Research Centers in Minority Institutions

National Center for Integrative Biomedical Informatics

Workshop on Translational Bioinformatics

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University of Michigan
Medical School

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Workshop Participants and Research Interests

Ney Alliey-Rodriguez, M.D., University of Chicago
Postdoctoral fellow

I'm a M.D., psychiatrist devoted to research, with particular interest in the genetics of mental disorders and behavioral traits taking active part in psychiatric diseases. I am currently on the clinical research team in Psychiatry with Dr. Elliot Gershon, and in the Molecular Genetics Lab with Drs. Chunyu Liu and Gershon. I'm performing association studies (GWAS) for personality traits in bipolar patients, as we hypothesize that some personality deviations are the base for this disorder. Also I'm working on clinical sub-phenotypes selected and built by principal components analysis for GWAS and copy number variation analyses. I'm open to collaborations on GWAS and building phenotypes from clinical data. Among my interests are to work with candidate genes networks related to psychiatric (and CNS) disorders, gene-gene interactions and Pharmacogenomics. Other interests are related to use of computational tools for research.

Leonard Anderson, Ph.D., Morehouse School of Medicine
Research Assistant Professor

Vascular diseases involving hyperproliferation of VSMCs, such as atherosclerosis, is one of the major causes of mortality in the U.S. and one of the leading causes of mortality among African Americans. VSMCs play a critical role in early vasculogenesis and blood vessel maintenance. The requirement for VSMC replenishment after vessel injury by putative stem cell progenitors suggest unique changes in the cellular transcriptome when compared to other cell lineages such as neurons, skeletal muscle, and cardiomyocytes. Our lab is currently interested in defining the process by which pluripotent stem cells become VSMCs at the transcriptional and hence, signal transduction level by utilizing various innovative genomics technologies (i.e. Agilent OligoArrays, Affymetrix GeneChips, and protein arrays) to identify novel genes and proteins that play a crucial role in early VSMC fate determination. We are functionally characterizing these genes in pluripotent mouse embryonal carcinoma stem cells (P19) and various clonal derivatives by utilizing either 'gain of-' or 'loss of-' function methodologies to alter expression levels of identified genes. These functional genomics studies will provide insight into the mechanism(s) by which specific genes are involved in early cell lineage determination within the vasculature. Although the therapeutic potential of ES cell-derived *ex vivo* therapy has been demonstrated in mouse models of atherosclerosis and restenosis after balloon angioplasty, the outcome of these studies suggest further understanding of the basic molecular mechanisms involved in this process is required. The outcome of our genomic studies will allow us to gain insight into these early signaling events and potentially generate modified ES cells with a predetermined VSMC, and thus, greater therapeutic efficacy *in vivo*.

Jaideep Chaudhary, Ph.D., Clarke Atlanta University
Associate Professor

My research focus is to understand molecular basis of prostate cancer development and progression. We currently have two projects in this area. The first project is focused on understanding the role of βHLH family of transcription factors in prostate cancer initiation and progression. Our current research on these proteins involves their use as diagnostic markers and therapeutic targets for prostate cancer. The second, relatively new project addresses how inflammation and infection causes prostate cancer. The observation that body's failure to effectively fight inflammation or infection causes cancer is the basis of this project. Our group is looking at molecular signatures (genetic polymorphism) in genes that cause inflammation that we hope will indicate if a person has increased susceptibility to prostate cancer. Our overall hypothesis is that body's inflammatory response, under the genetic control and influenced by race, environment and dietary habits is a major determinant of prostate cancer.

Mohamed Elsayed, D.V.M., Meharry Medical College
Research Assistant of Biomedical Science

