

CENTER FOR GENE REGULATION IN HEALTH AND DISEASE

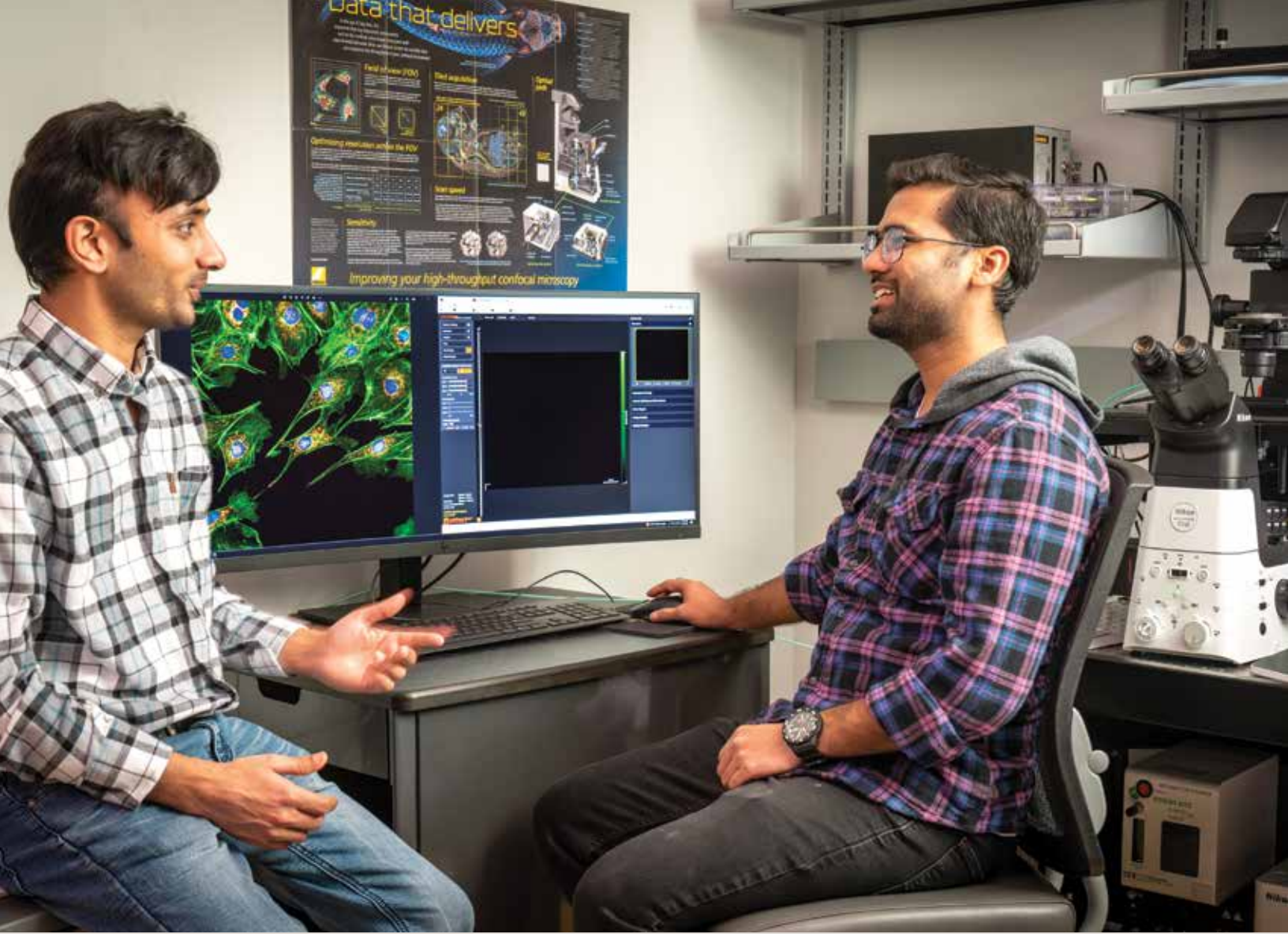
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FIFTEEN YEARS OF INNOVATIVE RESEARCH AND SUCCESSFUL STUDENT TRAINING



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The Center for Gene Regulation in Health and Disease (GRHD) is the home for modern biomedical research at Cleveland State University (CSU) with a mission to understand the underlying causes of many human diseases and develop treatments based on the molecular mechanisms discovered. GRHD is an Ohio Department of Higher Education recognized Center of Research Excellence at CSU and is also one of only two Strategic Research Centers at CSU that serve strategic university priorities to advance research, education, and engagement initiatives. The idea of an interdisciplinary Center with such a focus came to fruition when CSU received a \$900,000 grant from the Ohio Third Frontier Commission's Ohio Research Scholars Program, with help from Cleveland Clinic's Lerner Research Institute. The Center launched in October, 2008, initially bringing together eight researchers from the disciplines of biology and chemistry to work on understanding complex molecular mechanisms involved in the regulation of gene expression as well as understanding their relevance to the most devastating diseases, including cardiovascular disease and cancer.

Since its inception, GRHD has increased its number of investigators from 8 to 19 and has expanded its disciplines to include physics. GRHD researchers have produced numerous high-quality publications in top peer-reviewed journals, substantially increased extramural funding (nearly 5-fold), and received many generous private donations. Today, this highly collaborative and diverse environment brings together more than 100 researchers, including faculty, post-doctoral fellows, technologists, and students, who are making groundbreaking discoveries and contributing greatly to the local, national, and international scientific community and regional economy.

Five years ago, we celebrated our 10th anniversary with the special publication of the first edition of this brochure. The past 5 years brought many challenges to our lives. The COVID-19 pandemic dramatically changed the way we live, work and interact. Maintaining a strong work culture and ethic was especially difficult during this time and represented one of our biggest challenges both during and after the pandemic. Despite this, GRHD researchers continued to thrive and GRHD continues its upward development trajectory.

