



National Institute of
General Medical Sciences



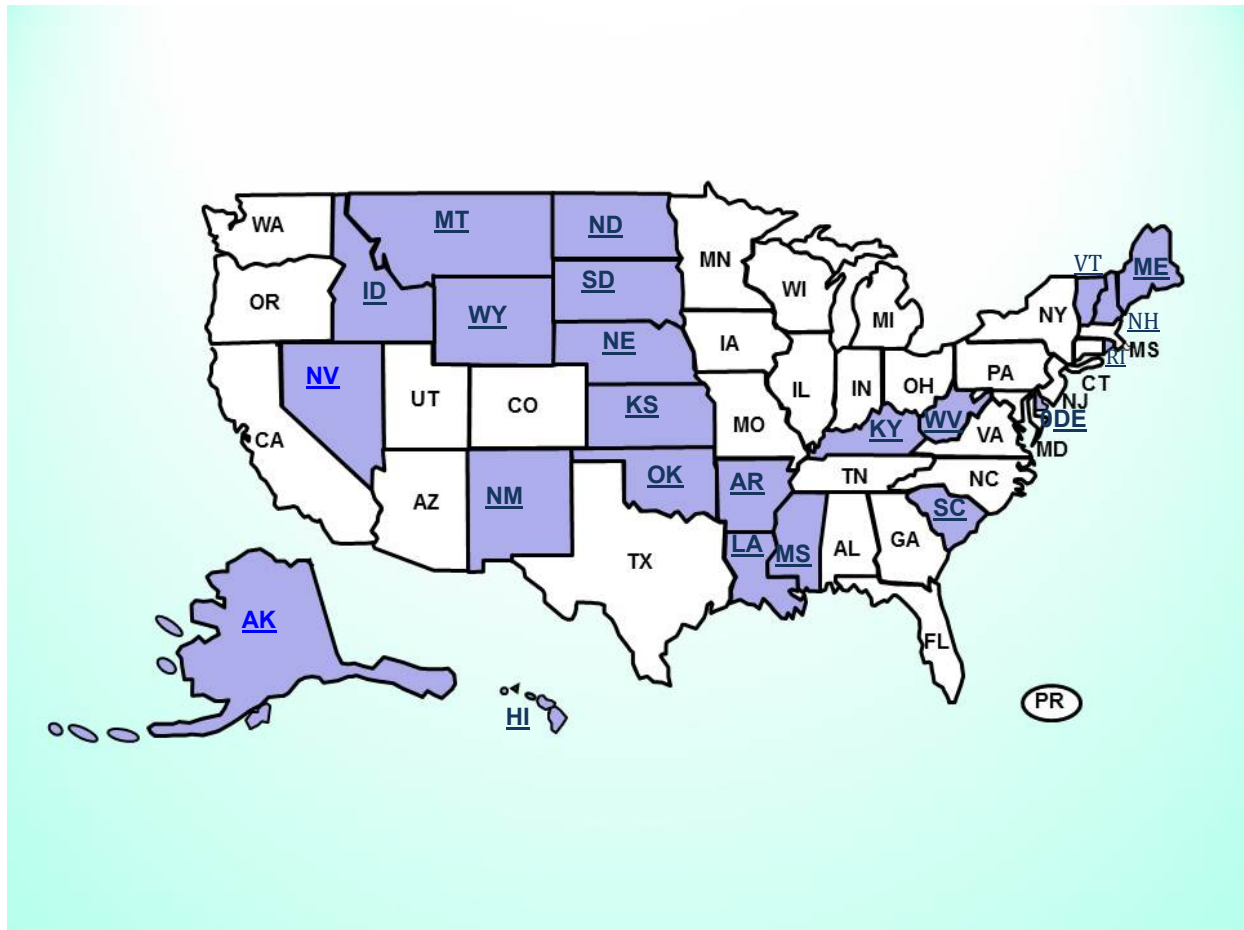
Centers of Biomedical Research Excellence (COBRE)

Directory of Active Awards By State

***Institutional Development Program (IDeA)
Capacity Building Branch
Training, Workforce Development, and Diversity Division
NIGMS, NIH***

December 2012

Map of COBRE States



Ctrl+ Click on 2-letter state abbreviation to view COBRE program.

Centers of Biomedical Research Excellence (COBRE) augment and strengthen institutional biomedical research capabilities by expanding and developing biomedical faculty research capability through support of a multidisciplinary center, led by a peer-reviewed, NIH-funded investigator with expertise central to the theme of the grant proposal.

Table of Contents

<u>State/Principal Investigator</u>	<u>Page</u>	<u>State/Principal Investigator</u>	<u>Page</u>
Alaska	3	Nebraska	56
<u>Boyer, Bert B.</u>	3	<u>Becker, Donald</u>	56
Arkansas	4	<u>Bronich, Tatiana</u>	57
<u>Garcia-Rill, Edgar E.</u>	4	<u>Johnson, Keith R.</u>	58
<u>Millett, Francis S.</u>	5	<u>Smith, Shelley D.</u>	59
<u>Smeltzer, Mark S.</u>	6	<u>Wood, Charles</u>	61
<u>Beebe, Thomas P.</u>	7	Nevada	62
Delaware	9	<u>Sanders, Kenton M.</u>	62
<u>Buchanan, Thomas S.</u>	9	<u>Von Bartheld, Christopher S.</u>	64
<u>Harrington, Melissa A.</u>	10	<u>Webster, Michael A.</u>	65
<u>Lenhoff, Abraham M.</u>	11	New Hampshire	66
<u>Shaffer, Thomas H.</u>	12	<u>Green, William R.</u>	66
Hawaii	13	<u>Moore, Jason H.</u>	67
<u>Shohet, Ralph V.</u>	13	<u>Stanton, Bruce A.</u>	68
<u>Ward, William Steven</u>	14	New Mexico	69
<u>Yanagihara, Richard</u>	15	<u>Calhoun, Vince</u>	69
Idaho	16	<u>Loker, Eric S.</u>	70
<u>Forney, Larry J.</u>	16	<u>Liu, Ke Jian</u>	71
Kansas	17	North Dakota	72
<u>Abrahamson, Dale R.</u>	17	<u>Geiger, Jonathan D.</u>	72
<u>Hanzlik, Robert P.</u>	18	<u>McCourt, Mark E.</u>	73
<u>Jaeschke, Hartmut</u>	19	<u>Sibi, Mukund P.</u>	75
<u>Lunte, Susan</u>	20	Oklahoma	76
<u>Lutkenhaus, Joe</u>	21	<u>Anderson, Robert E.</u>	76
<u>Marcus, Daniel C.</u>	23	<u>Dhanasekaran, Danny N.</u>	77
<u>Timmerman, Barbara N.</u>	24	<u>Gaffney, Patrick M.</u>	78
Kentucky	25	<u>James, Judith</u>	80
<u>Bhatnagar, Aruni</u>	25	<u>Ma, Jian-Xing (Jay)</u>	82
<u>Cassis, Lisa</u>	26	<u>McEver, Rodger P</u>	83
<u>Ebersole, Jeffrey L.</u>	27	<u>West, Ann</u>	84
<u>Greene, Robert M.</u>	28	Rhode Island	85
<u>Hersh, Louis B.</u>	29	<u>Atwood, Walter J.</u>	85
<u>Miller, Donald M.</u>	31	<u>Chen, Qian</u>	87
<u>Whittemore, Scott R.</u>	32	<u>Falanga, Vincent</u>	88
Louisiana	33	<u>Padbury, James F.</u>	89
<u>Bazan, Nicolas G.</u>	33	<u>Quesenberry, Peter J.</u>	90
<u>Cefalu, William T. (IDeA-CTR)</u>	34	<u>Ramratnam, Bharat</u>	91
<u>Deininger, Prescott L.</u>	36	South Carolina	92
<u>Gettys, Thomas W.</u>	37	<u>Kirkwood, Keith L.</u>	92
<u>Jazwinski, S. Michal</u>	38	<u>Markwald, Roger R.</u>	93
<u>Kapusta, Daniel R.</u>	39	<u>Nagarkatti, Prakash S.</u>	94
<u>Kousoulas, Konstantin G.</u>	41	<u>Ogretmen, Besim</u>	95
<u>Navar, Luis Gabriel</u>	42	<u>Tew, Kenneth D.</u>	96
<u>O'Callaghan, Dennis J.</u>	44	<u>Vyavahare, Naren R.</u>	97
<u>Ochoa, Augusto C.</u>	45	South Dakota	99
Maine	46	<u>Miskimins, W. Keith</u>	99
<u>Friesel, Robert E.</u>	46	<u>Rabinovitch, Alex</u>	100
<u>Meng, Ian</u>	47	Vermont	101
<u>Wojchowski, Don M.</u>	48	<u>Budd, Ralph C.</u>	101
Mississippi	50	<u>Irvin, Charles G.</u>	102
<u>Cutler, Stephen J.</u>	50	<u>Parsons, Rodney L.</u>	103
<u>Stockmeier, Craig A.</u>	51	West Virginia	104
Montana	52	<u>Gibson, Laura F.</u>	104
<u>Dratz, Edward A.</u>	52	<u>Spirou, George A.</u>	105
<u>Holian, Andrij</u>	53	<u>Sundaram, Uma (IDeA CTR)</u>	106
<u>Quinn, Mark T.</u>	54	Wyoming	108
<u>Sprang, Stephen R.</u>	55	<u>Flynn, Francis W.</u>	108

ALASKA

P30GM103325- Phase 3

Investigating Obesity and Chronic Disease-Related Risk Factors of Alaska Natives University of Alaska Fairbanks

Principal Investigator

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Thematic Scientific Focus

The prevention and treatment of obesity and metabolic disease, youth suicide and substance abuse among Alaska Native people, utilizing a community-based participatory research framework

Research Projects

- Currently in Phase III - no direct funding for research projects

Research Resources

- Experimental design, biostatistics and data services core
- Community engagement and clinical support core
- Nutrition and physical activity core

Index Terms

Alaska Native, obesity, metabolic disease, suicide, substance abuse, community-based participatory research

[Back to top](#)

Arkansas

P20GM103425- Phase 2
Center for Translational Neuroscience
University of Arkansas for Medical Sciences

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Thematic Scientific Focus

Establishment of a broad-based translational neuroscience research center

Research Projects

- A double-blind, placebo-controlled trial of modafinil in OEF/OIF combat veterans
- Nrf2/ARE signaling pathway and its implication for Amyotrophic Lateral Sclerosis
- Biomarkers of early brain injury in neonates with congenital heart disease
- Resting state brain activity to learn how rTMS mitigates phantom sound perception, preventing long term consequences of neonatal pain

Research Resources

- Human electrophysiology core
- Animal electrophysiology core
- Image analysis
- Transcranial Magnetic Stimulation (TMS) core
- Molecular biology core
- Behavioral core
- Telemedicine core

Index Terms

pediatric diseases, neurological disorders, psychiatric disorders, cardiovascular diseases

[Back to top](#)

Arkansas

P30GM103450- Phase 3

**Center for Protein Structure and Function
University of Arkansas at Fayetteville**

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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 Rigaku diffractometers with Saturn92 CCD detectors; robotic protein crystallization facility
- Mass spectrometry core – IonSpec 9.4 Tesla FTMS Fourier transform mass spectrometer equipped with MALDI and ESI sources; five other mass spectrometers
- Large-scale protein production facility – four Applikon bioreactors and ancillary equipment; Applied Biosystems protein 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

[Back to top](#)

Arkansas

P20GM103625- Phase 1

University of Arkansas for Medical Sciences

Center for Microbial Pathogenesis and Host Inflammatory Responses

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Thematic Scientific Focus

Understanding the dynamic interaction between human hosts and diverse microbial pathogens and its impact on disease processes

Research Projects

- Virus-host interactions in gammaherpesvirus pathogenesis
- Regulation of T-cell memory in chlamydial genital infection
- Plasma cells as antigen-presenting cells during malaria
- Mechanisms of reovirus cell killing for enhanced oncolytics

Research Resources

- The Administrative and Scientific Development Core A, with the support of internal and external advisory committees, provides administrative and fiscal support to all project leaders, fosters scientific growth through mentoring and faculty development, and fosters scientific growth and expansion of the center through the recruitment of new investigators
- The Research and Technical Advancement Core B provides direct scientific support through upgraded research instrumentation including enhanced, multi-color flow cytometry, confocal microscopy and systems to support molecular microbiological and cellular analysis. Supports all aspects of scientific development including animal use protocols, manuscript and grant preparation and statistical analysis

Index Terms

infection, pathogenesis, innate immunity, adaptive immunity, bacteria, viruses, parasites, malaria, reovirus, herpesvirus, oncolysis, inflammation, host response

[Back to top](#)

