrophil phenotyping in periodic and chronic arthritis
- Studies on immunotherapy for Alzheimer's disease
- APC rafts in antigen presentation
- Human B cells bearing IgVh4-34+ BCRS

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; Perkin-Elmer LS-50 spectrofluorimeter; Roche Lumi-imager for immuno-detection and quantification of proteins and nucleic acids on filters; BioRad medium-pressure chromatography system; Hunter thin layer electrophoresis apparatus; Molecular Dynamics Storm System for radiolabel quantification; transient transfection services
- Imaging core – Hitachi H-7600 transmission electron microscope; Zeiss Axiovert 200 inverted fluorescence microscope; Zeiss Axiostar upright microscope
- Peptide synthesis core – custom synthetic peptides for biochemical studies and solid-phase peptide epitope mapping experiments
- Microinjection core – production of transgenic and gene-targeted mice by zygote injection and injection of embryonic stem cells into blastocysts; rederivation of mouse strains; two inverted microscopes with Hoffman DIC and phase contrast optics, fitted with Narishige fine and coarse micromanipulators for embryo manipulation and a cooling stage for ES cells injections; three surgical microscopes (Nikon SMZ-2T, Nikon SMZ-U); deFonbrune microforge; Sutter P-97 pipette puller; laminar flow cell culture hood; CO2 incubator; inverted light microscope

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

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

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Thematic Scientific Focus:
Basic visual research with an emphasis on studying the retina and retinal diseases

Research Projects:
- The role of the interleukin-6 cytokine family receptor gp130 in diabetes complications
- Structure and function of cone cyclic nucleotide-gated channel
- *In vivo* role of caveolin-1 in modulating photoreceptor function
- Understanding the role of the retinol dehydrogenases RDH11 and RDH12 in vision
- Sphingolipid metabolism in the retina

Research Resources:
- Proteomics/bioinformatics core
- Image acquisition and production core
- Molecular biology/functional genomics 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

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

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Thematic Scientific Focus:
The molecular and genetic basis for autoimmune diseases

Research Projects:
- Discovery and testing of Novel Immunological Genes
- Characterization of IRF8 as a lupus susceptibility gene
- Estrogen receptor regulation of dendritic cells in homeostasis and autoimmunity
- Effects of lupus genetic susceptibility variants on B cell gene expression
- Functional manifestations of SLE risk haplotypes on EBV infection and related stimuli

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

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 Nikon ECLIPSE E600-FN intravital epifluorescence microscope with water immersion objectives connected to a Dage-MTI DC-330 3CCD color camera, a SVHS video cassette recorder, and a Microvessel Velocity OD-RT Doppler apparatus; Nikon SMZ800 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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Puerto Rico

Center for Molecular, Developmental and Behavioral Neuroscience
University of Puerto Rico Medical Sciences – P20 RR015565

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Thematic Scientific Focus:
Molecular mechanisms underlying neuronal injury, emotional memory, cocaine-seeking behavior, and the expression of maternal behavior

Research Projects:
- P2Y2 nucleotide receptor in ischemia
- Genomic basis of emotional learning and memory
- Neuropeptide modulation and gene expression in cocaine seeking behavior
- Neurosteroid effects in the structure and function of a sexually dimorphic network

Research Resources:
- Research core – DNA microarray instrumentation

Index Terms:
DNA microarray, neuroscience, stroke, ischemia, neuronal injury, molecular biology, schizophrenia, anxiety, memory, genomics, proteomics, drug abuse, endocrinology

UPR Protein Research Center
University of Puerto Rico, Mayaguez – P20 RR016439

Principal Investigator:
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http://cobre2.uprm.edu/

Thematic Scientific Focus:
Fundamental protein chemistry, proteomics and genomics, using x-ray diffraction, proteomic mass spectrometry, and computational techniques

Research Projects:
- Biophysics of unusual hemoglobins that show functions other than reversible oxygen binding
- The correlation between biophysical structure of an enzyme and its function
- Protein structure and function in unusual chemical settings (drug delivery systems)