Today, we mark our 15th anniversary with the publication of this 2d edition. All GRHD faculty were provided the opportunity to submit short pieces describing their research, and members of the community were invited to personally reflect on the evolution of GRHD over the years. I invite you to read about our history, our major achievements, and our vision for the future.

Anton A. Komar, PhD, Professor

*Director, Center for Gene Regulation in Health and Disease
Cleveland State University, Cleveland, OH*





Dr. Michael Schwartz, President, Cleveland State University (2002–2009) declaring the official opening of the Center.



Dr. Paul DiCorleto, Chair, Cleveland Clinic Lerner Research Institute (2002-2015) addressing the audience.



Dr. Crystal M. Weyman, founding Director, GRHD (2008-2010) addressing the audience.



Drs. George Stark, Chair, GRHD External Advisory Board, and Michael Schwartz, President, CSU.

CENTER FOR GENE REGULATION IN HEALTH AND DISEASE

VISION STATEMENT

To enhance and integrate research focused on Gene Regulation in Health and Disease leading to better understanding of the molecular mechanisms controlling these processes and the identification of therapeutic targets.

MISSION STATEMENT

The Mission of the Center is:

To develop and support research focused on Gene Regulation in Health and Disease.

To encourage and provide support mechanisms for the acquisition of extramural funding.

To encourage and provide support mechanisms for the dissemination of research results.

To create mechanisms to acquire resources to support research and student training focused on Gene Regulation in Health and Disease.

To develop and expand partnerships with relevant public and private community entities with similar interests.

To develop and promote Cleveland State University's reputation as a local, national and international leader in Gene Regulation in Health and Disease.





From its inception, GRHD has had the great fortune to recruit world-renowned scientists to serve on its external advisory board (EAB). Five of the seven members hold or have held endowed chairs, four are members of the National Academy of Sciences, and all are well recognized in their fields of expertise and have been distinguished with numerous awards.

The original members include Paul DiCorleto, PhD, Sherwin-Page Chair, Cleveland Clinic Lerner Research Institute (2002-2015); Richard W. Hanson, PhD, Leonard and Jean Skeggs Professor of Biochemistry and Chair, Department of Biochemistry, CWRU School of Medicine (1978-1999); Roy L. Silverstein, MD, John and Linda Mellows Professor and Chair, Department of Medicine, Medical College of Wisconsin (2011-present); and George R. Stark, PhD, Chair, Cleveland Clinic Lerner Research Institute (1992-2002), Distinguished Scientist of the Lerner Research Institute, National Academy of Sciences member (1987) and the Institute of Medicine, Royal Society of London fellow (1990). Sadly, Dr. Richard Hanson passed away in February 2014. This precipitated a reorganization of the EAB and the addition of 4 new members including William M. Baldwin, MD, PhD, Cleveland Clinic Lerner Research Institute; Stephen J. Benkovic, PhD, Evan Pugh Professor and Eberly Chair in Chemistry, Pennsylvania State University (1988-present), National Academy of Sciences member (1985), National Medal of Science recipient (2009); Carlos J. Bustamante, PhD, The Raymond and Beverly Sackler Professor in Biophysics and Howard Hughes Medical Institute Investigator, University of California, Berkeley (2000-present), National Academy of Sciences member (2002); and Harry F. Noller, PhD, Director, Center for Molecular Biology of RNA and Robert L. Sinsheimer Professor of Molecular Biology, University of California, Santa Cruz (1992-present), National Academy of Sciences member (1992).

The Advisory Committee has been continuously chaired by Dr. George Stark. The EAB meets yearly to evaluate GRHD's progress and aid advancement.



George R. Stark, Ph.D.
 External Advisory Board Chair
 Staff, Department of Cancer Biology
 Cleveland Clinic Lerner Research
 Institute, Cleveland, OH
 Distinguished Scientist of the
 Lerner Research Institute
 Member, National Academy of Sciences
 (1988)
 Fellow, the Royal Society of London
 (1990)



Paul E. DiCorleto, Ph.D.
 Immediate Past Vice President for
 Research and Sponsored Programs
 Kent State University, Kent, OH
 Past Chair, Cleveland Clinic Lerner
 Research Institute, Cleveland, OH



William M. Baldwin, M.D., Ph.D.
 Staff, Department of Inflammation
 and Immunity, Cleveland Clinic Lerner
 Research Institute, Cleveland, OH



Harry F. Noller, Ph.D.
 Director, Center for Molecular Biology of
 RNA; Robert L. Sinsheimer Professor of
 Molecular Biology; Professor Emeritus of
 MCD Biology
 University of California, Santa Cruz, CA
 Member, National Academy of Sciences
 (1992)



Stephen J. Benkovic, Ph.D.
 Evan Pugh Professor and Eberly Chair in
 Chemistry, Department of Chemistry
 The Pennsylvania State University,
 University Park, PA
 Member, National Academy of Sciences
 (1985)



Roy L. Silverstein, M.D.
 John and Linda Mellowes Professor and
 Chair of Medicine,
 Medical College of Wisconsin Division of
 Hematology and Oncology,
 Milwaukee, WI
 Senior Investigator
 Blood Research Institute, Blood Center of
 Wisconsin, Milwaukee, WI



Carlos J. Bustamante, Ph.D.
 The Raymond and Beverly Sackler Chair
 of Biophysics; Howard Hughes Medical
 Institute Investigator,
 College of Chemistry, University of
 California, Berkeley, CA
 Member, National Academy of Sciences
 (2002)