Delaware

P20GM103541- Phase 2 Molecular Design of Advanced Biomaterials University of Delaware

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Thematic Scientific Focus

Molecular design of advanced biomaterials

Research Projects

- A multidisciplinary approach to peptide-based antagonists of PCNA
- Experimental and computational methodologies for biomaterials characterization
- Elastomeric polymers with defined molecular architecture and tunable biological functions for vocal fold tissue engineering
- β -hairpin gels for liver regeneration
- High-throughput rheological screening of emerging therapeutic biomaterials
- Efficient preparation of glycopeptides via glycosylation of alkynyl residues
- Biomaterials for neuronal reprogramming
- Development of bioelectronic materials with tailorable molecular morphologies
- Functional polyester scaffolds with elastomeric properties for tissue engineering
- Development of methods for photochemically patterning surfaces
- An injectable solid hydrogel approach for direct drug delivery to medulloblastoma

Research Resources

- Circular dichroism (Jasco)
- Surface plasmon resonance (Biacore)
- Microcalorimeter (MicroCal)
- Dynamic light scattering (Brookhaven)
- Spectrofluorimeter (Jasco)
- Cell culture facilities (various)
- Prep-scale HPLC-MS/MS (Shimadzu)
- Instron tensile tester (Instron)
- ReactIR (Mettler Toledo)
- Cryo TEM tomography apparatus (Gatan)
- BioMAS probe for NMR (Agilent)
- Scintillation counter (Beckman)
- Dynamic light scattering (ZetaPALS)
- Fluorescence microscope (Nikon)
- Real-Time PCR #1 (Applied Biosystems)
- Air-Free PEO polymerization line (custom-built)
- Beowulf-type computer cluster (various)

- X-ray photoelectron spectroscopy (Thermo VG Scientific)
- Time-of-flight mass spectrometry (ION-TOF)
- Atomic force microscopy (Veeco)

Index Terms

biomaterial, biopolymer, biomimetic, hydrogel, protein, DNA, PNA, surface, surface analysis, molecular design, materials science, engineering, chemistry, biochemistry, chemical engineering, nanomaterials, organic chemistry, protein patterning, surface patterning, synthetic chemistry, photochemistry, NMR, XPS, TOF-SIMS, AFM, PCR, molecular modeling, drug delivery, drug payload

[Back to top](#)

Delaware

P30GM103333- Phase 3

Osteoarthritis: Prevention and Treatment

Delaware Rehabilitation Institute, University of Delaware

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Thematic Scientific Focus

Osteoarthritis: prevention and treatment

Research Projects (Pilot projects only in this COBRE III award)

- T-type calcium channel: a novel target for treatment of osteoarthritis
- Intra-articular administration of bisphosphonates for the prevention of post-traumatic osteoarthritis

Research Resources

- Patient-specific modeling core
- Cytomechanics core
- Clinical research core

Index Terms

osteoarthritis, physical therapy, orthopaedic surgery, biomechanics, cartilage, bone, muscle, tissue engineering

[Back to top](#)

Delaware

P20GM103653- Phase 1
Delaware Center for Neuroscience Research
Delaware State University

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Thematic Scientific Focus

Brain development and neuronal plasticity

Research Projects

- Molecular interactions of a dopamine auto-receptor involved in *C. elegans* behavior
- Role of the rodent medial prefrontal cortex in behavioral plasticity
- Fetal Alcohol Syndrome model: structure and function of prefrontal cortex
- Lasting epigenetic influence of early-life adversity on the BDNF gene
- CXCR4 controls neurite extension through direct regulation of actin dynamics

Research Resources

- Renovated rodent housing facility
- Equipment
 - Olympus Fluoview FV10i-LIV confocal microscope with integrated incubator for live-cell and time-lapse imaging
 - Olympus IX70 inverted fluorescent microscope with Sutter Instruments DG-4 monochromator

Index Terms

neuroscience, electrophysiology, developmental biology, epigenetics, molecular neuroscience

[Back to top](#)

Delaware

P30GM10351- Phase 3

COBRE on Membrane Protein Production and Characterization

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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

- The role of mitochondrial transport proteins in hepatocytes and adipocytes
- Protease digest conditions for membrane protein proteomics
- Molecular simulation of a GPCR dimer interface
- Molecular mechanism of a key switch in mesenchymal stem cell differentiation
- Studies of the transmembrane selenoprotein K and its role in oxidative defense
- The interaction of thrombin and ADP receptors in platelets
- Effect of protein-lipid interactions on the formation of aberrant prion protein conformations

Research Resources

- Protein production and purification core
- Biophysical characterization core
- Structural biology core
- Bioimaging core – multiphoton confocal microscopes; electron and scanning probe microscopy; laser capture microdissection system

Index Terms

membrane proteins, mitochondria, transport proteins, gluconeogenesis, metabolic flux analysis, systems biology, diabetes, proteomics, mass spectrometry, proteolysis, G-protein coupled receptor, molecular simulation, drug receptor, adenosine receptor, Parkinson's disease, schizophrenia, allostery, signaling pathways, protein folding, ligand binding, osteoporosis, bone morphogenic protein, stem cell differentiation, osteoblast, osteoclast, phosphorylation, oxidative stress, lipid oxidation, protein expression, selenium, platelet aggregation, co-immunoprecipitation, prion, amyloid, fibrillation, neurodegenerative disease

[Back to top](#)

Delaware

P20GM103464- Phase 2
Center for Pediatric Research
Alfred I. duPont Hospital for Children

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Developmental mechanisms of undescended testis
- Molecular mechanisms in Pelizaeus Merzbacher disease
- Peripheral nervous system in cerebral palsy
- Extracellular matrix remodeling in cardiovascular diseases
- Mechanisms of cell death in spinal muscular atrophy
- Oxygen and barotrauma effects on human airway epithelium
- Mechanistic biomarkers of endocrine disruption
- The medial olivocochlear bundle and speech-in-noise deficits
- Temporal regulation of localized mRNA translation in regenerating axons
- Prognostic synovial biomarkers in juvenile rheumatoid arthritis

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 - essential services in molecular biology and genetics; automated DNA sequencing; DNA fragment analyses and SNP analysis; Real-Time PCL; custom oligonucleotide synthesis; robotic liquid handling methodologies, etc.
- Bioinformatics core – specialized network and computing resources; support and training in experimental design; biostatistics; data analysis and data management, etc.

Index Terms

pediatric diseases, neurological disorders

[Back to top](#)

Hawaii

**P30GM10334- Phase 3
COBRE Center for Cardiovascular Research
University of Hawaii**

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Thematic Scientific Focus

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

Research Projects

- Effects of hypoxia-inducible factor-1 in the heart
- Ultrasound targeted microbubble destruction for gene therapy
- Endothelial gene expression in cardiovascular stress
- Effects of diabetes on cardiac signaling
- Immunological aspects of atherosclerosis
- Developmental biology of blood vessels and fibroblasts
- Calcium channels in the heart
- Epigenomics of cardiac stress
- 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, atomic force microscopy, calcium flux
- Mouse phenotyping core – high frequency echocardiography, murine surgery including myocardial infarction and ischemia reperfusion in vivo

Index Terms

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

[Back to top](#)

Hawaii

P20GM103457- Phase 1

Institute for Biogenesis Research: COBRE

University of Hawaii at Manoa, John A. Burns School of Medicine

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Thematic Scientific Focus

Fertilization and early development

Research Projects

- Mechanisms of sex differentiation in mouse germ cells
- Effects of specific spermatid-expressed Y chromosome genes on sperm function
- Cellular and molecular mechanisms of blastocyst development
- UGT1A enzymes in the human placenta across gestation: developmental regulation and effects on placental structure and function
- Transposase assisted transgenesis and gene therapy

Research Resources

- Transgenic mouse, ICSI and IVF core

Index Terms

fertilization, embryo, early development, gametes, sperm, egg, stem cells

[Back to top](#)

Hawaii

P20GM103516- Phase 2
Pacific Center for Emerging Infectious Diseases Research
University of Hawaii at Manoa

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Thematic Scientific Focus

Develop and deploy improved rapid diagnostics, effective treatments and affordable vaccines for newly recognized and re-emerging infectious diseases, which disproportionately affect underserved and geographically remote communities in the Asia-Pacific region

Research Projects

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

Research Resources

- ABSL-3/BSL-3 biocontainment core
- Bioinformatics core
- Molecular and cellular immunology core

Index Terms

emerging infectious diseases, health disparities, pathogenesis, Dengue virus, West Nile virus, *Burkholderia pseudomallei*

[Back to top](#)

Idaho

P30GM103324- Phase 3
Institute of Bioinformatics and Evolutionary Studies
University of Idaho

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Thematic Scientific Focus

The Institute for Bioinformatics and Evolutionary Studies (IBEST) is at the heart of a signature research area at the University of Idaho focused on evolutionary biology. Studies of evolution provide insight to the mechanisms that underpin the emergence of pathogens, the development and spread of antibiotic resistance, differences in susceptibility to disease and much more. The extensive data sets collected by biologists in contemporary studies of natural and experimentally evolved populations enable computational scientists to quantify the probabilities of various evolutionary events and develop models that can subsequently be empirically evaluated and refined by biologists. Many of these studies are facilitated by recent advances in technologies for DNA sequencing and transcriptome analysis as well as the increased speed and capacity for data analysis. This allows investigators to explore evolutionary biology in ways that were never before possible to make sense of biological processes.

Research Projects

- Harnessing the power of evolutionary genomics to advance human health
- Molecular dissection of adaptive evolution

Research Resources

- Computational resources core – supports computationally intensive projects on molecular modeling, statistical simulations, molecular phylogenetics, as well as machine learning and data mining
- Genomics resources core – next-gen DNA sequencing of genomes and amplicons, and transcriptome and microarray analysis of gene expression
- Optical imaging core – confocal and fluorescent microscopy, FACS and image analysis capabilities
- Mass spectrometry core – mass spectrometry, proteomics and chromatography capabilities

Index Terms

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

[Back to top](#)

Kansas

P20GM104936- Phase 2 Molecular Regulation of Cell Development and Differentiation University of Kansas Medical Center, Kansas City

Principal Investigator

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Thematic Scientific Focus

Basic mechanisms of cell and tissue development

Research Projects

- Functional analysis of histone demethylase activity in hypoxic cancer cells
- Targeting and regulation of O-GlcNAc transferase at M phase
- Impact of early experience on vulvovaginal sensitivity in adult mouse
- Molecular mechanism of THM1-mediated renal cystogenesis
- Role of cytoskeletal protein SPECC1L in facial morphogenesis and facial clefting

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

mitosis, development, differentiation, epigenetics, organogenesis, neurogenesis, neuropathy, ciliopathy

[Back to top](#)

Kansas

P20 GM 103420- Phase 2

Center of Biomedical Research Excellence in Protein Structure and Function The University of Kansas, Lawrence

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Thematic Scientific Focus

Health-related basic research in protein structure and function. Provides research support and mentoring to accelerate the career development of outstanding junior faculty researchers, and maintains core laboratory facilities that are available to researchers statewide

Research Projects

- Palladin and regulation of actin dynamics
- Modulating protein function by rational design
- Structural characterization of cysteine-dependent acyltransferases
- Mechanism of chaperone-assisted assembly of proteasome regulatory particle

Research Resources

- Protein production core laboratory (cloning, expression and purification of prokaryotic and eukaryotic proteins)
- Protein structure core laboratory (protein crystallization, X-ray data collection, data analysis, and structure solution and refinement)
- Biomolecular NMR core laboratory (maintains two high field NMR spectrometers in support of structural and dynamics studies of biomolecules)

Index Terms

protein structure, protein function, mentoring, protein X-ray crystallography, protein purification and production, bio-molecular NMR detection, genomics, cellular proteins, normal cell functioning and dysfunctioning underlying disease states, therapeutic interventions

[Back to top](#)

Kansas

P20GM103459- Phase 2

**Nuclear Receptors in Liver Health and Disease
University of Kansas Medical Center**

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Thematic Scientific Focus

Nuclear receptors and their role in liver health and disease

Research Projects

- Understanding ligand binding in the OCT1 drug transporter using 2D NMR and MD
- Genome and the environment factors in the development of obesity, metabolic syndrome and Type 2 diabetes
- To study the role and regulation of Sortilin 1 in hepatic steatosis and diabetic dyslipidemia
- Understanding how sterile inflammation modulates alcohol-induced hepatic fibrosis

Research Resources

- Biospecimen core
- Analytical core
- Histopathology core

Index Terms

bile acids, nuclear receptors, biomedical research, liver, liver dysfunction, liver function, liver repair, fatty acid glycerol esters, glucose, lipids, OCT1, ligand binding, metabolic syndrome, Type 2 diabetes, sortilin 1, diabetic dyslipidemia, alcohol, hepatic fibrosis