Wilfredo Hernandez, Ph.D., Ponce School of Medicine
Assistant Professor

Preventive medicine is the rational response to the rising medical costs. This response includes a renewed emphasis on antioxidant foods and supplements to lower risk from cancer, which is now the number one fatal disease. Our major aim is to evaluate suppression of mutagenesis by sulfhydryl antioxidant N-acetylcysteine (NAC), and alpha-lipoic acid, both of which potentiate glutathione activity, the gold standard of antioxidants. Surprisingly, few antioxidant studies have addressed directly the suppression of mutagenesis. Most rely on end points of survival times, anticarcinogenic activity, or chromosomal damage. We hypothesize that the sulfhydryl antioxidants will prevent mutations induced by gamma radiation, which mimics endogenous mutagenesis by OH radicals. Mutation frequencies (mf) will be quantitated by measuring mutations in a LacI repressor gene, contained in the chromosome of live transgenic Big Blue mice. Mutations will be detected because the inoperant LacI will not be able to repress the expression of the reporter gene (β-galactosidase) in a bacterial system, rendering the resulting plaque blue. DNA damage, a precursor to mutagenesis, will be assessed by quantification of apurinic/apirimidinic (AP) sites in the DNA. The degree of chemoprotection against mutations afforded by antioxidants in live Big Blue mice subjected to gamma radiation will be evaluated by two methods: LacI gene mutations and AP site production. Mutations will be isolated and sequenced to detect any patterns and to catalog them. This work will test the notion that antioxidants can effectively block mutations caused by oxidative damage. In addition, our results will provide a basis for a rational policy on the use of antioxidant supplements in humans, either as an anticancer strategy or for counteracting age-related diseases.

Raphael D. Isokpehi, Ph.D.,
Associate Professor of Biology & Director, Center for Bioinformatics & Computational Biology

The theme that ties my bioinformatics research interests is the integrative analysis of biological datasets with the goal of uncovering novel biological insights from observed patterns. The thematic emphasis permits my participation in a variety of projects that require the development and use of data integration pipelines. In the context of the NIH-NCRR-sponsored Research Centers in Minority Institutions (RCMI) Center for Environmental Health at Jackson State University, I lead a 5-year collaborative pilot project on arsenicogenomics, an aspect of toxicogenomics that provides a means to (i) understand how various genes respond to arsenic and (ii) how arsenic modifies the function and expression of specific genes in the genome. Arsenic is recognized as an environmental toxicant of global public health concern. Long-term exposure to arsenic principally through drinking water has been correlated with increased risk to diseases such as skin cancer, diabetes, blackfoot disease, spontaneous abortions, and arteriosclerosis. The avalanche of genome sequences combined with genome-enabled datasets from high-throughput gene expression, genotyping, haplotyping and protein assays is making it possible to gain biological insights into previously unknown gene-toxicant interactions. An output from the project is an Arsenic Sentence Database (http://compbio.jsums.edu/arsenic_pubmed) that provides a searchable catalog of sentences derived from the title and abstract text of PubMed records on arsenic. The arsenicogenomic research has used tools developed at the National Center for Integrative Biomedical Informatics (NCIBI) to gain molecular and systems level understanding of prioritized gene sets. For example, using BioSearch2D, a dynamic map of disease association of 19 arsenic interacting genes was generated that allowed the selection of 3 human genes (GSTT1, XPA, and ERCC2) based on their association with skin neoplasms. Subsequently, the Michigan Molecular Interactions (MiMI) and Gene Interaction Network (GIN) system were used to obtain protein interactions and gene networks.

Juliana Perez Laspiur, Ph.D., University of Puerto Rico
Research Associate

Human Immunodeficiency Virus (HIV)-associated Neurocognitive Disorders (HAND) is the mayor cause of dementia in HIV-positive young adults and is characterized by increased neuronal death via a cascade of events related to oxidative stress, mitochondrial damage, and apoptosis. The objective of this proposal is to study the neuroprotective potential of estrogen and fluoxetine during HAND. No studies exist investigating the changes in the neuronal proteome during HAND that may lead to a better understanding of the mechanisms of action of estrogen and fluoxetine. We propose to use an *in vitro* model of neurotoxicity simulating HAND by challenging cell cultures with cerebrospinal fluid (CSF) samples from the Hispanic-Latino Longitudinal Women Cohort repository. We hypothesize that estrogen and fluoxetine will mediate neuroprotection by enhancing mechanisms of cell survival, such as reduction/oxidation pathways and mitochondrial integrity. Our first objective is to establish an *in vitro* model of neurotoxicity at University of Puerto Rico Medical Science Campus. This will be accomplished by transferring techniques already set in place at Johns Hopkins University School of Medicine. We will validate the neurotoxic potential of CSF from women in our cohort diagnosed with HAND. This will be accomplished by measuring neuronal death using neurotoxic assays. We will then test the neuroprotective potential of estrogens and fluoxetine by pretreatment in neuronal cells when challenged with CSF of HAND patients. This will also be accomplished by measuring neuronal death using neurotoxic assays after pretreatment with neuroprotectors. CSF from non-demented HIV-seropositive patients will be used as controls. Finally, in an attempt to understand the mechanisms of neuroprotection of estrogens and fluoxetine, we will investigate changes in the neuronal proteome mediated by these two compounds using novel proteomics techniques such as two-dimensional differential in-gel expression and tandem mass spectrometry. The short-term goal of this proposal is to develop neurotoxic models for the characterization of these and other compounds with potential for neuroprotection in Hispanic women with HAND. The long-term goal is to generate preliminary data for a National Institute of Health (NIH) K award proposal submission by the PI in translational research.