IN MEMORIAM

Richard W. Hanson, Ph.D.
(1935-2014)
 Leonard and Jean Skeggs Professor
 of Biochemistry; Chair, Department of
 Biochemistry
 Case Western Reserve University,
 Cleveland, OH





Initially, the Center brought together these eight faculty members from the departments of Biological, Geological and Environmental Sciences (BGES) and Chemistry (CHM): Drs. G. Valentin Boerner (BGES), Michael Kalafatis (CHM), Anton A. Komar (BGES), Roman V. Kondratov (BGES), Bibo Li (BGES), Barsanjit Mazumder (BGES), Girish Shukla (BGES), and Crystal M. Weyman (BGES). Dr. Weyman served as founding director (2008-2010) and together with founding members Drs. Kalafatis, Komar, and Mazumder formed the governing body, the GRHD planning committee, which, then and now, oversees the Center's daily operations and budget issues and determines strategies for future development.

Throughout the years, additional members joined the Center, including Drs. Xue-Long Sun (CHM) and Aimin Zhou (CHM) in 2009, Drs. Andrew Resnick (Department of Physics) and Bin Su (CHM) in 2011, and Dr. Aaron Severson (BGES) in 2012. In 2010, CSU hired Dr. Sailen Barik from the University of South Alabama, College of Medicine. He served as GRHD director from 2010 to 2013 and retired in 2016.

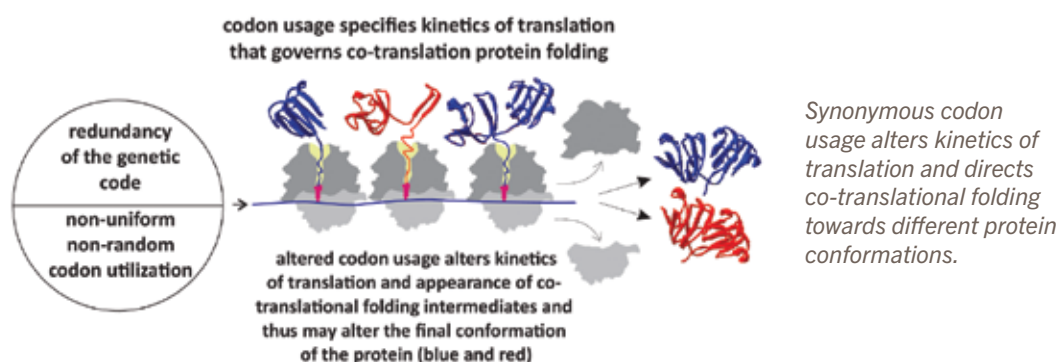
Dr. Anton A. Komar was appointed in January 2014 and currently serves as director. In order to continue to grow and develop the Center, GRHD, in coordination with the departments of BGES and Chemistry and with substantial support from CSU's upper administration including the Office of Research, the Provost and the President, recruited 6 dynamic, research active faculty over the past 4 years. Joining GRHD were Dr. Merlin Nithya Gnanapragasam (BGES) in 2019, Drs. Kailash Gulshan and Jingqi Yan (both BGES) in 2020, Dr. Peng Jiang (BGES) in 2021, and Drs. Jackson Taylor (BGES) and Junior Gonzales (CHM) in 2022.

Together the current 19 faculty members focus on research to improve the understanding of biological processes and how malfunction of these processes results in various diseases. This research has the significant potential to improve our understanding of the mechanisms and specific molecules that control reproductive health and the aging process as well as implications for the diagnosis and treatment of many of the most common global diseases, including neurological and infectious diseases, heart disease, and cancer.

ANTON A. KOMAR, PH.D., PROFESSOR AND DIRECTOR (GRHD)

**RESEARCH INTERESTS:** Translational control of gene expression

Dr. Komar's lab is interested in investigating protein synthesis, co-translational protein folding and translational control of gene expression in eukaryotic cells. Research in the laboratory has two major foci. We are particularly focused on investigating the link between synonymous codon usage and protein folding. The genetic code is degenerate, hence most amino acids are encoded by multiple, so-called synonymous codons. Synonymous codons were initially presumed to have entirely equivalent functions. However, synonymous codon usage is biased, as abundant and rare codons are distributed non-randomly in whole genomes and along the open reading frames of genes. We found that codon choice has functional implications beyond amino acid coding and that synonymous codons may modulate protein folding by tuning the kinetics of translation. These observations provided strong support for the hypothesis that synonymous codon usage serves as a secondary code for protein folding in the cell. The research in the laboratory is further devoted to the study of eukaryotic initiation factor eIF2A that does not function in major steps in the initiation process, but is believed to act at some minor/alternative initiation events such as reinitiation, internal initiation, and/or non-AUG initiation, important for translational control of specific mRNAs. We in particular found that eIF2A is involved in the control of lipid metabolism and that eIF2A-knockout mice reveal decreased life span and metabolic syndrome. Our work deepens the understanding of protein folding, one of the most fundamental mechanisms in the cell and helps elucidate unique features of translational control of gene expression.

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MICHAEL KALAFATIS, PH.D., PROFESSOR AND CHAIR (CHM)



RESEARCH INTERESTS: Blood coagulation and thrombosis, cancer and apoptosis

Blood Coagulation and Thrombosis. The coagulation system leans on a delicate balance between coagulant and anticoagulant factors. Any imbalance/defects in these systems can result in severe pathological conditions. The prothrombinase complex is the enzymatic complex responsible for timely thrombin formation at the place of vascular injury and is composed of the enzyme, factor Xa (fXa), the non-enzymatic cofactor factor Va (fVa), and the substrate prothrombin assembled on a lipid membrane in the presence of divalent metal ions. fVa contributes to the activation of prothrombin mainly by stabilizing the enzymatic complex and altering the kinetic mechanism of fXa (increased k_{cat}). Our data suggest that amino acids Leu⁴⁸⁰ and Gln⁴⁸¹ from prothrombin are crucial for proper recognition of the fVa-dependent site(s) for fXa within prothrombinase, thus modulating the enzymatic activity of fXa within the prothrombinase complex.