[Back to top](#)

Kansas

P20GM103638- Phase 1 Molecular Analysis of Disease Pathways University of Kansas

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Thematic Scientific Focus

Development of enabling technologies for the investigation of the genetic, biochemical and physical origins of disease

Research Projects

- Identifying mRNAs associated with a synaptogenic calcium-mediated pathway
- Functional analysis of Ewing Sarcoma proteins EWS/FLI1 and EWS in zebrafish
- Probing lipid-protein interactions in biological self-assembly
- Neurotransmitter interactions on sub-second timescales

Research Resources

- Microfabrication and microfluidics core
- Synthetic molecular probes core
- Genome sequencing core
- Model organisms (zebrafish and C-elegans)

Index Terms

imaging, genomics, sequencing, zebrafish, c-elegans, model organisms, microfluidics, molecular probes, microfabrication, microfluidics, sensors, cancer, pulmonary disease, neurological disorders, genetic diseases, molecular biology, bioengineering, bioanalytical chemistry, neuroscience

[Back to top](#)

Kansas

P30GM103326- Phase 3 Novel Approaches for Control of Microbial Pathogens University of Kansas Medical Center

Principal Investigator

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

Index Terms

pathogens, microbial infection, molecular structure, protein X-ray crystallography, mechanism-based enzyme inhibitors, drug development, cell mediated immune responses, development of the immune system

[Back to top](#)

Kansas

P30GM103330- Phase 3
Center for Epithelial Function in Health and Disease
Kansas State University College of Veterinary Medicine

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 <http://www.k-state.edu/cobre/Projects/currentProj.htm>

- CFTR regulation of thyroid anion transport
- Xenobiotic transport across the mammary epithelium
- Dietary supplements protect retinal pigment epithelial cells from apoptosis
- Salivary gland transcriptome and peptidome analysis in *Crocota crocuta*
- The function of anopheles serpins during malaria parasite invasion of mosquito epithelia
- Role of IL-1 β in cancer stem cell development and cancer recurrence
- Microbial ecology and epithelial immunity of *Lutzomyia longipalpis*

Research Resources

- Confocal microfluorometry – <http://www.k-state.edu/cobre/Cores/coreB.htm>
- Molecular biology core – <http://www.k-state.edu/cobre/Cores/coreC.htm>
- Epithelial electrophysiology core – <http://www.k-state.edu/cobre/Cores/coreD.htm>

Index Terms

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

[Back to top](#)

Kansas

P30GM103495- Phase 3

Center for Cancer Experimental Therapeutics

University of Kansas, Lawrence

Principal Investigator

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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

- Targeting EMT for identification of inhibitors of cancer stem cells by HTS
- Novel Beclin-mimetics for molecular cancer therapy via modulating autophagy
- Discovering drugs that induce degradation of oncogenic mutant p53
- Novel molecular cancer therapy targeting Musashi

Research Resources

- High throughput screening (HTS) 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

[Back to top](#)

Kentucky

P20GM103492- Phase 1
Center of Excellence in Diabetes and Obesity Research
University of Louisville

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Thematic Scientific Focus

The central scientific objective of the center is to support molecular, cellular, experimental, epidemiological and clinical investigations into the cardiovascular causes and consequences of diabetes and obesity

Research Projects

- Endothelial progenitor cell mobilization defects in diabetes
- Stem cells and diabetic cardiomyopathy
- Bioenergetic regulation of cardiac progenitor cells
- Foam cell formation and diabetic atherogenesis
- Resolution of diabetic vascular inflammation: role of lipid mediators

Research Resources

- Confocal microscopy and flow cytometry core
- Cardiovascular pathology core
- Transgenic mouse core
- Cardiovascular imaging and function core

Index Terms

diabetes, obesity, cardiovascular, inflammation, cardiac stem cells, lipid metabolism, oxidative stress, particulate matter, nitric oxide, endothelial progenitor cells, atherothrombosis, atherosclerosis

[Back to top](#)

Kentucky

P20 GM103527- Phase 1
Center of Research in Obesity and Cardiovascular Disease
University of Kentucky

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Thematic Scientific Focus

The central scientific objective of the center is to support molecular, cellular, integrative and clinical investigation into mechanisms linking obesity to cardiovascular diseases

Research Projects

- IKKbeta links macrophage inflammation to atherosclerosis
- Platelet activation with obesity promotes atherothrombotic vascular events
- Maternal consumption of a western diet promotes obesity and hypertension in offspring
- Quantifying the effect of obesity and comorbid hypertension on cardiac function in children and mice
- Role of bioactive lipids in the protective mechanisms of obesity in ischemic cardiomyopathy
- Role of adipose tissue TGF- β signaling on adipose dysfunction in obesity
- Role of Lipin1 in skeletal muscle mitochondrial homeostasis and oxidative energy metabolism

Research Resources

- Analytical research core
- Cardiovascular research core
- Diabetes research core
- Obesity research core
- Pathology research core

Index Terms

obesity, diabetes, inflammation, hypertension, coronary artery disease, thrombosis, myocardial infarction, atherosclerosis.

[Back to top](#)

Kentucky

P20GM103538-Phase 2
Center for the Biologic Basis of Oral/Systemic Diseases
University of Kentucky, College of Dentistry

Principal Investigator

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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 inflammatory bowel disease
- Ontogeny of innate immunity in gingival tissues
- HSV and chronic pain
- Inflammatory mediators in serum and secretions during gestation
- Behavioral interventional studies of CVD risk
- Genetics of chronic inflammatory diseases
- Bone responses to bisphosphonates and cancer

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

[Back to top](#)

Kentucky

P30GM103453- Phase 3 Molecular Determinants of Developmental Defects University of Louisville Birth Defects Center

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Developmental toxicity of cigarette smoke
- Identification of molecular signals involved in intermittent hypoxia-elicited white matter injury during CNS development
- Role of Vitamin A metabolism in congenital heart defects
- Genetic dissection of mouse secondary palate development
- Sphere-initiated reprogramming to generate induced pluripotent stem cells
- Impact of prenatal alcohol exposure on offspring health
- Integrated analysis of mRNA-microRNA (miRNA) interaction during orofacial 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, cleft palate, neural tube defects, cardiovascular defects, neurocognitive development, vitamin A, stem cells,

[Back to top](#)

Kentucky

P20GM103486- Phase 2

**COBRE in the Molecular Basis of Human Disease
University of Kentucky College of Medicine**

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- A study into understanding the molecular basis of epigenetic transcriptional silencing
- Understanding the role of Shoc2 protein in spatio-temporal regulation of extracellular signal-related kinase (ERK) kinase cascade
- Structural biology of the ESX secretion system from pathogenic mycobacteria
- Molecular mechanism of mammalian autophagy

Research Resources

- Protein analytical core – quantitative and qualitative protein profiling and identification analysis including characterization of protein modifications. Instruments include a Qstar XL quadrupole time-of-flight MS, a 4800 MALDI-TOF-TOF MS, an LTQ Velos Orbitrap and a TSQ Vantage triple quadrupole mass spectrometers. Eksigent and Shimadzu HPLC systems and multiple PCs for data acquisition and analysis including site licenses for Mascot, ProteomeDiscoverer, ProteinPilot, Sequest and PDQuest software
- 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), Nikon A1 hybrid scanning confocal microscope
- Proteomics core – quantitative and qualitative protein profiling and identification analysis including Qstar XL quadrupole time-of-flight MS, 4800 MALDI-TOF-TOF MS, and 4000 Q-Trap MS, LTQ Velos Orbitrap. 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
- Organic synthesis core – synthetic capabilities for the preparation of a variety of organic compounds to support research projects
- Viral production core - production of recombinant, replication-deficient lentivirus, adenovirus, and adeno-associated viruses expressing genes of interest to the user

Index Terms

transcriptional regulation, cancer genes, pathogens, autophagy

[Back to top](#)

Kentucky

P20GM103482- Phase 2 COBRE in Molecular Targets University of Louisville

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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 – affymetrics 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 calorimetric, 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

[Back to top](#)

Kentucky

P30GM10350- Phase 3
Central Nervous System Injury and Repair
University of Louisville

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Thematic Scientific Focus

Developing and characterizing clinically relevant animal models. Making available necessary equipment for human SCI, neurological disease and stroke patient analysis. Bringing new investigators from other fields into spinal cord injury research

Research Projects

There are no individual research projects as this is now a P30 grant

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, two photon spectral imaging
- Human locomotor core – partial body weight treadmill training, EMG and kinematic analyses, cardiopulmonary analyses

Index Terms

neurobiology, cell culture, molecular biology, surgery, behavior, electrophysiology, microscopy, apoptosis, immunology, signaling, central nervous system, spinal cord injury, stroke, Parkinson's disease, traumatic brain injury, stem cells, human, rodent, kinematic, gait analysis

[Back to top](#)

Louisiana

P30GM103340- Phase 3
Mentoring Neuroscience in Louisiana
Louisiana State University Health Sciences Center

Principal Investigator

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Thematic Scientific Focus

Core support for 19 neuroscience laboratories; dendritic integration in the hippocampus; define differently distributed synaptic input, the form of dendritic integration and action potential output in the apical dendrites of hippocampal CA1 neurons; neuroprotectin D1 and in the beginning to define inflammatory resolution circuits in the brain and other tissues; simulation and modeling; cellular and molecular imaging; experimental stroke, active dendritic processing and Alzheimer's disease

Research Projects

- Descending modulation of complex auditory processing
- Corneal nerve regeneration in experimental diabetes
- Antisense oligonucleotides as a novel therapeutic for Usher Syndrome
- Molecular mechanisms of FUS-related neurodegeneration
- Identify and characterize parkin ubiquitin substrates that mediate parkin's role in mitochondrial quality control

Research Resources

- Computational neuroscience core – development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of neurobiological systems
- Mediator-lipidomics core – contains ultra-performance liquid chromatography – tandem mass spectrometers, thin layer chromatography, and all necessary materials for the isolation, purification, identification, quantification, and storage of lipid mediators and their precursor lipids
- Multiphoton microscopy core – allows for simultaneous imaging and photo-release of caged compounds, in combination with electrophysiological recordings
- Imaging core –state-of-the-art technologies for 3-D tissue analysis and stereology

[Back to top](#)

IDeA -CTR

Louisiana

U54GM104940

**Louisiana Clinical and Translational Science Center
LSU Pennington Biomedical Research Center**

Principal Investigator

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Thematic Scientific Focus

LA CaTS Center supports a wide range of clinical and translational research interests. However, major research thematic areas are:

- Nutrition, obesity, type 2 diabetes and other prevalent chronic diseases
- Health disparities
- Cancer studies
- Cardiovascular disease
- Preventative approaches to health, including vaccine development. These parallel the needs of the population we serve and represent current areas of focus in our research portfolios

Research Projects

- Discovering the role of putative microRNAs in prostate tumorigenesis
- Evaluation of ACE2 as a biomarker for neurologic hypertension
- Metabolic effects of short term sugarcane bagasse supplementation
- MicroRNAs as prognostic markers of breast cancer
- Relationship of uAGT to blood pressure and response to antihypertensive therapy
- Transcriptional profiling of gastritis progression using high throughput sequencing of tissue microRNA
- Using serum microRNAs as biomarkers for cognitive impairment in HIV patients
- Urinary excretion of renin and soluble prorenin receptor in hypertension

Research Resources

- Administrative core
- Clinical and translational pilot grants program
- Clinical research education, mentoring and career development core
- Clinical research design, epidemiology and biostatistics core
- Clinical research resources
- Community engagement and outreach resource
- Biomedical informatics core
- Ethics and regulatory knowledge resource
- Health literacy core
- Communications core

Index Terms

diabetes, obesity, cancer, hypertension, infectious diseases, health disparities, health literacy, community engagement, education, biostatistics, medical informatics

[Back to top](#)

Louisiana

P20GM103518- Phase 2 Mentoring a Cancer Genetics Program Tulane University Health Sciences Center

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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

- L1 retroelements causing genetic instability in cancer growth and development
- Error prone polymerase mutations in prostate cancer
- Interleukin-17 and inflammation in prostate cancer progression
- Circadian regulation and prostate cancer
- Chronic inflammation in colon cancer
- Epigenetic regulation of miRNAs in triple negative breast cancer

Research Resources

- Cell assay core – employs a series of devices for gene function, expression and mutagenesis assays
- Bioinformatics core – provides computing and assistance for investigators to analyze next-generation sequence data

Index Terms

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

[Back to top](#)

Louisiana

P20GM103528- Phase 2 Mentoring Obesity and Diabetes Research in Louisiana Pennington Biomedical Research Center