Research Resources:
- Computational facilities – capable of protein dynamics simulations
- X-ray crystallography facilities
- Proteomic mass spectrometry facilities
- FT-IR/RAMAN facilities
- Light scattering facilities
- Circular dichroism (CD) facilities
- Transient kinetics: flash photolysis, stopped-flow spectrophotometry

Index Terms:
proteomics, genomics, protein chemistry, protein structure, protein function, enzymology, proteomic mass spectrometry, x-ray diffraction, biophysics, drug delivery

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Rhode Island

Center for Cancer Research Development
Rhode Island Hospital – P20 RR017695

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Thematic Scientific Focus:
Molecular targets for cancer intervention

Research Projects:
- Biomarkers for predicting response to therapy, prognosis, staging
- Targets for molecular intervention using siRNA, specific inhibitors
- Targeting signaling pathways that increase sensitivity to conventional treatments
- Molecular pathways targeted by environmental, physiological, or infectious agents

Research Resources:
- Proteomics Core – Bio-Rad/Ciphergen protein chip analyzer, HPLC expertise and ABS mass spectrometry system: makes state-of-the-art protein and analysis/purification instrumentation and techniques available for specific research projects; 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; 1250 ft^2 facility is equipped with an Aperio ScanScope digital tissue scanner, Arcturus AutoPix automated laser capture microdissection instrument, Olympus BX41 with CoolSnap Camera from Media Cybernetics and Image Pro-Plus Software, Stratagene MX4000 quantitative real-time PCR system, BioRad iCycler, Agilent BioAnalyser, Ventana Discovery automated immunohistochemistry processor, microtome and cryostat, Beecher tissue arrayer, and 40 ft^3 of -80°C 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, signal transduction

Center for Genomics and Proteomics
Brown University – P20 RR015578

Principal Investigator:
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http://www.brown.edu/Research/CGP/

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
- Functional studies of E3 ubiquitin ligase
- Genetic damage by lipid peroxidation
- Supv3L1 helicase knockout mouse
- Bayesian inferences of cis-regulatory modules and signal transduction pathways

Research Resources:
- Transgenic and knockout mouse facility
- Flow cytometry core
- Confocal imaging 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

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

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http://bms.brown.edu/COBRE/

Thematic Scientific Focus:
The molecular basis of cardiopulmonary signal transduction and development during fetal and postnatal life

Research Projects:
- Determine the role of the cell cycle inhibitor p57KIP2 in ventricular myocyte differentiation
- Elucidate the signaling pathways that regulate cardiomyocyte proliferation
- Identify the mechanotransduction mechanisms that regulate lung alveolar differentiation
- Define the role of Fas-mediated apoptosis in perinatal lung remodeling

Research Resources:
- Molecular biology and histology core – radiographic imaging, multifluorescent 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

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

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http://www.lifespan.org/rih/services/cobre_cshr/default.htm

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
- Molecular Biology and Imaging core

Index Terms:
Cartilage, bone, growth plate, skeletal dysplasia, joint degeneration, osteoarthritis, chondrosarcoma, angiogenesis, tissue engineering

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:
- MoFlo high speed cell sorter from Cytomation, BD FACS scan and BD FACS caliber
- Zeiss fluorescent motor-driven microscopes: upright Axioplan 2, inverted Axiovert 200M, Zeiss 510 confocal laser-scanning microscope capable of four-color imaging
- IVIS system for live imaging
- Genepix 4200A microarray scanner with three lasers
- IncuCyte time lapse photography system

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

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South Carolina

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

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Thematic Scientific Focus:
Molecular, biochemical, genetic, and lifestyle factors that affect colorectal cancer and its treatment

Research Projects:
- The role of C-MYC in neovascularization and intestinal cancer
- Genetic alterations that drive colorectal cancer metastasis
- Regulation of cyclooxygenase expression in intestinal neoplasia
- Novel biosensors for detection of colon cancer
- The nature and role of the microbiome in mouse models of colon cancer
- Community-based colorectal cancer prevention in South Carolina