Cancer and Apoptosis. Cancer is the primary cause of death worldwide. The traditional way to treat cancer today is “cut, poison, and burn” which correlates to surgery, chemotherapy, and radiation respectively with the known devastating side effects. Human tumor necrosis factor-related apoptosis-inducing ligand (hTRAIL) is a cytokine that has the capability to induce both pathways of apoptosis (first extrinsic and then intrinsic) in cancer cells while it does not harm normal non-transformed cells. We have demonstrated that recombinant hTRAIL together with several natural compounds are efficient in inducing apoptosis in previously described TRAIL-resistant cancer cell lines. Thus, by using natural non-harmful substances and rhTRAIL, under the conditions established, only cancer cells will be specifically destroyed while normal cells will not be affected.

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BARSANJIT MAZUMDER, PH.D., PROFESSOR



RESEARCH INTERESTS: Post-transcriptional mechanism of resolution of inflammation, role of ribosomal protein in mammalian development, viral genetic elements of SARS-CoV-2 and its role in translation control and viral homeostasis

My laboratory at Cleveland State University discovered a novel translational silencing-dependent mechanism for controlling inflammation in myeloid cells. This involves the assembly of the ribosomal protein L13a-dependent multi-protein RNA-binding complex (IFN-gamma-activated-inhibitor of translation) or “GAIT” complex in the 3’ untranslated region (UTR) of target mRNAs. We have generated myeloid-specific L13a-knockout (KO) mice. Induced endotoxemia, colitis, and high-fat diet-induced atherosclerosis in these mice were more severe than control, thus, showing the role of this mechanism in the endogenous resolution of inflammation. However, the role of this mechanism in normal macrophage development from bone marrow and their plasticity is not known. Using an ex-vivo bone marrow-derived macrophage development model, our recent results strongly support the role of the L13a-dependent post-transcriptional mechanism in macrophage development and plasticity. Recently our laboratory also identified an extra-ribosomal function of ribosomal protein L13a in the embryonic development of the preimplantation morula stage to implanted blastocyst. In addition, our laboratory recently discovered a novel and structurally conserved RNA element in the genomic RNA of SARS-CoV-2 and respiratory syncytial virus. This study showed that these RNA elements regulate the translation of viral proteins mediated by L13a-dependent RNA-binding complex formation in response to viral protein-induced signaling. Detailed studies on these novel roles of this protein are ongoing in our laboratory.

Select references:

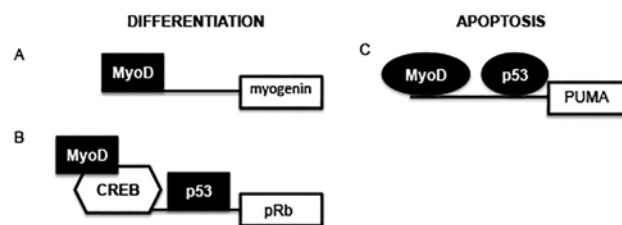
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CRYSTAL M. WEYMAN, PH.D., PROFESSOR AND CHAIR (BGES)



RESEARCH INTERESTS: Coordinate regulation of differentiation and apoptosis

Differentiation (cell type specialization) and apoptosis (programmed cell death) are coordinately regulated in most, if not all, cells. Dr. Weyman's lab utilizes the model system of skeletal myogenesis to investigate this coordinated regulation. Treatment options relevant to the amelioration of muscle trauma or disease states include maximizing the regenerative potential of adult muscle stem cells as well as improving the efficacy of protocols utilizing skeletal myoblast transfer or skeletal muscle tissue engineering. For each option, a better understanding of the molecular events controlling skeletal myogenesis could identify targets for better therapeutic manipulation. To this end, we have determined that MyoD, the pioneer transcription factor long known to control muscle differentiation through both direct and indirect binding to DNA (A and B), is also responsible for controlling the coordinated apoptosis via the direct transcriptional regulation of the pro-apoptotic protein PUMA (C). Moreover, we have determined that MyoD works with the transcription factor p53 to drive PUMA expression. p53 is well known for its role in tumor suppression as a pivotal transcription factor responsible for interpreting the extent of DNA damage into either cell cycle arrest or apoptosis. p53 is less well known for its role in skeletal myoblast differentiation. We propose that post-translational modification(s), portrayed in the figure as shape changes, could explain the mutually exclusive, dual, biological roles in differentiation or apoptosis for both of these key transcription factors. Moreover, we are gathering data that suggests that cell cycle position plays a role in these respective post-translational modifications.



Proposed model for the coordinated regulation of differentiation and apoptosis by MyoD and p53.