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Gene-environment interactions and high-density lipoproteins: an integrated genomic, biological and behavioral approach
- Exploration of the role of carnitine octanoyl transferase in preventing lipid-induced insulin resistance
- Astrocytes as CNS gluco-detectors
- Epigenetic regulation of lipid metabolism
- Role of NT-PGC-1 α in mitochondrial biogenesis and function

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
- C FL 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

[Back to top](#)

Louisiana

P20 GM103629- Phase 1 Mentoring Research Excellence in Aging and Regenerative Medicine Tulane University of Louisiana

Principal Investigator

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Thematic Scientific Focus

Spatial attention in cognitive aging; genetics and epigenetics of human aging; cardiovascular and microvascular aging and regenerative medicine; inflammation and cell signaling in pulmonary fibrosis

Research Projects

- Effect of donor age on mesenchymal stem cell-dependent angiogenesis
- Spatial attention networks and cognitive aging
- Genetics and epigenetics of healthy aging in twins
- The role of Sirtuin 1 and 3 in the prevention and pathogenesis of pulmonary fibrosis
- The effect of age-related microvascular patterning alterations on network resistance in spontaneously hypertensive rats

Research Resources

- Biostatistics and genomics core

Index Terms

genetics, molecular and cell biology, signaling, immunology, stem cells, cardiovascular biology, cognitive aging, biology of aging

[Back to top](#)

Louisiana

P20GM103514- Phase 2 Mentoring in Cardiovascular Biology Louisiana State University Health Sciences Center

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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

- Role of lysyl oxidase enzyme and downstream signaling pathways in volume overload-induced left ventricular remodeling in rats
- Protective effect of GAPDH against oxidant-induced apoptosis, impaired DNA repairing, suppression of vascular smooth muscle cell migration, and diet-induced atherosclerosis
- Heparin sulfate sulfation in transforming growth factor signaling and pathophysiology of pulmonary fibrosis

Research Resources

- Cell and molecular analysis core – cell culture, molecular biology, and cell signaling assay services; real time PCR analysis; 2-D gel electrophoresis, mass spectroscopy, HPLC
- Imaging and histology core – tissue processing, staining, imaging, and pathology analysis
- Cardiac and vascular function core – telemetry, in vivo ultrasound imaging, stereotaxic microinjection, cardiac, renal, and pulmonary function services

Index Terms

cardiovascular disease, atherosclerosis, hypertension, ischemic heart damage, oxidative stress, cell signaling and trafficking, G protein-coupled receptors

[Back to top](#)

Index Terms

neuroscience, stroke, neurotrauma, epilepsy, neurodegenerative diseases, Alzheimer's disease, retinal degenerations, lipidomics, imaging, molecular biology, cell biology

[Back to top](#)

Louisiana

P20GM103458- Phase 2
Center for Experimental Infectious Disease Research
Louisiana State University

Principal Investigator

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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 and microsporidia coinfection

Research Resources

- Molecular biology and immunology core – providing DNA sequencing; library construction
- microarray analysis, FACS analysis, confocal microscopy, live imaging microscopy, real time 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

[Back to top](#)

Louisiana

P30GM103337- Phase 3

COBRE Phase III: Translational Research in Hypertension and Renal Biology Tulane University School of Medicine

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Angiotensin in distal nephron ontogeny
- Angiotensin receptors in renal microvascular physiology
- Beneficial effects of physical activity on blood pressure among African-American females
- Citrate transport in the proximal tubule
- Distal nephron renin and prorenin receptor in angiotensin II-dependent hypertension
- Endothelial dysfunction, adipocytokines, inflammation and chronic kidney disease
- Functional role of pro-renin receptor in the collecting duct to the development of hypertension
- Heme oxygenase in angiotensin II hypertension
- Heme-heme oxygenase-carbon monoxide system in salt-induced hypertension
- Macronutrient composition of diet and risk factors for cardiovascular disease
- Mechanism of resistance artery structural remodeling in hypertension
- Regulation of inhibitory circuits in the RVLM by angiotensin II
- Role of p53 in nephron progenitor cell renewal and differentiation
- Transcriptional control of ureteric bud growth and branching
- Tubular renin-angiotensin system in hypertension
- The effect of microvascular patterning alterations on network resistance in spontaneously hypertensive rats
- The role of genetic polymorphisms in the epoxygenase pathway in hypertension

Research Resources

- Molecular, imaging and analytical core – provides major support to COBRE and other Tulane investigators and includes: RIA, ELISA, gel documentation system, real-time PCR system, licor's odyssey system, stratagene, qiagen biorobot system, dako cytometry's autostainerplus, fluostar optima microplate reader, and PTI ratiometer
- Transgenic and gene-targeted animal core – maintains breeding colonies of rat and mouse transgenic strains used by investigators in the hypertension and renal center

- Mouse phenotyping core – maintains and operate state-of-the-art methodologies for assessing arterial blood pressure, neural autonomic status and renal function in mouse models of hypertension and associated renal and cardiovascular diseases
- Clinical and translational core – promotes and facilitates clinical and translational studies in hypertension, kidney disorders and related cardiovascular diseases

Index Terms

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

[Back to top](#)

Louisiana

P20GM103433- Phase 2
Center for Molecular and Tumor Virology
Louisiana State University Health Sciences Center

Principal Investigator

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<http://www.lsu.hsc.microbiology.com/cmtv-overview.htm>

Thematic Scientific Focus

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

Research Projects

- Role of CD4+ Th cells in Theiler's virus persistence and pathology
- Immune correlates of BK virus persistence and reactivation
- Mechanism by which the EHV-1 IR2 protein inhibits viral gene expression
- Role of the human cytomegalovirus UL97 protein kinase in viral replication
- The 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

[Back to top](#)

Louisiana

P20GM103501- Phase 2 Mentoring Translational Researchers in Louisiana Louisiana State University Health Sciences Center

Principal Investigator

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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

- Genetic profiles of gastric lesions in patients with gastritis and mice infected with helicobacter pylori
- L-Arginine availability regulates proliferation of malignant T cells
- HSV-2 subversion of the innate immune response by targeting cell-intrinsic pathways
- Identification of protective and pathogenic human B cell epitopes in dengue virus
- Modulating L-Arg metabolism through Arginase and iNOS to inhibit growth
- Tumor microenvironment and B cell lymphomas
- Alterations in cell signaling pathways by human neurotropic JC virus in colon cancer
- Polycyclic aromatic hydrocarbons and malignant transformation of neural progenitors

Research Resources

- Immunology and cell analysis core – flow cytometry, cell sorting and cell separation services
- Illumina and genomics core – low cost sequencing and GeneChip preparation and analysis services
- Biostatistics and bioinformatics core
- Grants and development core

Index Terms

inflammation, host defense, immune response, T cells

[Back to top](#)

Maine

**P30GM103392- Phase 3
Phase III COBRE in Vascular Biology
Maine Medical Center Research Institute**

Principal Investigator

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Thematic Scientific Focus

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

Research Pilot Projects:

- Evaluation of tumor microvasculature with targeted micro-bubble contrast-enhanced ultrasound
- Cthrc-1 is a marker for activated mesenchymal progenitor cells

Research Resources

- Structural biology core – capillary-based automated DNA sequencing; protein mass spectrometry with quadrupole tandem mass spectrometers; confocal microscope
- Transgenic mouse and small animal imaging 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

[Back to top](#)

Maine

**P20GM103643- Phase 1
Interdisciplinary Center of Excellence for the Study of Pain and Sensory Function
University of New England**

Principal Investigator

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Thematic Scientific Focus

The neurobiology of chronic pain and sensory function

Research Projects

- Interaction between calcitonin-gene-related-peptide and CD40 on CNS glial cells in neuropathic pain
- Genes involved in antinociception in drosophila melanogaster
- Function of the transcription factor Sox11 in regulating the plasticity of nociceptive neurons after nerve injury
- Triptan-induced modulation of blood-brain barrier integrity and nociception

Research Resources

- Histology and imaging core
- Behavioral core

Index Terms

pain, nociception, neurobiology, sensory, behavior, neuropathology

[Back to top](#)

Maine

P20GM103465- Phase 2
Center for Regenerative Medicine
Maine Medical Center Research Institute

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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

- Mechanisms of de novo human blood vessel formation
- Roles of podocalyxin during the onset and progression of acute myeloid leukemia
- Notch signaling and skeletal muscle function
- MAP37K: An intersection between inflammatory and regenerative signaling in kidney injury
- Molecular mechanisms of adipogenic conversion of skeletal muscle stem cells: Crosstalk between myostatin and WNT signaling

Research Resources

- Progenitor cell analysis core – analytical flow cytometry; FACS and MACS cell isolation; high through-put colony/cell imaging, fluorimetry, luminometry; stem and progenitor cell culture; basic murine and human ES cell services
- Molecular phenotyping core – automated nucleic acids purification, microarray analysis, quantitative PCR, automated fluorescence cell marker analysis and screening
- Histopathology core – fixation and processing of specimens for frozen, paraffin and plastic embedded sectioning; comprehensive spectrum of histological and specialty stains; immunohistochemistry; capacity to prepare custom tissue microarrays
- Physiology core – arrays of enzyme-linked, colorimetric and radio-immunoassays for hematologic, metabolic and skeletal phenotyping; complete metabolic phenotyping through the use of metabolic cages plus DXA scanning approaches; cellular and mitochondrial bioenergetics via analysis of oxidative phosphorylation and glycolysis of isolated cells and mitochondria

Index Terms

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

[Back to top](#)

Mississippi

P20GM104932- Phase 2
Center of Research Excellence in Natural Products Neuroscience
University of Mississippi

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Thematic Scientific Focus

Identification and characterization of psychoactive properties of natural products

Research Projects

- Chemical and biological evaluation of psychoactive plants
- Sigma receptors and the endocannabinoid system
- Delta-8-tetrahydrocannabinol in the management of glaucoma
- Rational design and testing of novel cannabinoid ligands

Research Resources

- Sourcing, acquisition and isolation core – isolation; structure elucidation; analysis of biologically active natural products
- Chemistry core – semi-synthesis; scale-up synthesis; structure-activity-relationship; DMPK
- In vitro pharmacology core – in vitro functional assays to evaluate natural products
- In vivo pharmacology core – in vivo models to evaluate acute behavioral properties of natural products
- Biopharmaceutics-clinical and translational core – pre-formulation and formulation studies; stability testing; product and regulator development

Index Terms

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

[Back to top](#)

Mississippi

P30GM103328- Phase 3
Center for Psychiatric Neuroscience
University of Mississippi Medical Center

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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 and psychoactive substance abuse

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 –provides post-mortem brain specimens from psychiatrically characterized subjects and matched normal control subjects for studies of human brain biology
- Animal behavior 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 – provides 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

[Back to top](#)

Montana

P20 GM103394- Phase 1

Center for Analysis of Cellular Mechanisms and Systems Biology Montana State University

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Thematic Scientific Focus

Developing predictive models of cellular signaling and metabolic mechanisms of bacterial and eukaryotic systems in health and disease.

Research Projects

- Global proteomic analysis of nutrient limitations in bacterial and yeast metabolism: implications for microbial pathogenesis and nutrient interactions in systems biology of bacterial consortia
- Brain astrocyte genomic and proteomic responses to *Toxoplasma gondii* parasites with different virulence phenotypes
- New probes of protein nitrosylation and global proteomic analysis of nitrosative stress during virus infection
- Proteomic and metabolomic mechanisms of helminth infection on the intestinal microbiome in inflammatory bowel disease in animal models and in humans
- Developing a systems biology understanding of osteoarthritis, using proteomic and metabolomics tools in animal models and in humans

Research Resources

- Proteomics and metabolomics core, including mass spectral and NMR approaches and integrative analysis of genomics and metabolomics
- Proteomic reagent synthesis core, including multicolor fluorescent probes for differential analysis of protein levels, enzyme activities and protein posttranslational modifications
- Systems biology modeling core

Index Terms

proteomics, metabolomics, genomics, systems biology, host-pathogen interaction, microbial pathogenesis, microbial consortia, *Toxoplasma*, brain parasites, protein nitrosylation, nitrosative stress, helminth infection, hygiene hypothesis, inflammatory bowel disease, osteoarthritis

[Back to top](#)

Montana

P30GM103338- Phase 3
Center for Environmental Health Sciences
University of Montana, Missoula

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Thematic Scientific Focus

Effects of environmental agents on human health and disease, focusing primarily on adverse effects on immune and neurological outcomes as well as cancer

Research Projects

- Regulation of macrophage function by components of wood smoke
- Regulation of inflammasome activation by AhR
- Innate immunity in ozone-induced asthma exacerbations
- Relationships of DNA methylation patterns to breast cancer and biomarker discovery
- Mechanisms of nanomaterial activation of NLRP3 inflammasome and autophagy
- Cannabinoid agonists as novel therapeutic agents to suppress allergic airway inflammation
- AhR activation in dendritic cells and induction of systemic immune suppression
- Impact of the herbicide Atrazine on the activation and differentiation of FoxP3+ CD4 Tcells
- Protein production related to lung fibrosis and role of SPARC in airway remodeling
- Pulmonary and systemic effects of woodstove smoke on mice and humans
- Influence of obesity on particulate-induced pulmonary diseases
- Tumor suppressor genes in human cancer models

Research Resources

- Inhalation and pulmonary physiology core –resources to conduct animal exposures to various particulates (wood smoke, ambient PM, nanomaterials), volatile and semivolatile compounds and invasive and noninvasive procedures to assess pulmonary function
- Molecular histology and fluorescent imaging core – full complement of high throughput histology and staining; and Olympus Fluoview 1000 confocal
- Fluorescent cytometry core – BDFacsAria II, CompuCyte ICys and assorted fluorescent microscopes

Index Terms

environmental health, toxicology, immunology, development, nanomaterials, asbestos, woodsmoke, oxidative stress, carcinogenesis, receptor signaling, innate and adaptive immunity

[Back to top](#)

Montana

P20GM103500

**Center for Zoonotic and Emerging Infectious Diseases
Montana State University**

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Thematic Scientific Focus

Many of the important and emerging infectious diseases of humans are zoonotic, and most are also potential weapons of bioterrorism. Furthermore, a number of these diseases have reservoirs in the livestock and wildlife of our nation. The goal of this COBRE is to support new investigators and provide the resources needed to advance our understanding of infectious disease pathogenesis and facilitate development of novel therapeutic treatments.

