Ongoing and Pending Research Support – Jeremy C. Smith.

Ongoing

DOE – OBER
Title: ORNL Scientific Focus Area "Biofuels"
Funding period: 10/1-10-10/1-13
Amount: $2.1M
Effort: 1 month/year
Role: Co-PI.
Abstract: Continuation of LAB 07-12 program. To combine neutron scattering and computer simulation for multiple length scale, real-time imaging of biomass during pretreatment and enzymatic hydrolysis. The combined capabilities of the Spallation Neutron Source, the High Flux Isotope Reactor, and the National Center for Computational Sciences at Oak Ridge National Laboratory will provide new information on lignocellulosic degradation.

DOE – OBER
Title: Bioenergy Science Center
Funding Period: 2007-2012
Amount: $125M
Effort: 1 month/year
Role: Co-PI and Task Leader.
Abstract: Our task in this center is to perform computer simulations of enzymes involved in cellulose deconstruction, including cellulosome component modeling and quantum mechanical/molecular mechanical investigations of cellulase action.

DOE – EpsCOR Implementation Award
Title: DE-FG02-08ER46528 Neutron Scattering Research Network for EPSCoR States.
Funding Period: 10/1/12-10/1/15
Amount $1.97M plus 50% U. Tenn. matching.
Effort: 0.5 months/year
Role: Co-PI
Abstract: With the completion of the Spallation Neutron Source (SNS) and upgrading of the High-Flux Isotope Reactor (HFIR) at the Oak Ridge National Laboratory (ORNL) the state of Tennessee is poised to lead the world in the capability of neutron scattering research. This proposal aims at directing the great impact of these facilities to the EPSCoR states and Tennessee in particular, by creating a research collaboration network around these facilities, and making the access to the facilities much easier for the researchers in the EPSCoR states. The plan consists of five parts: (1) Seeding research collaboration among the core participants and with the ORNL researchers, (2) Purchasing equipment widely used by the participants, (3) Supporting travels by the graduate students and participating researchers to the neutron facilities at the ORNL, (4) Partially supporting sabbatical leaves by the participating researchers, and (5) Holding workshops and schools on the application of neutron scattering for biological, life and physical sciences and engineering.

DOE - OBER Science Focus Area
Title: Biogeochemical and Molecular Mechanisms Controlling Contaminant Transformation in the Environment
Funding Period: 10/09-10/14
Amount $3M/year

Effort: 1 month/year
Role;. Co-PI Task leader.
Abstract: The ORNL Science Focus Area (SFA) Program responds to Environmental Remediation Science Program (ERSD) needs by addressing the scientific issues that limit contaminant remediation at the Oak Ridge Reservation (ORR). Over the initial 5-10 year period, ORNL's SFA will address significant knowledge gaps regarding biogeochemical transformations that determine uranium (U) subsurface mobility and mercury (Hg) toxicity. This program integrates geochemical, microbiological, molecular, and modeling-simulation sciences to understand contaminant behavior in the field.

DOE-OBER
Title: Active Biosystems Imaging.
Funding Period: 05/01/2014-31/09/2017
Amount: $4M
Effort: 1 month/year
Role: Co-PI.
Abstract: Understanding how observable biological processes, carried out over wide ranging temporal and spatial scales, arise from molecular scale events represents a grand challenge facing biological and environmental research. Underpinning this challenge is the need to monitor the flow of materials and information in response to environmental perturbations. Therefore, we propose to develop and apply an adaptive approach to imaging, wherein computational modeling and simulation guide interactive, molecular imaging measurements to couple systems models to observable phenomena. We will apply the unique resources of ORNL and our academic collaborators to advance and integrate new instrumentation, stable-isotope probes and supercomputer-driven simulation tools to trace the production, transport and fate of selected metabolites in bacterial systems. Our pilot efforts will focus on understanding the structure and organization of cellular membranes and the movement of chemicals within and between cells and within their environment. The resulting capability will serve as a framework for designing and implementing bioimaging experiments that reach across the hierarchies and dimensions of biological systems to provide understanding to a diverse array of biological and environmental processes.

NSF 07-597 EF - BIO CENTERS:
Title: Nimbios – Center for Synthesis of Mathematics and Biology
Funding Period: 10/1/12-10/1-17
Amount: $15,907,538.
Effort: 0.5 months/year
Role: Co-PI.
Abstract: A major goal of mathematical models and analysis in biology is to provide insight into the complexities arising from the non-linearity and hierarchical nature of biological systems. The Center fosters the maturation of cross-disciplinary approaches in mathematical biology and fosters the development of a cadre of researchers who are capable of conceiving and engaging in creative and collaborative connections across disciplines to address fundamental and applied biological questions. The Center : 1) addresses key biological questions by facilitating the assembly and productive collaboration of interdisciplinary teams; and 2) fosters development of the critical and essential human capacity to deal with the complexities of the multi-scale systems that characterize modern biology.