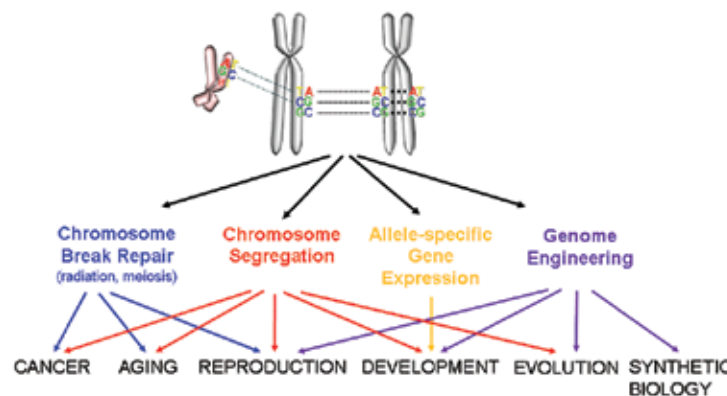
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G. VALENTIN BÖRNER, PH.D, PROFESSOR

**RESEARCH INTERESTS: Mechanisms of chromosome segregation during meiosis**

Chromosomes are the carriers of genetic information in all higher organisms including humans. Each chromosome consists of a single DNA fiber packaged into a sausage-shaped structure. When the DNA fiber breaks, genetic material is frequently lost. Errors in chromosome break repair result in birth defects, premature aging and cancer. Chromosome breaks are induced by radiation treatment and chemotherapy thereby stopping the growth of cancer cells. Cells also induce breaks in their own chromosomes to reshuffle the genetic material for sexual reproduction. The central questions of the Börner lab are: how do cells repair chromosome breaks and how do they prevent the loss of genetic information? Our research focuses on DNA repair by homologous chromosome interactions. This type of repair is especially accurate as it uses a highly similar chromosome segment as template. Several surprising discoveries have resulted from our work. We have developed a US-patented approach to identify chromosome segments involved in recognition of homologous stretches of DNA. We are now identifying the machinery that brings homologous chromosome segments together among the myriads of DNA segments within a nucleus. We have also discovered that a cellular protein degradation machinery called the proteasome assists in the DNA break repair process. Unexpectedly, the proteasome relocalizes to chromosomes while break repair is ongoing, thereby ensuring the elimination of proteins that block access to DNA damage. Ultimately, our research will contribute to a better understanding of the machinery that keeps the molecule of inheritance stable.



Chromosome break repair and segregation impacts many cellular processes and affects human health at multiple levels.

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MERLIN NITHYA GNANAPRAGASAM, PH.D., ASSISTANT PROFESSOR



RESEARCH INTERESTS: Mammalian Erythropoiesis and Hemoglobin Gene Regulation

The overarching goal of our laboratory is to delineate the processes that regulate tissue proliferation and differentiation, and how dysregulation of these pathways contributes to human diseases. Our studies utilize erythroid cells as a model system.

Our current research goals are to understand how transcriptional regulation in erythroid cells ensures that the cell cycle machinery is able to accommodate the rapid pace of the erythroid terminal cell divisions and enucleation, and to investigate the molecular pathogenesis of Congenital Dyserythropoietic Anemia IV. This severe anemia is caused by a hypomorphic mutation in EKLF/KLF1 (a master regulator of erythropoiesis) that arises due to a failure in terminal cell divisions and results in binucleate erythroblasts and erythroblasts with DNA bridges. Additionally, we are interested in understanding the mechanisms of hemoglobin switching to ameliorate and potentially cure Sickle Cell Anemia and β -thalassemia. Here, our goal is to identify factors that induce fetal hemoglobin in adult erythroid cells due to its ameliorating effects in these anemias.

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JUNIOR GONZALES, PH.D., ASSISTANT PROFESSOR

**RESEARCH INTERESTS: Mechanisms and imaging pain via ion channels**

As we have always been fascinated by the resources of the Amazonian Rainforest, our work is highly influenced and strongly revolves around the idea of extracting, and using, very potent physiochemical substances from the highest Bio-diverse space on the planet, (e.g. small molecules, peptides), which are waiting to be found to help ameliorate human disease(s). Our research is heavily invested in transforming bio-active substances into quantitative tools/methods for imaging “diseased” nerves using fluorescence or PET modalities. Imaging unhealthy nerve structures is the first step in providing and deploying urgently needed therapies for pain related diseases, and alternatively addresses the analgesic-resistance problem, potentially rendering a formidable approach to the standard of care, with a benefit to cancer, diabetic, and terminally ill patients.

Another aspect of our research program studies sodium channel NaV1.7. We are particularly interested in the molecular and mesoscopic changes of these channels and their relationships to the initiation and/or progression of human diseases. NaV1.7 is highly expressed in peripheral nerves, the dorsal root ganglia, and some cancers. There are seminal studies indicating that dysregulations and changes to the distribution of channel NaV1.7 triggers the development of neuropathies in patients. Examples of human afflictions that could benefit from sensing/monitoring the associated changes in channel NaV1.7 include chemotherapy-induced peripheral neuropathy, a dysfunction affecting cancer patients and survivors and diabetic neuropathy. Both afflictions lead to the loss of anatomical function and result in enduring chronic pain long after treatment. Despite their widespread and chronic nature, no tools or methods currently exist to quantify or provide a readout of these afflictions.

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KAILASH GULSHAN PH.D., ASSISTANT PROFESSOR



RESEARCH INTERESTS: Interplay between PIP2, cholesterol, and inflammation in CVD and lung cancer

The overall research focus of the Gulshan lab revolves around the role of PIP2 metabolism/trafficking and Gasdermin D (GsdmD) mediated IL-1 β release in inflammation, cardiovascular disease (CVD), and lung cancer. Our lab uses a wide variety of mouse models to study inflammasome activity, progression of atherosclerosis, and metastasis of lung cancer. We employ a variety of cutting edge techniques such as unbiased lipidomics, RNAseq, Crispr-Cas9 mediated genome engineering, bone marrow transplants (BMTs), 16s rDNA sequencing for microbial profiling, high-resolution STED/STORM, electron and atomic Force microscopy, 10X genomics single cell RNAseq, liposome (LUVs & GUVs) based protein-lipid interactions, unbiased screening of drug libraries, and recombinant adeno-associated virus (rAAV) and baculovirus mediated gene expression in mice and insect cells. We have a long-standing interest in mechanisms regulating cross talk between ABC transporters, GsdmD, PIP2, and cholesterol and other lipid species (*PNAS* 2015, *Autophagy* 2015). We described a novel role for ABCA1 as a PIP2 floppase (*Circulation Research* 2016). We identified anti-atherosclerotic and microbiome-altering activities of a FDA approved drug Miltefosine (*Scientific Reports* 2019, *iScience* 2023). Our lab showed that GsdmD, a substrate of various caspases (1,4-5/11) promotes atherosclerosis, as well as lung cancer (*Front Cell Dev Biol* 2021, *iScience* 2023).