Research Projects

- Mechanisms of RNA-guided adaptive immunity in bacteria
- Bone marrow failure and immune responses to pulmonary fungal infections
- Determining how vaccine vectors shape memory CD8 T cell development

Research Resources

- Cellular analysis core – flow cytometry, histology, and confocal fluorescence microscopy services
- Animal models core – technical support to investigators utilizing animal models of infectious disease pathogenesis, resources and expertise to assist investigators in utilizing and/or developing new animal models to enhance or expand their research programs, access to the BSL-3 and ABSL-2 animal research facilities

Index Terms

zoonotic diseases, infectious agents, bacterial pathogenesis, fungal pathogenesis, innate immunity, adaptive immunity, bone marrow failure

[Back to top](#)

Montana

P20GM103546- Phase 1
Center for Biomolecular Structure and Dynamics
The University of Montana

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Thematic Scientific Focus

Apply the methods and concepts of biophysics, structural biology and mathematics to understand the mechanistic basis of biological processes in health and disease

Research Projects

- Structural studies of arenaviral envelope glycoprotein
- Computational comparison of the mechanism of adenylyl cyclase in mammals and in pathogens
- Studies of the reaction mechanism in heme dioxygenases using oxygen isotope fractionation techniques
- Structural and functional analysis of genetic polymorphisms in the P-glycoprotein (ABCB1) drug transporter
- Catalysis with non-covalent interactions
- A role for germ granules in promoting mRNA silencing in germline stem cells

Research Resources

- Macromolecular x-ray diffraction core
- Macromolecular NMR spectroscopy core
- Molecular computation core
- Biospectroscopy core
- Mass spectrometry core

Index Terms

biophysics, structural biology, structural studies, pathogens, mammals, fractionation, functional analysis, genetic polymorphisms, P-glycoprotein, drug transporter, catalysis, non-covalent interactions, germ granules, mRNA, silencing, stem cells, cancer, diffraction, disease, isotopes, oxygen, glycoprotein, biological processes, crystallization, spectroscopy, biospectroscopy, spectrometry, cellular biology, pharmacology, neurobiology, biochemistry, synthetic chemistry, macromolecular X-ray crystallography, nuclear magnetic resonance spectroscopy, NMR, mass spectrometry, molecular computation

[Back to top](#)

Nebraska

**P30GM103335- Phase 3
Redox Biology Center
University of Nebraska-Lincoln**

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Thematic Scientific Focus

Underlying scientific theme is redox biology which encompasses the study of reduction-oxidation events in metabolism, signaling pathways, stress response, and cellular repair that are essential for proper growth and development. Investigators are exploring fundamental questions in redox biology in systems from microbes to mammals that are of significant importance to human health

Research Projects

- Protein quality control in mitochondrial homeostasis and signaling
- Redox regulation of neuronal cell death
- Linking mitochondrial dysfunction to environmental stressors

Research Resources

- Metabolomics and proteomics
- Spectroscopy and biophysics
- NMR metabolomics
- Electron paramagnetic resonance spectroscopy
- Macromolecular crystallography
- Bio-imaging

Index Terms

redox biology, oxidative stress, redox signaling, reduction-oxidation, metabolism, redox regulation, mitochondria, reactive oxygen species, metal ion homeostasis, cancer, Parkinson's disease, aging, cataracts, cardiovascular disease, neurodegeneration

[Back to top](#)

Nebraska

P20 GM103480- Phase 1
Nebraska Center for Nanomedicine
University of Nebraska Medical Center

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Thematic Scientific Focus

The development of effective nanomedicines for human disease diagnosis and therapy including cancer, neurodegenerative and cardiovascular disorders, polymer-based nanomaterials and drug delivery platforms delivery systems for various biological agents (proteins, siRNA, anticancer drugs)

Research Projects

- Nanoformulations of redox enzymes for treatment of stroke, Parkinson disease and hypertension. Deliver drugs and recombinant DNAs to focal areas of disease or to tumors to maximize clinical benefit while limiting untoward side effects
- Antiviral peptide nanocomplexes for treatment of HCV/HIV co-infection
- Novel metabolically cleavable radiotherapeutic copolymers
- Polymer conjugates for the treatment of oxidative damage induced by traumatic brain injury
- MUC4-based vaccine for pancreatic cancer

Research Resources

- Nanomaterials core facility
- Bioimaging core facility

Index Terms

nanotechnology and engineering , drug delivery, gene therapy, neuroscience, medicine, cancer biology, polymer science

[Back to top](#)

Nebraska

P20 GM103489- Phase 2
Nebraska Center for Cellular Signaling
University of Nebraska Medical Center

Principal Investigator

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Thematic Scientific Focus

Elucidation of cellular signaling transduction mechanisms with particular emphasis on growth regulation, DNA methylation, apoptosis, metastasis, invasion and cell adhesion receptors

Representative Research Projects

- Role of DNMT3b in myc-induced lymphomagenesis
- Role of kinases in recovery from DNA damage
- Hippo signaling
- Endocytosis of GPI-anchored proteins

Research Resources

- Microscopy core
- Histology core
- Molecular biology core
- High throughput screening facility
- Flow cytometry core
- Microarray core
- Biostatistics core
- Human tissue bank
- Protein structure core facilities
- Animal facility
- Transgenic mouse facility

Index Terms

signal transduction, DNA methylation, DNA damage, endocytosis, cell adhesion, prostate cancer, oral cancer

[Back to top](#)

Nebraska

P20GM103471- Phase 2

**Center for the Molecular Biology of Neurosensory Systems
University of Nebraska Medical Center**

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Investigate the pathogenesis of mutations causing Usher syndrome by determining the role of the CDH23, PCDH15, VLGR1 and clarin-1 proteins in the development and function of the hair cell synapse in a zebrafish model
- Determine the role of genes DCDC2 and MACF1 on hippocampal neuronal connectivity in a mouse model and test the hypothesis that these genes are inter-related in the pathogenesis of neurodevelopmental disorders
- Define the role of the glycosaminoglycan keratin sulfate in the pathogenesis of hearing loss by determining its effects on ear development, function and susceptibility to ototoxic drugs in zebrafish
- Address the treatment of chronic inflammatory disorders by determining the roles of $\alpha 1$, $\alpha 2$ and $\beta 1$ integrins and VEGF in corneal wound healing through their effects on lymphangiogenesis

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 and sequencing core – services to determine global gene expression patterns, transcriptional profiling and DNA-protein interactions

Index Terms

neurosensory disorders, central nervous system, inner ear development, developmental neuroscience, neurodevelopmental disorders, inflammation, hearing loss, vision loss, Usher syndrome, ototoxicity, autism, lymphangiogenesis

[Back to top](#)

Nebraska

P30GM103509- Phase 3
Nebraska Center for Virology
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Thematic Scientific Focus

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

Research Resources

- 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
- Bioinformatics core – data analysis for high throughout sequencing

Index Terms

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

[Back to top](#)

Nevada

P20GM103513- Phase 2
Smooth Muscle Plasticity: A COBRE
University of Nevada School of Medicine

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Develop new methods to analyze and diagnose movement defects in diabetes and other disorders affecting gastric emptying
- Determine the importance of Ca²⁺ sensitization mechanisms (ROCK2 and protein kinase C phosphorylation of MYPT1 and CPI-17) in regulation of contraction in the proximal and distal stomach and the role of these mechanisms in the pathophysiology of diabetic gastroparesis
- Determine the role of S100A4, a calcium binding protein, in the development of atherosclerosis and arterial stenosis, constrictive remodeling of arterial wall.
- Examine the physiological changes that occur during obstructive bowel disease; specifically, analyze microRNA regulation of the smooth muscle phenotype
- This project is examining the molecular mechanisms of estrogen regulation of TREK-1 channels (a molecular candidate of stretch-dependent potassium channels in the bladder) and how loss of these channels leads to impaired regulation of bladder excitability

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 for all projects by RT-PCR and qPCR
- Protein expression and analysis core – provides immunohistochemical and protein analysis support for projects, including Western blots, immunoprecipitation, confocal microscopy
- Dynamic imaging facility – provides expertise in fluorescent imaging; employs multiple high speed fluorescent imaging systems and a ratio metric (Fura 2-AM) imaging system for use with intact smooth muscle tissues and isolated cells. Provides imaging analysis for digital video imaging of movement and Ca²⁺ signals

Index Terms

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

[Back to top](#)

Nevada

P20GM103554- Phase 1 Cell Biology of Signaling Cross Membranes University of Nevada, Reno

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Thematic Scientific Focus

- Cell biology of signaling across membranes: signaling proteins in neuroscience
- Signal transduction, ligand-receptor interactions, glycosylation of secreted proteins, modulation of mitochondrial function by kinases and phosphatases, NMDA receptor signaling, neuron-glia interactions

Research Projects

- Neurotrophic signaling in *Drosophila*
- Secretion of signaling molecules
- The roles of glia and neural activity in the development of neuromuscular synapses.
- Modulation of mitochondrial quality control and function by serine/threonine kinases and phosphatases in neurons
- Apoptosis signaling in Parkinson's disease

Research Resources

- Imaging core
- Tissue culture core
- Electron microscopy core

Index Terms

cell biology, molecular biology, neuroscience, signaling, glycobiology, neurodegeneration

[Back to top](#)

Nevada

P20GM103650- Phase 1
Center for Integrative Neuroscience
University of Nevada, Reno

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Thematic Scientific Focus

Integrative neuroscience; mechanisms of normal brain function and neural deficits

Research Projects

- Understanding the neural basis of working memory to improve WM function
- Behavioral and neural investigations of spatiotemporal form integration in healthy and brain-injured persons
- Temperature control of the *C. elegans* circadian clock
- Analysis of sleep-deprivation induced memory loss
- Engineering magnetofluorescent nanoparticles for neurological disease diagnosis

Research Resources

- Neural imaging resources core
- Special populations patient database

Index Terms

cognitive neuroscience, cellular neuroscience, genetics, neuroimaging, traumatic brain injury, neural disorders

[Back to top](#)

New Hampshire

P30GM103415- Phase 3
Center for Molecular, Cellular, and Translational Immunological Research
Dartmouth Medical School

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Thematic Scientific Focus

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

Research Projects

- 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

[Back to top](#)

New Hampshire

P20GM103534- Phase 1
Quantitative Biology Research Institute
Dartmouth College

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Thematic Scientific Focus

Bioinformatics

Research Projects

- Immunogenomic analysis of gene-environment interaction in zebrafish
- False-discovery rate methods for the analysis of gene-environment interaction
- Computational prediction of regulatory motifs in environmental response genes
- Bayesian network analysis of gene-environment interaction in human populations

Research Resources

- Integrative biomedical sciences core
- Northern New England computing grid

Index Terms

bioinformatics, biostatistics, genomics, genetics

[Back to top](#)

New Hampshire

P20GM103413- Phase 2

Cellular and Molecular Mechanisms of Lung Disease

Geisel School of Medicine at Dartmouth

Principal Investigator

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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

- Molecular mechanisms of Aurora Kinase A dysfunction in lung cancer
- A novel regulator of *P. aeruginosa* virulence genes
- Humanizing alginate depolymerase: new strategies for de-immunizing enzyme therapies
- Biodiesel and petroleum diesel: exposure profiles and public health consequences