Chunmei Liu, Ph.D., Howard University
Assistant Professor

Dr. Chunmei Liu's research interests include Algorithms, Computational Biology Graph Theory, and Theory of Computation. Her previous research developed a graph tree decomposition model and used it to solve a number of bioinformatics problems such as non-coding RNA gene search in genomes, protein structure prediction, and tandem mass spectral analysis. She also developed Machine Learning-based techniques for protein domain prediction and protein fold classification. Her research also studied parameterized complexity technique and analyzed the complexities of previous graph algorithms and developed new parameterized algorithms for some graph problems with better time and space bounds. To date, she has published 30+ referred journal and conference papers and spoken in several international conferences, workshops, and seminars.

Chun-yu Liu, Ph.D., University of Chicago
Assistant Professor

My major research interests are in the areas of genetics, genomics, and epigenomics of neuropsychiatric diseases, particularly Bipolar Disorder and Schizophrenia. Four major ongoing projects are: 1) microRNA in bipolar disorder and schizophrenia: looking for variants in miRNAs that might be related to the diseases; 2) gene expression regulation in human brain: map gene expression controllers in brain; 3) CNVs and SNPs in whole genome association study of bipolar disorder: looking for SNP/CNV association with the disease; 4) G72 transgenic mice: study biochemical, genomic, and behavioral changes in a human BAC transgenic mice that may serve as a model for human psychiatric diseases.We have evaluated SNP associations in numerous candidate genes, pathways and genomic regions. We discovered the rare copy number variant burden in bipolar disorder patients. Recently, we successfully performed genome-wide expression QTL mapping and methylation QTL mapping in human brain, and identified cis- and trans-regulatory elements for gene expression and DNA methylation.

Angel Mayor, M.D., Unversidad Central del Caribe
Associate Professor

Dr. Mayor is a medical doctor with a master's degree in epidemiology. He is an assistant professor in the internal medicine department of the Universidad Central del Caribe, School of Medicine. He was involved in the creation, coordination and implementation of the program, RCRII Clinical Research Center at the UCC. He is the program epidemiologist of the RRC, RCMI/NIH of Bayamón Puerto Rico and the PI of a prevention/intervention study to reduce the Hepatitis C co-infection in HIV-infected IV drug users. Dr. Mayor has been involved in the study of acute and chronic conditions related to the HIV infection in the Puerto Rican population. He had study the prevalence of AIDS related condition, neoplasm, diabetes mellitus, renal damage and liver damage in Puerto Rican HIV infected population. Around 45% of this population reported drug use as a HIV risk behavior. In addition he evaluates the mortality rates and mortality causes of this population.

Dr. Mayor is also an associate professor of rheumatology section of internal medicine department in the Puerto Rico Health Medical Campus at the University of Puerto Rico. In this setting his primary study focus is rheumatologic disease, principally autoimmune disease including systemic lupus erythematosus, rheumatoid arthritis, fibromyalgia and scleroderma and other conditions.

Guylaine Poisson, Ph.D., University of Hawaii
Assistant Professor

The focus of my current research is on the development of algorithms and tools for large-scale dataset analysis, including protein pattern prediction, metagenomics sequencing simulation, comparative genomics, mosaic viruses representation and metagenomics assembly.