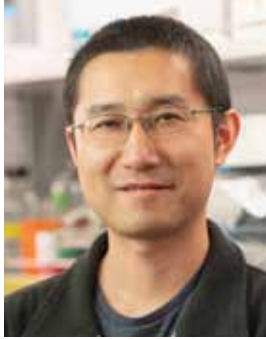


High-resolution microscopy of giant unilamellar vesicles (GUVs), showing lipid-protein interaction on the membrane surface.

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PENG JIANG, PH.D., ASSISTANT PROFESSOR


RESEARCH INTERESTS: Computational Biology, Multi-Omics data Integration, Single-cell RNA-seq, Machine Learning, Tissue Regeneration

The Jiang Lab is focused on developing computational methods and software to investigate multi-source high-dimensional omics data. We have developed several statistical methods and software, such as **TimeMeter** – a dynamic time warping (DTW) algorithm-based statistical method and R package to assess temporal gene expression similarity and identify differentially progressing genes, **MPBind** – a Meta-motif-based statistical framework and pipeline to predict the binding potential of SELEX-derived aptamers, and **CRSP** – a comparative RNA-seq pipeline for species lacking both sequenced genomes and reference transcripts. One unique aspect of our research is that we integrate a variety of statistical/ bioinformatic methods, such as network modeling, machine learning, and genomic and transcriptomic data analysis, to leverage complex/large-scale omics datasets. These integrative computational approaches allow us to maximize the knowledge learned from the data to gain novel insights into the fundamental and translational aspects of human diseases.

One special focus of our research is that we are particularly interested in leveraging omics data to investigate tissue regeneration processes. A key and broad question we want to address is whether regeneration in adult mammals can be activated with appropriate treatment or a series of treatments. We are closely collaborating with scientists from basic science and surgeons in a clinical setting to (a) identify key regulators for tissue regeneration; (b) compare the regenerative response to endogenous versus exogenous expression of transcriptional factors; (c) develop and evaluate different strategies (e.g., ECM, exosome and electric stimulation) for intervention.

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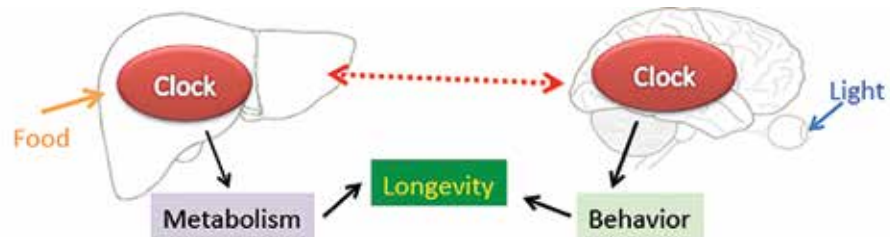
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ROMAN V. KONDRATOV, PH.D., PROFESSOR AND ASSOCIATE VICE PRESIDENT FOR RESEARCH (CSU)



RESEARCH INTERESTS: Circadian control of metabolism and aging

Dr. Kondratov's laboratory is interested in how the circadian clock regulates an organism's metabolic response to diet. The circadian clock is an internal time keeping system that generates daily rhythms known as circadian rhythms. The circadian clock controls an organism's metabolism, physiology and behavior. Dr. Kondratov found that circadian clock disruption results in accelerated aging and reduced lifespan. Now we are focused on the role of the circadian clock in health and longevity. It is well known that diet might affect physiology and that wrong diet might significantly compromise health. On the contrary, some good diets, such as calorie restriction, improve health and even extend lifespan in many organisms including primates. We found that the circadian clocks are part of the calorie restriction mechanisms and that functional circadian clocks are necessary for the full benefits of calorie restriction for metabolism and longevity. We continue to work on understanding how the circadian clock and diet can be used to increase longevity.



Circadian clock controls organism metabolism, physiology and behavior. Functional circadian clock is necessary for the full benefits of calorie restriction for metabolism and longevity.

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BIBO LI, PH.D., PROFESSOR



RESEARCH INTERESTS: Chromosome Biology (Telomere Functions), Molecular Parasitology (Antigenic Variation), Gene Expression Regulation, DNA Damage Repair, Genome Stability

Similar to aglets that prevent ends of a shoelace from fraying, telomeres, the nucleoprotein complex at linear chromosome ends, prevent the natural chromosome ends from being recognized as DNA breaks. Telomeres protect chromosome ends from illegitimate degradation, repair, and rearrangement. Hence, telomeres are essential for genome integrity and chromosome stability. Telomere shortening in human somatic cells has been implicated in organismal aging, and genome instability often leads to tumorigenesis. Therefore, studies on telomere biology in the Li lab has a great impact on improving human health and life quality. Telomeres are also important for eukaryotic parasites. *Trypanosoma brucei* is a protozoan parasite that causes debilitating sleeping sickness in humans. It sequentially expresses distinct VSGs, its major surface antigen, to evade the host's immune response, which is essential for a long-term infection. Although *T. brucei* has a large VSG gene pool, VSGs are expressed exclusively from telomere-adjacent regions one at a time (in a monoallelic fashion). The Li lab has shown that loss of telomere proteins in *T. brucei* is detrimental to parasite survival, making telomere proteins potentially good drug targets, since parasite telomere proteins are distinctive from their human homologs. Additionally, the Li lab has shown that *T. brucei* telomere proteins are essential for monoallelic VSG expression and regulate VSG switching frequencies. Therefore, targeting parasite telomere proteins can also paralyze the key immune-evading mechanism of these human pathogens.