Research Resources

- Host pathogen interaction core - facilitate research on biological mechanisms that contribute to lung disease and accelerate therapeutic development
- Live cell imaging core - facilitate research on biological mechanisms that contribute to lung disease and to accelerate efforts to identify candidate therapeutic targets. The infrastructure and expertise of the core supports live cell imaging, as well as protein localization and host-microbe interaction studies
- Translational research core - provide support to basic science investigators and physician-scientists focused on translational research who require access to clinical specimens from patients with lung disease to support their work and expand preliminary observations into human subjects

Index Terms

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

[Back to top](#)

New Mexico

P20GM103472- Phase 1

Neural Mechanism of Schizophrenia: Use of Multiple Neuroimaging Tools to Examine The Mind Research Network

Principal Investigator

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The Mind Research Network

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Thematic Scientific Focus

Examining the neural mechanisms of schizophrenia and evaluating the use of multiple neuroimaging tools to examine dysfunctions in neural integration

Research Projects

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

Research Resources

- An in-house 3 Tesla Siemens Trio whole body scanner equipped with Sonata gradient subsystem (40 mT/m amplitude, 200 μ s rise time, 100% duty cycle).
- A 306 channel Elekta Neuromag MEG System
- A state-of-the-art high density electroencephalography (EEG) lab
- Administrative, clinical assessment and stability (ACAS) core
- Image analysis core (IA)
- Image data acquisition core (IDA)
- Biostatistics and neuroinformatics (STATNI) core

Index Terms

schizophrenia, auditory integration, visual integration, resting fMRI, MEG, EEG, DTI, cognition, gating

[Back to top](#)

New Mexico

P20GM103452- Phase 2
Center for Evolutionary and Theoretical Immunology
University of New Mexico

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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

- Modeling of host immune responses and antiviral therapy against Hepatitis C virus infection: in vivo and in vitro
- Characterization of the opossum T cell receptor mu complex
- Computational study of molecular motions involved in peptide, MHC and TCR binding
- The evolution of nasal-associated lymphoid tissue in early vertebrates

Research Resources

- Molecular biology facility – Roche FLX 454 sequencer, 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
- Cell biology facility – Microm HM 550 cryostat, Attune flow cytometer, inverted Ti Nikon microscope, two Conviron E8 reach-in environmental chambers and one Conviron C1006 controlled environment room; a fully equipped tissue culture room
- Bioinformatics core

Index Terms

evolutionary immunobiology, theoretical immunology, innate immunity, immunology, RNAi, comparative immunology, evolution, host-pathogen interaction, hepatitis C, T cell

[Back to top](#)

New Mexico

P30GM103400- Phase 3 Integrative Program in CNS Pathophysiology Research University of New Mexico

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Thematic Scientific Focus

The Biomedical Research and Integrative NeuroImaging (BRaIN Imaging) Center is a multimodal integrative neuroimaging facility for central nervous system pathophysiology research at the UNM Health Sciences Center

Research Projects

The BRaIN Imaging Center hosts constituents from numerous HSC and main campus departments, UNM's Clinical and Translational Science Center and others investigating stroke, traumatic brain injury, epilepsy and other neurological diseases at the molecular level

Research Resources

- Magnetic resonance imaging
- Electron paramagnetic resonance spectroscopy and imaging
- Confocal laser scanning microscopy
- Animal surgery models

Index Terms

central nervous system, pathophysiology, stroke, brain injury, neuroimaging, neurological disorders

[Back to top](#)

North Dakota

P30GM103329- Phase 3

COBRE in Pathophysiological Signaling in Neurodegenerative Disorders

University of North Dakota School of Medicine & Health Sciences

Principal Investigator

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Chair, Pharmacology, Physiology and Therapeutics

Interim Chair, Anatomy and Cell Biology

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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 Resources

- Mass spectrometry core – Waters G2S high-resolution electrospray-quadrupole/time-of-flight MS, Waters TQS electrospray-triple quadrupole MS, and Polaris Q 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

[Back to top](#)

North Dakota

P20GM103505-Phase 2
Center for Visual and Cognitive Neuroscience
North Dakota State University

Principal Investigator

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Thematic Scientific Focus

Empirical and theoretical analysis of human visual and cognitive performance in normal and dysfunctional states

Research Projects

- Mechanisms of own- and other-race face processing
- Neural mechanisms and processing strategies underlying brightness and lightness perception
- Testing a quantitative model for the perception of depth from motion parallax
- Vigilance and avoidance in affective visual processing

Research Resources

- High-density EEG core facility
 - (2) ETS Lindgren EM-, RF-, and acoustically shielded recording chambers
 - (4) IAC EM and RF-shielded anechoic recording chambers
 - (2) 168-channel Biosemi HD-EEG recording systems
 - (1) 64-channel EGI HD-EEG recording system
 - (1) 128-channel Neuroscan HD-EEG recording system
 - (1) 64-channel ASA TMS-compatible HD-EEG recording system
 - Magstim Rapid2 air-cooled TMS system with 3D digitizer/positioning system
- Driving simulator core facility
 - DriveSafety DS-600c research driving simulator
- High dynamic range imaging core facility
 - (1) Brightside Technologies (Dolby Laboratories, Inc.) DR-37P 37" HDR display monitor
 - (1) Sim2 Multimedia HDR47E HDR display monitor
- Immersive virtual reality core facility
 - IVR system #1
 - IVR system #2
- ElectroOptical instrumentation core facility
 - (1) Konica-Minolta luminance meter (LS-110)
 - (1) PR-650 SpectraColorimeter (PhotoResearch, Inc.)

- (2) Professional-grade digital cameras (Canon EOS-1D Mark II; Nikon D3)
- (1) Casio High Speed Exilim (Ex-zr100) digital
- (1) Minolta VIVID 9i high precision 3D laser
- (1) VariSpec Liquid Crystal Tunable Spectral Filter
- (1) Extech 407764 Data-logging Sound Level Meter
- (1) Protek B803 Sweep Function Generator
- (1) Instek GDS-820S 150 Mhz Digital Storage Oscilloscope
- (1) B+K Precision model 2120B dual trace oscilloscope (30 MHz bandwidth).
- (1) CircuitSpecialists CSI 825A SMD Rework station
- (1) CircuitSpecialists CSI474 thermostatically controlled desoldering station
- (1) CircuitSpecialists CSI 3005X5

- Eyetracking core facility
 - (2) Eyelink II head-mounted high-speed video eyetrackers
 - (3) Eyelink 1000 video-based eyetrackers with a sampling rate up to 1000 Hz
 - (1) Tobii X120 (Tobii Technology, Inc.) video-based binocular eyetracker
 - (3) Applied Science Laboratories (Model 504, upgraded to Eye-Trac6 capabilities) remote video eyetrackers
 - (1) Skalar IRIS IR Limbus Eye Tracker
 - (1) FaceLAB (Seeing Machines, Inc.)

- Technical services core facility
 - (2) Computer programmers (versed in C, C++, Python, Matlab, Mathematica, Presentation, e-Prime, VisualStudio).
 - (1) Computer/electronics engineer (responsible for design and fabrication of custom electronic and/or mechanical devices, as well as hardware interfaces).
 - (1) Laboratory coordinator
 - (1) EEG technician
 - (1) Web development specialist

Index Terms

visual processing, vision, eye movements, neural activity, EEG/ERP, cognition, attention, RT

[Back to top](#)

North Dakota

**P30GM103332- Phase 3
Center for Protease Research
North Dakota State University**

Principal Investigator

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Thematic Scientific Focus

Novel strategies for targeting human diseases through protease inhibition: understanding the role of proteases in disease, structural biology driven drug discovery, inhibition of matrix metalloproteinases and histone deacetylases

Research Projects

- Synthesis of HDAC inhibitors
- Fungal asthma
- Epigenetics and cancer
- Prostate cancer regulation
- Autophagy
- Cardiovascular signaling
- Environmental pathogenesis
- New methods for biochemistry education
- MMPs and innate immunity

Research Resources

- Molecular biology facility: fluorescence/chemifluorescence imager, flow cytometer, PCR, RT-PCR, microarray scanner
- Bioassay facility: microplate spectrophotometer, microplate fluorometer
- Cell and tissue culture facility: inverted microscope, Bright Field microscope
- Core synthesis facility and analytical services: combinatorial synthesis equipment, microwave synthesizer
- Mass spectroscopy facility: HRMS, GC-MS and MS-MS
- Microscopy facility: confocal microscope, laser capture microscopy
- Nuclear magnetic resonance facility: 500, 400, and 300 MHz spectrometers

Index Terms

cancer, asthma, arthritis, obesity, structural biology, reactive oxygen species, histone deacetylase, epigenetics, autophagy, synthesis of inhibitors

[Back to top](#)

Oklahoma

P30GM103334- Phase 3 Mentoring Vision Research in Oklahoma University of Oklahoma Health Sciences Center

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Protective role of cerium oxide nanoparticles in retinal degenerations
- Role of surfactant-binding proteins in retinopathy of prematurity
- In vivo role of caveolin-1 in modulating photoreceptor function
- Sphingolipid metabolism in the retina
- Endophthalmitis complicated by diabetes

Research Resources

- Image acquisition and production core
- Molecular biology
- Animal resource core – live animal imaging and testing
- Lipid analysis core

Index Terms

vision research, retinal disease, retinal biochemistry, light-induced signal transduction, immunology, neurodegeneration, diabetes, angiogenesis, vascularization, microbiology, neuroprotection

[Back to top](#)

Oklahoma

P20 GM103639- Phase 1 Mentoring Translational Cancer Research in Oklahoma University of Oklahoma Health Sciences Center

Principal Investigator

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Thematic Scientific Focus

Tumor biology: resistance to cancer therapy and mitigating strategies

Research Projects

- Hur: role in mediating resistance to radiation
- Molecular determinants of gemcitabine transport in lung cancer therapy
- Tumor resistance mechanisms to anti-VEGF therapy in prostate cancer
- Targeted therapy against rel-orchestrated neuroblastoma

Research Resources

- Histology and immunohistochemistry core
- Small animal imaging core
- Biospecimen pathology core

Index Terms

cancer, metastasis, chemotherapy, radiation-therapy, resistance, tumor cell biology

[Back to top](#)

Oklahoma

P20GM103456- Phase 2 Molecular Mechanisms and Genetics of Autoimmunity Oklahoma Medical Research Foundation

Principal Investigator

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Thematic Scientific Focus

This COBRE focuses on the molecular and genetic basis of autoimmune diseases

Research Projects

- Discovery and testing of novel immunological genes
- Functional analyses of B-Cell expressed susceptibility genes in SLE
- Ro- and La- specific T cells in Sjogren's Syndrome
- Identification of novel variants influencing autoinflammation in Sarcoidosis
- The prothrombotic potential of Anti-PDI autoantibodies in SLE
- Immunogenic associations of accelerated damage in an inception cohort of Systemic Lupus Erythematosus
- Whole transcriptome profiling of Sjogren's Syndrome using RNA sequencing
- Functional study of SLE-associated risk loci
- Epstein-Barr viral mimics in SLE pathogenesis: collaborative roles for molecular mimic EBNA-1 and CD40 functional mimic LMP1 in a mouse model of lupus

Research Resources

- Nucleic acids analysis core – Next generation sequencing, Sanger sequencing, genotyping, custom expression arrays; Illumina Immunochip, Illumina OMNI and OMNI-S genotyping chips, Illumina Golden Gate arrays
- Data analysis core – education and participation in experimental design, biostatistics, database construction and publication
- Bioinformatics core – provides support via the analysis of high-dimension data as well as the development and the implementation of novel computational approaches to investigating complex data systems
- Biorepository core – provides a centralized access point for assist junior COBRE investigators to indentify possible sample procurement resources, select which samples to use in their projects, procure samples, and gather available collaborative data about the same individuals

Index Terms

autoimmune disease, inflammatory rheumatic diseases, systemic lupus erythematosus, sjogren's syndrome, sarcoidosis, Epstein-barr, autoantibody, autoantigen

[Back to top](#)

Oklahoma

P30GM103510- Phase 3 Science in a Culture of Mentoring Oklahoma Medical Research FDN

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

Epstein-Barr viral mimics in SLE pathogenesis: collaborative roles for molecular mimic EBNA-1 and CD40 functional mimic LMP1 in a mouse model of lupus; tools for lineage tracing in fibrosis and inflammation; generating disease-specific thymic epithelial progenitors from human T1D patient-derived iPSCs; varicella zoster reactivation and vaccination in individuals with systemic lupus erythematosus