Large Scale Motif Prediction: This goal of this project is the development of tools and new methods to find irregular conserved patterns in protein and DNA sequences. The automatic discovery of those patterns is an important problem that can give a better understanding of the structure and function of a biological sequence. We use machine learning methods since they can work with the subtleties of sequence variations.

Environmental Genomics: In metagenomics all the genomes composing an environment are analyzed simultaneously. Many new computational challenges emerged from this complexity. Traditional bioinformatics tools and methods developed for single genome are not designed to deal with the presence of fragments pertaining to different genomes. This adds multiple dimensions to the problem. My areas of interest in metagenomics touch the assembly and representation of metagenomes and the simulation of the sequencing effort for metagenomes experiments.

John V. K. Pulliam, Ph.D., Morehouse School of Medicine
Postdoc Research Fellow

Stroke is the third leading cause of death in the United States and the major cause of long-term disability. Little progress has been made in development of treatments for acute stoke. The goal of our laboratory is to determine the genetic and molecular interactions associated with neuroprotection and/or neurorepair of stroke injury. Recently, transcription factors have been associated with stroke injury. We will utilize microarray technology and bioinformatic tools to determine putative transcriptional regulators of stroke by computational analysis. Furthermore through molecular biology, we will validate the role of transcription factors within in vitro and in vivo models of stroke.

Microarray analysis was conducted using brain tissues from control, MCAO and MCAO + NRG treated rats. Genes exhibiting a 2-fold or greater increase in mRNA expression were identified. Gene accessions were loaded into the RESOURCER program and human orthologs were identified. Next, human ortholog-associated gene symbols were loaded into the Netaffx program to determine the matching reference sequence ID for the human gene ortholog. Putative transcriptional regulators of the data set were identified using the conserved transcription factor binding site finder (CONFAC) program. CONFAC is a program that provides statistical methods that facilitate the prediction of transcriptional regulators of gene lists derived from results of a microarray analysis. We employed CONFAC analysis to find transcription factor binding sites (TFBS) that were over-represented in a list genes associated with neuroprotection by NRG-1. CONFAC compared our gene list to a random set of 250 genes and analyzed using a Mann-Whitney test. Significantly over-represented TFBS were identified as using the p-value ($p<0.05$). Changes in the expression of specific transcription factors were then investigated from previously obtained microarray data set between control, MCAO and MCAO+NRG treatment conditions.

CONFAC analysis revealed several TFBS that were over-represented following MCAO and NRG-1 treatment. Consistent with previous reports, AP1 and NFκB appear to be associated with ischemia-induced gene expression. We also identified members of the ETS family of transcription factors as potential mediators of ischemia-induced gene expression that was suppressed by NRG-1. Subsequent analysis of the microarray data set revealed that Ets-1 and the AP1 transcription factors jun and c-fos were upregulated following ischemia and suppressed upon treatment with NRG-1.

Taken together, these data indicate that NRG-1 is a powerful neuroprotectant in ischemia and appears to involve the transcriptional repression of genes associated with cell neuronal death and inflammation. Transcription factors identified in theses studies may be potential novel targets for the treatment of acute stroke.

Jeremy Ross, Ph.D., University of Texas at El Paso
Postdoctoral fellow

It is well established that while Hispanics comprise slightly greater than ten percent of the US population, they account for a disproportionately higher percentage of disease when compared to non-Hispanic whites. This consists of certain types of cancer including acute lymphocytic leukemia (ALL) where Hispanics have the highest incidence and poorest survival rates compared to non-Hispanic whites. Even more disturbing is that Hispanic children exhibit the highest rates of ALL when compared to non-Hispanics and also Hispanic adults. Extensive data analysis by the Leukemia and Lymphoma Society also indicate that Non-Hodgkin lymphoma is the eighth leading cause of death for Hispanics. For many afflicted with these cancers, stem cell transplantation is often their only therapeutic option. Unfortunately, Hispanic recipients display some of the poorest survival rates in response to this type of intervention. Given these statistics it is clear that there is a critical need to identify new therapeutic strategies to effectively treat these patients. Given our location within the El Paso del Norte region of Texas and outstanding research core facilities, we are interested in addressing this key medical need in the area of health disparities. To do so, we must understand the health disparities issues at the molecular level which has been a relatively ignored area of study for these tumors. We seek to identify novel molecular pathways that we hope will yield the next generation of therapeutic strategies for treating these types of hematopoietic disorders. Our goal is to isolate, bank and test Hispanic derived leukemia and lymphoma samples and use innovative multiplexing technologies to identify intracellular and extracellular proteins that will yield insight for early detection and treatment possibilities for these malignancies. We will also use and develop novel antibodies and tools coupled with mass spectrometry analysis to identify and expand biomarkers for these diseases. Lastly, we will employ novel inhibitors against a key tyrosine kinase known as Janus tyrosine kinase 3, which according to earlier results from our group, may play a critical role in many of these cancers. At the conclusion of this work we expect to gain insight into new therapeutic approaches and characterize viable compounds for the treatment of leukemia and lymphoma for this underserved population.