Research Resources:
- Animal/mouse core
- Histology/imaging core
- Pathology core – pathologic tissue diagnosis with detailed description, image illustration, and pathologic consulting for immunohistochemistry, digital quantitation, tissue microarray analysis, and tissue microdissection
- Biometry core – statistical support and new statistical methods

Index Terms:
colon cancer, cell biology, DNA repair, apoptosis, inflammation, cellular proliferation, chemotherapy, chemoprevention, nutrition, epidemiology

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

Principal Investigator:
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http://biochemistry.musc.edu/cobre/

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 and impact on chemotherapy
- ATP-binding cassette transporter-2 (ABCA2) regulation of APP processing
- Modeling the roles of bioactive lipids in gene expression systems
- Protein-lipid interactions: structural analysis of *Pseudomonas aerufinosa* ceramidase

Research Resources:
- Lipidomics core – expertise, analysis and synthetic molecular tools to perform research in sphingolipidomics; conceptual and practical training in various aspects of lipidology, qualitative and quantitative analysis of more then 80 distinct sphingolipid components (metabolomic profile) from different biological materials (cells, tissue, and biological fluids) employing high performance liquid chromatography-tandem mass spectrometry (LC-MS/MS) technology; synthetic molecular tools to study lipid metabolism and diversified synthetic lipids and analogs for cellular *in vitro* and *in vivo* studies (e.g., organelle-targeted sphingolipids and organelle-targeted inhibitors of sphingolipid metabolizing enzymes)
- 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

South Carolina COBRE for Cardiovascular Disease
Medical University of South Carolina – P20 RR016434

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http://cba.musc.edu/COBRE/index.htm

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

Research Resources:
- Transgenic mice core
- Imaging core
- DNA microarray core
- Proteomics core

Index Terms:
cardiovascular disease, proteomics, genomics, apoptosis, cell biology, DNA microarray

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:
- Epidemiology of oral disease and diabetes: cytokine genes and inflammation
- Oral health in African American adolescents with diabetes in rural areas
- *Candida albicans*-associated oral biofilms
- Metastasis-associated proteins in oral and head and neck cancer
- Role of the extracellular matrix in oral cancer
- Oral cancer prevention by dietary flavonoids: role of salivary beta-glucosidase

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 methods for proteomics research
- 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 (including genotype analysis, laser scanning cytometry, and SearchLight proteome multiplex ELISA arrays)

Index Terms:
oral health, periodontal disease, cytokines, diabetes, oral cancer, genetic polymorphisms, health disparities, health education intervention

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South Dakota

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

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http://www.usd.edu/neurogroup/COBRE.cfm

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 tolloid-like 1 expression in the hippocampus

Research Resources:
- Biological imaging core – Olympus FluoView 500 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
- Behavioral core – Noldus Ethovision video tracking system; ObserverXT data analysis system; watermaze, elevated plus maze, 8 arm radial maze

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

Mechanisms of Cardiovascular Remodeling
University of South Dakota School of Medicine – P20 RR017662

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Thematic Scientific Focus:
Multi-disciplinary, highly integrated, approach toward understanding cardiovascular disease

Research Projects:
- α1-adrenergic receptor signaling and cardiac remodeling
- Integrin signaling in dilated cardiomyopathy
- Mechanisms of doxorubicin induced heart failure
- Myotonic dystrophy protein kinase in myocyte development
- Thyroid hormone regulation of vascular growth

Research Resources:
- Physiology testing core
- Cell culture core
- Molecular biology core
- Cell imaging core

Index Terms:
cardiovascular disease, heart failure, remodeling, signal transduction, α1-adrenergic receptors, integrins, cardiotoxicity, myotonic dystrophy, thyroid hormones, dystrophin complex, sarcoglycan, dystroglycan, molecular biology, autophagy, apoptosis, angiogenesis