Research Resources

- Clinical core
- Human immunophenotyping and immune function core – attune acoustic focusing cytometer; BioTek Synergy HT multifunction plate reader; BD 4-laser LSRII and ARIA systems; multiparameter flow cytometry with cellular barcoding; cell surface biomarker expression/levels on cellular subsets; phospo-flow cytometry; intercellular cytokine and biomarker staining; proliferation assays
- Human monoclonal antibody – offers production of fully-human, full-length antigen-specific antibodies; cloning of antibodies into expression vectors; ELISA; hybridoma sequencing; site-specific mutagenesis or reversion of antibody or germline; non-antibody protein expression
- Imaging core – available microscopes include: Hitachi H-7600 transmission electron microscope; Zeiss Axiovert 200 inverted fluorescence microscope; Zeiss AxioStar upright microscope; Zeiss Laser TIRF Imaging Microscope system; Zeiss AxioPlan 2i Upright fluorescent microscope; Zeiss LSM-510META Laser Scanning Confocal microscope; Olympus SX12 Dissecting Fluorescent Microscope
- Microarray core – experimental design/project consulting, quality control analysis of RNA, microarray processing for Illumina and Affymetrix commercial microarrays (whole genome, miRNA, exon arrays), data warehousing, bioinformatics and statistical analyses of microarray data
- Serum analyte and biomarker core – provides investigators with access to high-throughput and multiplex autoantibody and cytokine/chemokine assays in order to advance basic science and clinical disease research. This core offers project/assay consultation, high-throughput multiplex assays, autoantibody testing (including anti-viral and cotinine antibodies), Vitamin D testing, serum analyte profiling, cytokine/chemokine testing, solid phase epitope mapping, BioRad Bio-Plex 200 and BioRad Bio-Plex 2200 assays

Index Terms

immunology, vaccine, signaling, inflammation, inflammatory disease, DNA microarray, imaging, proteomics, immunodeficiency, autoimmune disease, SLE, arthritis, genomics

[Back to top](#)

Oklahoma

P20GM104934- Phase 2 Mentoring Diabetes Research in Oklahoma University of Oklahoma Health Sciences Center

Principal Investigator

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Thematic Scientific Focus

To mentor and train junior investigators in diabetes research and establish core facilities for diabetes research

Research Projects

- Mechanisms of mitochondrial dysfunction in diabetic cardiomyopathy
- The 26S proteasome functionality and endothelial dysfunction in diabetes
- GRP78-dependent modulation of ER stress response in diabetes
- VEGF signaling in photoreceptors

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

[Back to top](#)

Oklahoma

P20GM103441- Phase 2 Interdisciplinary Research in Vascular Biology Oklahoma Medical Research Foundation

Principal Investigator

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Thematic Scientific Focus

Interdisciplinary research in vascular biology

Research Projects

- SWI/SNF-regulated postnatal angiogenesis
- Epsin-regulated VEGFR-3 signaling in lymphangiogenesis
- Mechanisms of CXCL16-mediated atheroprotection
- Obesity and aging in osteoarthritis
- Podoplanin regulation of lymphatic endothelial cell identity In vivo

Research Resources

- In vitro microscopy core – provides expertise and the equipment to perform a diversity of techniques that include bright field 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

[Back to top](#)

Oklahoma

P20GM103640- Phase 1

**Oklahoma Center of Biomedical Research Excellence (COBRE) in Structural Biology
University of Oklahoma-Norman**

Principal Investigator

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Thematic Scientific Focus

Structural biology approaches to study macromolecules that are promising targets for rational drug design

Research Projects

- Structure-function studies of MsvR, a methanogen-specific transcriptional regulator
- Structural and mechanistic studies of essential microbial kinases
- Structural characterization of gamma-glutamyl transferase enzymes

Research Resources

- X-ray crystallography core
- Protein production core

Index Terms

x-ray crystallography; structure/function studies; structural biology; transcription; protein kinases; cancer; antimicrobial drug targets; oxidative stress

[Back to top](#)

Rhode Island

P30GM103410-Phase 3 COBRE Center for Cancer Signaling Networks Brown University

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Changes in spatial organization in the aging genome
- Computational and functional genomic analysis of the notch signaling pathway in ovarian cancer
- Creation of viable knock-in mice expressing an engineered bungarotoxin-sensitive nicotinic $\alpha 3$ receptor subunit to facilitate functional analysis of $\alpha 3$ in spinal cord mediated pain and in diabetic neuropathy in the sympathetic nervous system
- Determining the dynamic molecular architecture that regulates dopamine neuron diversity
- Do steroid hormones induce gene amplification in cancer
- Dynamic translational profiling
- Engineering mouse models of neurodevelopmental disorders due to GPT2 mutations
- Functional characterization of the olfactory subsystem of TAAR-expressing neurons
- Generation of SHP-1 and SHIP-1 conditional deficient mice
- Novel UV receptors in human skin
- The role of mechanosensitive microRNA-365 in cartilage development

Research Resources

- Animal care facility
- Confocal imaging core
- Flow cytometry and sorting facility
- Genomics facility
- Molecular pathology research core, superfund basic research program
- Mouse transgenic and gene targeting facility
- MRI research facility
- Proteomics facility
- Rhode Island Biobank
- Core Research Laboratories at Rhode Island Hospital
- Rhode Island Hospital COBRE Core Facility

- Rhode Island Genomics and Sequencing Center at the University of Rhode Island
- RI-INBRE Centralized Research Core Facility at the University of Rhode Island

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

[Back to top](#)

Rhode Island

**P20GM104937- Phase 2
COBRE for Skeletal Health and Repair
Rhode Island Hospital**

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Biomechanical regulation of chondrocyte differentiation
- Articular cartilage calcification in osteoarthritis (OA)
- Mechanical characterization of stem cell differentiation

Research Resources

- Bioengineering core
- Molecular biology and imaging core

Index Terms

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

[Back to top](#)

Rhode Island

P20GM103414- Phase 2 New Approaches to Tissue Repair Roger Williams Hospital

Principal Investigator

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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

[Back to top](#)

Rhode Island

**P20GM103537- Phase 2
COBRE for Perinatal Biology
Women and Infants' Hospital of Rhode Island**

Principal Investigator

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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
- Define the role of Fas-mediated apoptosis in perinatal lung remodeling

Research Resources

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

Index Terms

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

[Back to top](#)

Rhode Island

P20GM103468- Phase 1 Stem Cell Biology: New Directions in Clinical and Basic Research Rhode Island Hospital

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Web: <http://www.lifespan.org>

Thematic Scientific Focus

Studies of stem cell biology and have evolved the theory of the stem cell continuum which is largely based on the cell cycle status of long-term re-populating hematopoietic stem cells. Also, working on cell fate determination by cell-derived microvesicles and translation of those studies to tissue restoration in injury models

Research Projects

- Injured lung and its influence on marrow cell phenotype
- Determining the transcriptional regulation and cell signaling events that shape the molecular identity of dopamine neuron progenitors and specify subtypes of midbrain dopamine neurons
- Tyrosine phosphatase Shp2 in hematopoietic stem cell property maintenance
- The study of cycling hematopoietic stem cells
- Human induced Pluripotent Stem Cell (iPSC) technology applied to brain disease

Research Resources

- Administrative core
- Flow core
- Molecular core

Index Terms

stem cell biology, stem cell continuum, cell cycle, circadian rhythm, microvesicles, BrdU

[Back to top](#)

Rhode Island

**P20 GM103421- Phase 2
COBRE Center for Cancer Research Development
Rhode Island Hospital**

Principal Investigator

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Thematic Scientific Focus

The mission of COBRE Center for Cancer Research Development at Rhode Island Hospital is to create, interpret and apply new knowledge based on original, collaborative, multidisciplinary laboratory studies of the cellular and molecular pathways leading to cancer

Research Projects

- Post-translational modification of survivin: a novel therapeutic approach for cancer
- The RKIP-STATs axis in colon cancer: molecular profiles for prognosis and therapeutic intervention
- Involvement of stem-like cells in models of spontaneous transformation
- Mapping conformational changes in growth factor receptors using DXMS
- Growth regulation of liver progenitor cells

Research Resources

- Proteomics core
- Molecular pathology core

Index Terms

cell biology, molecular biology, proteomics, cancer, signaling, angiogenesis

[Back to top](#)

South Carolina

P30GM103331- Phase 3
MUSC Center for Oral Health Research (COHR)
Medical University of South Carolina

Principal Investigator

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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

- Clinical core (C-COHR)
- Laboratory core (L-COHR composed of four distinct but interactive facilities: 1) Oral Preclinical Research Facility, 2) Mineralized Tissue Facility, 3) Gnotobiotic Animal Research Facility, and 4) Laser Capture Microdissection Facility
- Pilot and feasibility project program

Index Terms

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

[Back to top](#)

South Carolina

P30GM103342- Phase 3

South Carolina COBRE for Developmentally Based Cardiovascular Diseases Medical University of South Carolina

Principal Investigator

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Thematic Scientific Focus

Elucidating the developmental mechanisms underlying the etiology of congenital heart disease and adult cardiovascular diseases

Research Resources

- Core B: Morphology, imaging and instrumentation core – microscopy and instrumentation resources including basic and confocal microscopy; histology services, including image analysis and 3D reconstruction; flow cytometry
- Core C: Proteogenomics and bioinformatics core – protein related services include surface plasmon resonance and multiplex bead array-based analysis of phosphoproteins and cytokines; genomic related services using next generation sequencing technology include genomic resequencing, RNA-seq, ChIP-seq, methyl-seq and small RNA profiling. DNA microarray analysis, RNA quality assessment and real time quantitative PCR analysis
- Core D: Gene function core - DNA construct design and fabrication; transgenic mouse generation in either FVB/N or C57BL/6; gene targeting in either 129Sv/Ev and C57BL/6 ES cells with chimera production and breeding to confirm germline transmission

Index Terms

cardiovascular disease, proteomics, genomics, apoptosis, cell biology, DNA microarray, morphology, 3D-reconstruction transgenic mice, gene targeting, next generation sequencing, genomic resequencing, RNA-seq, ChIP-seq, methyl-seq and small RNA profiling, DNA microarray

[Back to top](#)

South Carolina

P20GM103641- Phase 1 COBRE Center for Dietary Supplements and Inflammation South Carolina Research FDN

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<http://cobre.med.sc.edu/index.asp>

Thematic Scientific Focus

The Center for Dietary and Inflammatory Diseases integrates faculty from six of University of South Carolina's colleges to conduct research on the mechanism of regulation of inflammation by dietary supplements during chronic inflammatory processes associated with cancer, obesity, hypertension, diabetes, Alzheimer's and several other autoimmune diseases

Research Projects

- Study the role of a new Chinese herb-derived selective Toll-like receptor antagonist (Sparstolonin B) as an anti-inflammatory agent to treat atherosclerosis
- Anti-inflammatory capabilities of plant polyphenols for the treatment of Alzheimer's disease
- American Ginseng-mediated autophagy and suppression of inflammation in pathological cardiac remodeling and dysfunction
- Macrophage-induced inflammation in high fat diet enhanced breast cancer: benefits of Quercetin.

Research Resources

- Administrative core
- Flow cytometry and cell sorting core
- Immune monitoring core
- Microscopy and imaging core

Index Terms

dietary supplements, inflammation, Quercetin, Ginseng, Sparstolonin B, plant polyphenols, atherosclerosis, Alzheimer's disease, cardiac remodeling, cardiac dysfunction, high fat diet, breast cancer, macrophage, toll-like receptors, amyloid- β protein, autophagy, NF-kB, SIRT1, Nrf2, COBRE

[Back to top](#)

South Carolina

P30GM103339- Phase 3
Department of Biochemistry and Molecular Biology
Medical University of South Carolina

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Thematic Scientific Focus

Center in lipidomics and pathobiology focusing on bioactive lipids and related metabolites, such as sphingolipids, which constitute a complex network of diverse pathways regulating key physiologic functions in the pathobiology of specific diseases

Research Projects

- Lipid metabolism and signaling
- Enzymes of lipid metabolism
- Preclinical and genetic models of lipid metabolizing enzymes

Research Resources

- Lipidomics core
- Protein science translational core
- Animal pathobiology core

Index Terms

sphingolipids, lipidomics, sphingolipid metabolism and signaling

[Back to top](#)

South Carolina

P20GM103542- Phase 1

South Carolina COBRE in Oxidants, Redox Balance and Stress Signaling Medical University of South Carolina

Principal Investigator

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Thematic Scientific Focus

Oxidants, redox balance and stress signaling

Research Projects

- The role of mitochondrial DNA stability in the development of mitochondrial diseases
- Novel AML therapy targeting HDAC6 and Hsp90 chaperone complex
- ROS/RNS and the unfolded protein response
- Glutathione S-transferase pi mediated redox regulation modulates cocaine sensitivity
- Role of glutathione and mitochondrial pathology in models of amyotrophic lateral sclerosis

Research Resources

- Cell and molecular imaging
- Mass spectrometry
- Metabolomics

Index Terms

oxidants, redox balance, stress signaling

[Back to top](#)

South Carolina

P20GM103444- Phase 1 Center of Biomaterials for Tissue Regeneration (CBTR) Clemson University

Principal Investigator

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Thematic Scientific Focus

The overarching theme of this research center is tissue regeneration through cell-biomaterials interactions using distinctive biomaterials-based approaches. Tissue regeneration involves bringing together scaffolds, cells, biological signals and a microvascular network in three-dimensional constructs. A combination of factors working independently and in concert, such as scaffold composition, cell selection, cell-matrix interactions and mechanical cues, determines the success of tissue regeneration; therefore, interdisciplinary research is required. Here, Clemson University's unique strengths in bioengineering, tissue engineering, biomaterials, and fiber and film technology is complemented by expertise in medicine and developmental biology at Medical University of South Carolina and University of South Carolina.