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ANDREW RESNICK, PH.D., PROFESSOR



RESEARCH INTERESTS: Ciliary science

My lab has developed several innovative new approaches to probe ciliary function by assaying single living cilia. We have developed optical trapping and perfused tissue culture methods as quantitative probes of ciliary mechanics and physiology. Our current work draws upon my prior expertise. I have been applying optical techniques to the study of soft matter systems for nearly 20 years. I began by studying fluid flow in microgravity and developed ‘spaceflight’ versions of confocal microscopes and optical traps. The Light Microscopy Module (LMM) has been performing world-class research onboard the International Space Station from 2009 to 2021 (<https://www.youtube.com/watch?v=SdhmXRHFprs>). I now use optical traps and fluid dynamics to better understand how the kidney regulates salt and water balance, maintaining homeostatic function in the presence of normal cell turnover. I seek to understand how changes in flow through a ‘healthy’ tubule can promote disease progression by aberrant stimulation of the primary cilium. Along with my collaborators Y-N Young (NJIT), Z. Peng (Notre Dame) and J. Garvin (CWRU), we now study how mechanical properties of the primary cilium relate to flow sensitivity and how the cilium base could mechanistically act as a gate to distinguish between mechanical and chemical stimulation. *My long term goal is to bridge the gap between Biology and Physics* to better understand how: 1) solute and water absorption along the nephron is regulated by fluid flow; 2) stimulation of the primary cilium connects with intact tissue response; and 3) these processes contribute to homeostatic kidney function and injury recovery.

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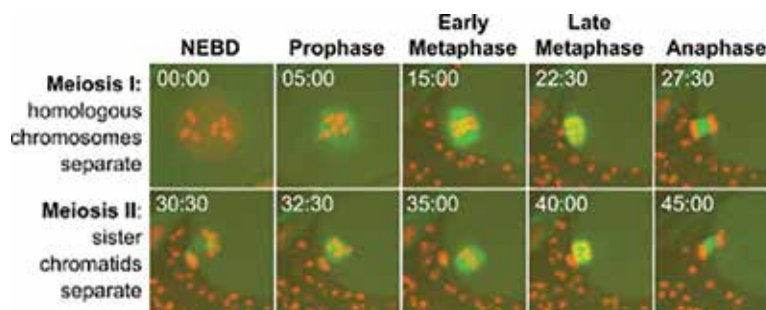
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AARON F. SEVERSON, PH.D., ASSOCIATE PROFESSOR

**RESEARCH INTERESTS: Chromosome Segregation and Reproductive Health**

As a result of mistakes that occur during the formation of sperm and eggs (also called gametes), approximately one in four human embryos has too many or too few chromosomes. These errors in chromosomal inheritance have a major impact on reproductive health, causing infertility, miscarriage, and congenital birth conditions like Down Syndrome.

My lab studies the processes that ensure that every sperm and every egg inherits a single copy of each chromosome to identify where in this chain of events mistakes are likely to occur. We have identified previously unknown factors important for producing healthy gametes, explained apparent differences in the mechanisms that form sperm and eggs in different organisms, and revealed unexpected features of gametogenesis that appear widely conserved in plants and animals. We are currently elucidating a surveillance mechanism that finds and destroys a meiotic protein, called REC-8, when it fails to bind to chromosomes. REC-8 is a key factor that distinguishes meiosis from mitosis, and we believe that this mechanism ensures that REC-8 is not inherited by mitotically dividing embryos. Finally we have developed, and continue to develop, tools to increase the efficiency of genome editing and to speed up and simplify genetic analysis. Our research has the potential to lead to tests that predict the likelihood of an abnormal pregnancy and interventions that can improve outcomes for those at risk.



Chromosome segregation during meiosis. Microtubules (green) mediate the segregation of meiotic chromosomes (red) as chromosome copy number is precisely reduced.

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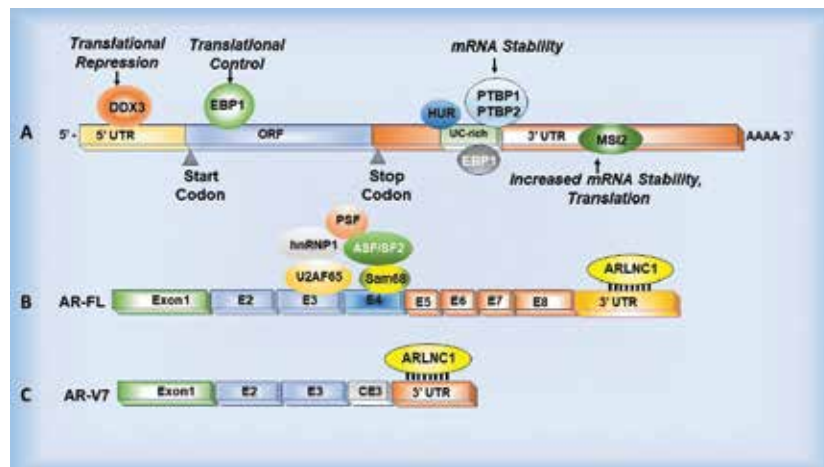
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GIRISH C. SHUKLA, PH.D., PROFESSOR



RESEARCH INTERESTS: RNA Metabolism Dynamics in Normal and Cancer Cells

Cancer remains the second leading cause of mortality in the United States. The dysregulation of molecular and cellular processes modulates the malignant transformation of a normal to a cancer cell. Cancer cells exhibit altered RNA metabolism, which promotes intrinsic carcinogenic pathways. Our research has functionally linked the dysregulated RNA metabolism to prostate tumorigenesis. My lab studies post-transcriptional regulation of androgen signaling, lipid biosynthesis, and steroid metabolism. We have established links between the androgen receptor mRNA metabolism, long noncoding RNA ARLNC1, and microRNA dynamics in normal and cancer cells. We are studying the link between WT and AR-V7 spliced isoforms and their interplay mediated by ARLNC1 in chromosomal remodeling and global gene expression.