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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 – Noran laser scanning confocal microscope; DeltaVision Restoration microscopy system; BioRad Radiance dedicated multiphoton confocal microscope; Nikon TIRF (total-internal reflection fluorescence) microscope; Nikon/Sutter ratiometric imaging system with patch-clamp capability; and Andor imaging workstation with EMCCD camera and Andor iQ-CORE
- Cellular and molecular biology core – Zeiss Palm microlaser dissection system; Ciphergen SELDI-TOF mass spectrometer for biomarker analysis; two Applied Biosystems 7500 Fast quantitative real-time PCR systems; LI-COR Odyssey infrared imaging system for multicolor Western blotting; BioRad Calligrapher array printer for printing antibody/protein/RNA/DNA arrays; Nanodrop spectophotometer; Biorad Chemidoc XRS gel documentation system; Microbrightfield Neurolucida neuroanatomical analysis system for 3D measurements, neuron tracing and morphometrics; and 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

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

Principal Investigator:
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Thematic Scientific Focus:
Translating basic laboratory research into clinical applications to fight lung disease, while creating a stimulating research environment for promising new investigators

Research Projects:
- Airway epithelial signaling cascades evoked by nitrogen dioxide
- Airway parenchymal mechanical dysfunction in asthma
- Role of altered pulmonary proteolysis in pathogenesis of asthma
- Th2 mediated airway inflammation in the delta-f508 mouse

Research Resources:
- Transgenic animal core
- Biomedical engineering core

Index Terms:
physiology, lungs, asthma, biomedical engineering, transgenic animals, signaling, inflammation

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

Principal Investigator:
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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

Research Resources:
- Microarray and Bioinformatics core – Affymetrix GeneChip 2500 system that includes Hybridization Station 640, Fluidics Station 400 and Scanner 2500; Agilant 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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http://www.hsc.wvu.edu/mbrcc/research/cobre.asp

Thematic Scientific Focus:
Molecular changes in cell signaling proteins that occur in cancer; the relationship between cancer cell growth, metastasis, and signal transduction, using proteomics

Research Projects:
- SHP2-mediated cross talk between the EGFr/HER2 and WNT Signaling
- A novel computational model system for constructing molecular classifiers of human cancers
- A novel tumor suppressor gene
- Role of cortactin in head and neck cancer
- Caveolin polarity and endothelial cell migration
- VE-cadherin trafficking and angiogenesis

Research Resources:
- Flow cytometry core
- Mass spectrometry core

Index Terms:
cell biology, molecular biology, proteomics, cancer, signaling, angiogenesis

COBRE in Sensory Neuroscience
West Virginia University – P20 RR015574

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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:
- Spatio-temporal encoding of odor
- fMRI of auditory attention to complex environmental sounds
- Functional convergence in visual cortex
- Regulation of intracellular transducin homeostasis by phosducin in vertebrate rods
- Genetics of ocular disease
- Role of AIPL1 in inherited retinal neurodegenerative disease

Research Resources:
- Histology core
- Non-linear optical imaging core
- Transgenic animal core
- Molecular biology core (Affymetrix genechip reader)
- Center for Advanced Imaging

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

Transcription Factors in Cancer
Marshall University – P20 RR020180

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Thematic Scientific Focus:
The role of transcription factors in promoting cancer, with an emphasis on the function of retinoids or their signaling pathways as a unifying focus

Research Projects:
- β-catenin function and retinoic acid in melanoma
- Retinoids, NF-κβ and superoxide dismutase in neuroblastoma
- Sap, a potential zebrafish oncogene
- Ski and Sno transcription factors in testicular cancers

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

Index Terms:
retinoids, transcription factors, 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 – real time PCR; nitric oxide analyzer; Versadoc 3000 imaging system with phosphoimager; atrix assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry; Agilent 8453 UV-Vis spectrophotometer
- Microscopy imaging facility – Hatachi TEM with 4K by 4K cooled CCD digital camera (Gatan); Leica and BioRad laser scanning microscopes; epifluorescent microscopes; scanning electron microscope

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

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