Research Projects

- Stem cell-myocyte electrical coupling via a laser patterned cell bridge
- Biomaterials for guided neural regeneration
- Biomechanics and mechanobiology of atherosclerotic plaque failure
- Stem cell differentiation and cardiovascular tissue engineering in diabetes
- Mechanically guided urological tissue regeneration in vitro
- Improved reactor control for stem cell expansion to meet therapeutic needs
- Nanoparticles for targeted delivery of neuroprotective antioxidant enzymes to CNS
- Combinatorial development of biomaterials for cardiac tissue regeneration
- Neuron-specific polymeric micelle delivery system for neural regeneration

Pilot Project

- Developing non-invasive luminescent tension-indicating orthopedic screws

Research Resources

- Materials synthesis, characterization and testing core – a Jasco FTIR-480 spectrophotometer, Jasco J-810 circular dichroism spectropolarimeter, Reichert AR700 refractive index instrument, Kruss DSA-20 contact-angle goniometer, Sopra GES-5 variable-angle spectroscopic ellipsometer, Perkin Elmer AAnalyst 200 flame atomic absorption instrument, Biacore X SPR spectrometer, MTS Synergie 100 mechanical test machine, Waters HPLC System, Harrick plasma surface treatment system, and a MTI Corp. VTC-100 programmable spin-coater system.
- Cell and molecular engineering core – the major equipment in the Cell and Molecular Engineering lab include a CyAN ADP Cell Analyzer, MoFlo Astrios High Speed Sorter, Invitrogen Countess Cell Enumeration /Viability Counter, Amaxa Nucleofector, and Bio-Rad iCycler RT-qPCR detection system. We also have all matter of accessory equipment for cell

harvest, cell culture, tissue processing, conventional and confocal microscopy, protein analyses and RT-PCR analyses

- Histology and imaging core - the Clemson Light Imaging Facility is housed in the newly constructed Life Sciences Building, and contains the following state of the art light microscopes: Zeiss LSM 510 Confocal Microscope, CytoViva wide field hyperspectral imaging system, Leica TCS SP8 multiphoton spectral confocal, Nikon Eclipse Ti, inverted microscope with confocal and spectral imaging, Nikon AZ100 Multizoom and the Nikon Eclipse LV/UDM

Index Terms

biomaterials, tissue engineering, organ replacements, tissue regeneration, cardiac tissue engineering, neural tissue engineering, drug delivery

[Back to top](#)

South Dakota

P20GM103548- Phase 1
Center for Cancer Biology Research
Sanford Research/USD

Principal Investigator

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Sanford Research/USD

Sanford Center

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Thematic Scientific Focus

Basic biology of cancer cells with emphasis on the identification, functional characterization, and targeting of tumor specific markers and antigens

Research Projects

- Autoantibody profiling as a novel method for early and personalized diagnosis for prostate cancer
- Protein Kinase D function in cancer
- Therapeutic effects of antibodies against Fc-receptor like proteins in hematological malignancies
- EPHRINB1: signaling ligand and regulator in head and neck squamous cell carcinoma
- The interaction between Notch Pathway and Atonal Homolog 1 (Atoh1) in Sonic Hedgehog-dependent Medulloblastoma

Research Resources

- Molecular pathology core
- Imaging core
- Tumor biology core
- Flow cytometry

Index Terms

cancer biology, tumor markers, tumor specific antigens, cancer signaling pathways, cancer immunology, mouse models of cancer, breast cancer, prostate cancer, head and neck cancer, medulloblastoma, lymphoma

[Back to top](#)

South Dakota

P20GM103455

**Mechanisms of Cardiovascular Remodeling
University of South Dakota School of Medicine**

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- α 1-adrenergic receptor signaling and cardiac remodeling
- 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 remodeling, lipid mediators, lipoprotein metabolism, fatty acids, cardio protection, autophagy, doxorubicin, apoptosis, α 1A-adrenergic receptor, heart failure, benign prostate hyperplasia, hypertension

[Back to top](#)

Vermont

P20GM103496- Phase 2

**The Vermont Center for Immunology and Infectious Diseases
University of Vermont**

Principal Investigator

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Thematic Scientific Focus

The immune and host response to infectious agents and microbial pathogenesis

Research Projects

- Identification of the hantavirus-host interactome
- Chemically interrogating bacterial martx toxin function
- The role of NFAT in the effector functions of memory CD4 T cells
- Pathogenesis of *Pseudomonas aeruginosa*
- Regulation of the RIG-I/interferon pathway by viruses

Research Resources

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

Index Terms

innate and adaptive immunity, viral, bacterial, and parasite pathogenesis, T cells, genetic regulation of the immune response

[Back to top](#)

Vermont

P30GM103532- Phase3 Translational Research in Lung Biology and Disease University of Vermont & State Agricultural College

Principal Investigator

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Thematic Scientific Focus

Translating basic laboratory research into clinical applications to diagnose and treat lung disease, while creating a stimulating research environment for promising new investigators

Pilot Research Projects

- Predictors of dyspnea/fatigue syndrome in breast cancer survivors before and after an exercise intervention
- Epithelial Duox1, IL-33 and allergic inflammation
- Mechanisms of stretch-induced SPC expression
- Non-invasive detection of airway injury associated with airway closure in asthmatic subjects
- Role of DARC, the Duffy antigen receptor for chemokines, in eosinophil induced airway pathology
- Design study of a sterile disposable attachment for measuring respiratory impedance in ventilated patients

Research Resources

- Transgenic animal core
- Pathophysiological phenotyping core
- Clinical support core

Index Terms

physiology, lungs, asthma, biomedical engineering, transgenic animals, signaling, inflammation, chronic obstructive pulmonary disease

[Back to top](#)

Vermont

**P30GM103498- Phase 3
Center for Neuroscience Excellence
University of Vermont**

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Thematic Scientific Focus

- Stroke and neurovascular interactions
- Neural regulation of autonomic nervous system development, function and disorders

Research Project

Determinants of multipotency and neurogenesis from reactive astrocytes

Research Resources

- Imaging/physiology core – this multi-user facility houses a Noran confocal microscope, DeltaVision restoration microscope, Biorad Radiance Dedicated Multiphoton Microscopy System equipped with a Coherent Chameleon laser, and a TIRF microscopy system. This year a new Zeiss multiphoton will be added
- Cellular/molecular biology core – this multi-user facility houses the equipment required for neuroscience investigators and others within the university community to apply cutting-edge molecular techniques to their projects

Index Terms

autonomic neurobiology, stroke, neurodegeneration, neurodevelopment

[Back to top](#)

West Virginia

**P30GM103488- Phase 3
COBRE for Signal Transduction and Cancer Phase III
Mary Babb Randolph Cancer Center at West Virginia University**

Principal Investigator

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Thematic Scientific Focus

Molecular changes associated with disease initiation and progression including EMT, invasion, metastasis and tumor stem cell biology

Research Projects (during P20):

- Role of ankyrin complexes in anoikis
- Sumoylation and epigenetics
- Hef-1/Ajuba regulates Aurora kinases
- Cortactin and head and neck cancer
- Myosin II and cancer cell migration

Research Resources

- Flow cytometry
- Microscope imaging facility
- Animal models and imaging
- Protein purification
- Bioinformatics and biostatistics
- Biospecimen processing

Index Terms

flow cytometry, imaging, biospecimens, EMT, invasion, stem cells

[Back to top](#)

West Virginia

**P30GM103503- Phase 3
COBRE in Sensory Neuroscience
West Virginia University**

Principal Investigator

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Thematic Scientific Focus

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

Research Projects

- Novel phosphodiesterases in retina and brain
- Wearable devices for neuroimaging humans in action
- Construction of an electronic nose

Research Resources

- Histology core
- Non-linear optical imaging core
- Transgenic animal core
- Molecular biology core (Affymetrix genechip reader, Illumina NextGen Sequencing)
- Center for advanced imaging

Index Terms

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

[Back to top](#)

IDeA-CTR

West Virginia

U54GM104942

West Virginia IDEA-CTR

West Virginia University

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Thematic Scientific Focus

The overall goal of the West Virginia Clinical and Translational Science Institute's (WVCTSI) IDeA-CTR Program is to establish a competitive clinical and translational science infrastructure and expand our capacity to conduct clinical and translational research in order to meet our long term goal of eliminating health and healthcare disparities amongst West Virginians/Appalachians

Research Cores

- Administrative – establishes and maintains the administrative and operational structure required to support clinical and translational research within the WVCTSI
- Biomedical Informatics Resources – contributes to the development of robust clinical and translational research projects that have enhanced extramural competitiveness by virtue, in part, of their utilization of unique clinical data
- Community Engagement and Outreach – ensures the rapid application of WVCTSI research into clinical practice and public health strategies through knowledge synthesis, targeted communication and evidence-based dissemination
- Clinical Research Design, Epidemiology, and Biostatistics – provides a transdisciplinary team of biostatisticians and epidemiologists who work collaboratively with clinical and translational researchers statewide
- Clinical and Translational Faculty Recruitment and Resources – recruits magnet clinical and translational faculty and junior investigators and builds resources for them in all five Schools at the West Virginia University Health Sciences Center
- Clinical Research Education, Mentoring, and Career Development – educates a workforce of trained health professionals and scientists (especially clinical faculty) to be competitive for NIH funding to support research aligned with the major diseases impacting the West Virginia's population
- Ethics, Regulatory Knowledge and Support – coordinates components of the individual regulatory programs, integrates training and education, enhances contract and technology transfer guidelines and develops an overarching program in research ethics and the responsible conduct of research
- Clinical And Translational Pilot Grant Program – provides a mechanism for soliciting and awarding clinical, translational, and community engagement projects, from concept to competitiveness for external funding

- Tracking, Evaluation and Quality Improvement Program – responsible for gathering Program data and analyzing them to determine whether or not adequate progress is being made toward each overall CTR Aim, and whether each core is effectively carrying out their planned activities and progressing toward meeting their specific aims

Research Resources

- Pilot grant funding
- Integrated data repository
- Human subjects' research and responsible conduct of research training
- Clinical and translational science master's and graduate certificate programs
- Research bootcamp
- Research scholar program
- Research mentors
- Research pathfinder
- Research participant advocacy program
- Online portal of clinical and translational resources
- Biostatistics walk-in clinics and huddles
- Pre- and post-award support

Index Terms

clinical and translational science, clinical, translational, Appalachia, West Virginia, rural, health disparities, infrastructure, West Virginia Clinical and Translational Science Institute,

[Back to top](#)

Wyoming

P30GM103398- Phase 3 Neuroscience Center University of Wyoming

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Thematic Scientific Focus

The Neuroscience Center is comprised of neuroscientists who combine expertise in neurophysiology, neuroanatomy, behavioral neuroscience, systems physiology and molecular biology to identify mechanisms that guide normal brain development, synaptic plasticity across the life span, and those that underlie neuropathological processes. The overall goal of the Neuroscience Center is to increase the effectiveness of Center investigators to complete current research projects and to foster synergies between researchers that combine various expertise to answer pressing neurological health issues.

Research Resources

Microscopy Imaging - The microscopy core has four main components: epi fluorescence and bright field microscopy, confocal laser scanning microscopy, transmission electron microscopy and scanning electron microscopy

- Hitachi scanning electron microscope (TM-1000)
- Hitachi Transmission electron microscope with 4K by 4K cooled CCD digital camera (Gatan)
- Zeiss 710 laser scanning confocal with inverted microscope and live cell imaging capacity
- Zeiss 700 laser scanning microscope with upright microscope
- Nikon and Olympus inverted epi-fluorescence microscopes
- Raman Microscope (DeltaNu ExamineR)

Index Terms

neuroscience, neuroplasticity, nociception, somatosensory, neuroendocrine, confocal microscopy, ultrastructure, receptor signaling

[Back to top](#)