NIH - PEER
Title: Program for Excellence and Equity in Research
Funding Period: 01/10/09-01/10/14
Amount $3.9M.
Effort: 0.5 months/year

Role;. Senior Personnel.
Abstract: The University of Tennessee Knoxville's (UTK) Program for Excellence and Equity in Research (PEER), an Initiative for Maximizing Student Diversity (IMSD) program in the MORE Division, through UTK's partnership with Oak Ridge National Laboratory (ORNL) and the partnership's UTK/ORNL Graduate School for Genome Science and Technology (GST), proffers underrepresented minority (URM) Scholars the opportunity to train in an unprecedented atmosphere of scientific excellence, engage in team-science fostered through the UTK-ORNL partnership, gain crucial 21st century professional skills, and be mentored by world class scientists, all within a supportive community created by and for the Scholars. PEER's goal is to leverage these attributes to create a "program of excellence" that will produce from PEER, the GST, and across the university, an increased number of accomplished, competitive and determined URM Ph.D.s who attain careers in biomedical research characterized by significant contributions to their fields, and thus contribute to our nation's health and well being.

NIH Grant Number: 1KL2RR031974-01
Title: Georgetown-Howard Universities Center for Clinical and Translational Science (GHU)
Funding Period: 07/01/2010 – 03/31/2015
Amount: $1,254,365
Role: Senior personnel
Effort: 0.5 month/year
Abstract: The Georgetown-Howard Universities Center for Clinical and Translational Science (GHUCCTS) is a collaborative research center that includes two major universities and three affiliated hospital and research systems. The specific aims of GHUCCTS are to accelerate improvements in human health by stimulating innovative, multidisciplinary and cross-institutional research among the GHUCCTS investigators; to support the careers of clinical and translational investigators through a variety of educational programs paired with focused mentorship; and to enhance local and national clinical and translational research in underserved populations, including minorities, the elderly, and those with disabilities. GHUCCTS also will support collaborative research projects, using the supercomputing and translational tools of the Oak Ridge National Laboratory to explore and develop novel translational methodologies.

NSF 13-1439
Title: SI2-SSI: A Productive and Accessible Development Workbench for HPC Applications Using the Eclipse Parallel Tools Platform,
Funding Period: 05/01/2013-03/31/2014
Amount: $100,687.00
Effort: 1 month/year
Role: Subcontractee from Univ. Illinois
Abstract: Our goal is to reduce or eliminate at least some of the factors that hinder productive development of petascale scientific codes. Our starting point will be the development environment that plays a crucial role in the application development lifecycle. Long experience by the software engineering community has demonstrated that the use of integrated development environments is a key mechanism for improving productivity, so our intention is to use the open source Eclipse platform as the basis for the project.

NIH NIAMS 3R01AR045955 - 15S1 PI: Quarles
Title: REGULATION AND FUNCTION OF FGF23
Funding period: 05/14-05/15
Amount: $150,000
Effort: 1 month

Role: Co-PI
In this application we are employing the power of the supercomputing capacity at Oak Ridge National Laboratory and a new interdisciplinary collaboration between computational scientists at UT/ORNL and biologists and physician-scientists at UTHSC to identify compounds that modulate FGF23 interactions with a-Klotho, the co-factor required for FGF23 activation of FGF receptors. A comprehensive knowledge of targetable conformations of the protein will identify candidate molecules that bind to a-Klotho which will be tested in cell-based assays for their ability to activate or inhibit FGFR/ a-Klotho signaling. These small molecules will be useful tools to manipulate FGF23 signaling and serve as an initial step toward developing pharmaceutical agonists or antagonists modulate the function of the FGF23 endocrine network regulating phosphate and vitamin D metabolism.

INTEL Corporation.
Title: "Porting and Optimization of the General-Purpose Molecular Dynamics Code GROMACS on Next-Generation Intel-Based Computers",
Funding Period: 10/01/2013-10/01/2014
Amount: $150,000
Effort: 1 month/year
Role: PI
Abstract. This grant is for the Porting and Optimization of the General-Purpose Molecular Dynamics Code GROMACS on Next-Generation Intel-Based Computers.

Pending:

NIH NIAMS R-01 (Ranked: 6th percentile.)
Title: Transport Across Two Membranes by AcrAB-TolC.
Funding Period: 10/14-10/19
Role: Co-PI
Effort: 1 month per year
Abstract: Our long-term goal is to understand the molecular mechanism of drug efflux in Gram-negative bacteria and to develop approaches to inhibit multidrug efflux transporters. Our findings exposed a previously unknown vulnerability of multidrug pumps that could be targeted in development of new inhibitors. The objective of this application is to characterize this vulnerability in molecular details and to discover new effective inhibitors of drug efflux in Gram-negative bacteria. We will pursue three specific aims: (i) to investigate the activation of multidrug efflux pumps; (ii) to investigate the mechanisms of drug efflux inhibition; (iii) to identify new allosteric inhibitors of drug efflux transporters. The expected outcome of the proposed studies is detailed understanding of how multidrug efflux pumps are activated and new allosteric inhibitors acting on this critical step in drug efflux.

NIH NCI R01
Title: Drug Design for Prostate Cancer via GPRC6A Antagonism
Role: Co-PI
Effort: 1 month per year
Abstract: GPRC6A is the biologically relevant receptor for osteocalcin, and a molecular mechanism for linking osteocalcin to GPRC6A-mediated prostate cancer progression. GPRC6A is a common receptor that mediates the "non-genomic" effects of T and possibly effects dietary factors on PC progressionAntagonists to GPRC6A can be developed to attenuate prostate cancer progression.
We will define the role of GPRC6A in prostate cancer progression in mouse models, and pursue pre-therapeutic lead design of antagonists and agonists for GPRC6a using the unique computer power and computational biology modeling available at UTK/ORNL for drug discovery.