Gregory Strayhorn, M.D., Ph.D.; Morehouse School of Medicine; Professor

My current work and funding center on developing a clinical research data repository that will be used for clinical, translational, and health services research. I am currently working on a project that looks at whether access to health care resources are sufficient for disease management relative to income/financial resources external to the health care setting.

Zhiwei Wang, M.S., University of Texas San Antonio
Director of Computational Biology Initiative

The overall objective of the Computational Biology Initiative (CBI) is to provide a world-class facility supporting the research of current as well as future biologists at UTSA as well as the training of students. The CBI, constructed with funding from the RCMI, supports a range of research from sophisticated studies of genomes, to analysis of the dynamics of the regulation, control and expression of proteins, to increasingly complex efforts to construct models at all levels of biological organization.

Huan Xie, Ph.D., Texas Southern University
Assistant Professor

My research interests are on nanoparticle-based drug formulation, drug delivery system, cancer therapy and diagnostics. Nanotechnology is the creation and utilization of materials, devices and systems through the control of matter on the nanometer-length scale. The most important applications in healthcare are in diagnostics, drug delivery and nanosurgical procedures. Those applications are of special interest because they can provide solutions to the challenges that current medical and pharmaceutical industry are facing while no other methods could solve, such as guiding drugs to specific targets, optimizing the effect of drug dosages and reducing toxic side effects. Sometimes, a single nanoparticle can be decorated with therapeutic molecules, targeting molecules and imaging molecules and achieves multi-purpose simultaneously.

I have solid knowledge and rich industrial experience on conjugation chemistry and nanotechnology-based drug design and delivery. Before joining TSU, I was a senior scientist at a biotech company in Houston for four years. During my employment, the company successfully developed a novel type of nanometer-sized gold shells for photo-thermal ablation cancer therapy. I have investigated various biomolecules and modified nanoparticles for enhanced target delivery. I also designed and synthesized radioactively labeled nanoshells and studied their pathway in live animals by PET and SPECT imaging, which is the pioneer work in this field. My research has greatly contributed to the FDA approval of clinical trial on this nanomedicine. Now it is in the phase I clinical trial.

My current research at TSU is focused on developing an integrated approach using gold nanorods as a scaffold and arginine-glycine-aspartic acid (RGD) peptide as intergin αvβ3 binding moiety for tumor neovascular targeting. Nanorods have emerged as precisely plasmonic tunable novel nanomaterials by controlling their aspect ratios (length vs. width). The peak absorbance of the nanorods can be engineered to fall into the specific radiation band of near-infrared (NIR) laser, which can penetrate tissues to a certain depth without observable tissue damage. The combination of gold nanorods and NIR laser hence makes a promising tool for thermal ablation of tumors. Research has determined that the integrin αvβ3 is over-expressed on endothelia in angiogenesis but not on normal endothelial cells, resulting in significant interest in the use of this target for imaging and therapy. A cyclic RGD peptide targeting αvβ3 has been successfully used in clinic. The proposed work will conjugate RGD peptide with nanorods to achieve more efficient and specific accumulation in tumor site, therefore improving the efficacy of this nanoparticle-based photo-thermal cancer therapy. This therapy could potentially synergize with radiation therapy and chemotherapy to eliminate residual or recurrent tumor cells.

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