AR mRNA Metabolism: (A) Various RNA binding proteins bind AR mRNA and control its stability and translation. (B) Splicing factors can bind the WT-FL AR mRNA. (C) AR-V7 variant and possible interaction with the ARLNC1.

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BIN SU, PH.D., PROFESSOR

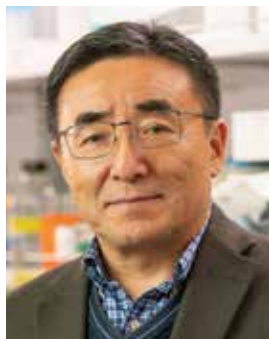
**RESEARCH INTERESTS: Anti-trypanosomiasis and Anti-cancer drug development**

Dr. Su's lab focuses on drug development research. One research direction is anti-cancer drug discovery. We synthesize small molecules to inhibit heat shock proteins that play important roles in tumor progression and drug resistance. The research involves drug design, synthesis, molecular target identification, in vitro and in vivo evaluation, and pharmacokinetic investigation. Currently, our disease model is Androgen Receptor (AR) overexpressed glioblastoma. Another research direction is anti-trypanosomiasis drug discovery. Trypanosomal parasites cause human African sleeping disease, which is an orphan disease. The current treatment is toxic, less effective and needs hospitalization, which is difficult in most countries in Africa. Dr. Su's team focuses on the development of oral active small molecules that can selectively target the parasites without harming the hosts. By collaborating with Dr. Bibo Li, the team already identified several lead compounds that showed great selectivity to the parasites.

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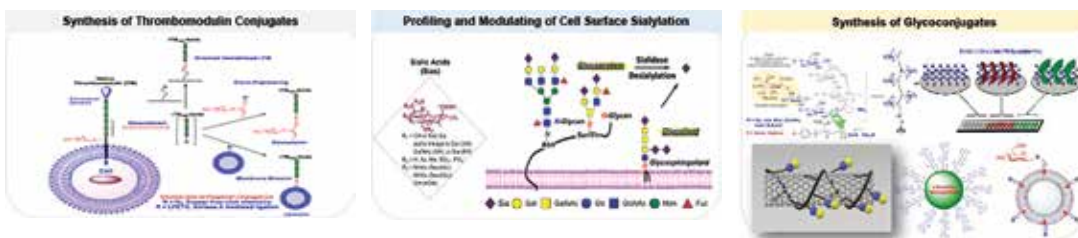
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XUE-LONG SUN, PH.D., FAHA, PROFESSOR



RESEARCH INTERESTS: Profiling and Modulating Glycosylation Pathway and Glyco-engineering

Dr. Sun's laboratory is working in the Chemical Biology and Medicinal Chemistry areas. We are interested in cell surface and receptor glycosylation patterns and changes under pathological pathways. One major research project is developing novel chemical probes and enzyme inhibitors to profile and modulate sialylation and desialylation of receptor proteins in immune cells, including monocytes and macrophages related to infection, immune response and inflammation. The long-term goal of this research is to discover the sialylation molecular mechanisms in infection, immune response and inflammation and identify novel targets and lead compounds for antiviral infection and anti-inflammation drug development for flu and coronavirus infection and sepsis. In addition, we are interested in the biomimetic synthesis of native biomolecule thrombomodulin (TM) for the compensation of its loss in the pathological site, as an on-demand anticoagulant and anti-inflammatory therapeutic strategy. Specifically, we are developing TM-liposome conjugates that mimic the native endothelial antithrombotic mechanism of both TM and lipid components and thus will provide a more forceful antithrombotic agent. Also, we are developing TM-glycosaminoglycan (GAG) conjugates and investigating the significance of GAG on the antithrombotic activity and pharmacokinetic properties of TM. Furthermore, we are developing biomimetic glyco-ligands for microarray, carbon nanotube, quantum dot and liposome surface functionalization for biosensor and drug delivery applications.



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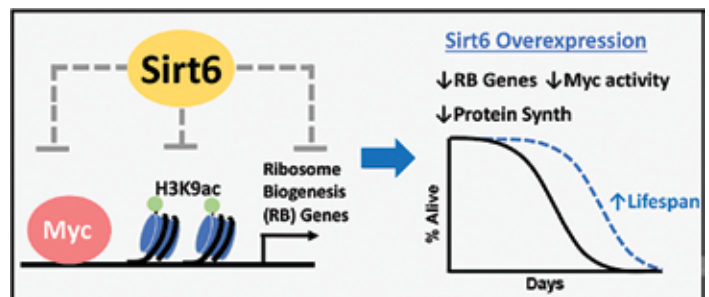
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JACKSON R. TAYLOR, PH.D., ASSISTANT PROFESSOR

**RESEARCH INTERESTS:** Epigenetic regulation of longevity and age-related disease

Most of the genes in our genome are activated or silenced by a variety of naturally-occurring chemical modifications to DNA, called “epigenetic modifications.” These modifications change substantially as we grow older, altering gene activity. In the Taylor Lab, we seek to better understand the relationship between epigenetic modifications and the aging process. Our lab uses *Drosophila melanogaster* (fruit flies) to study (i) how epigenetic modifications change with age and disease, and (ii) how experimental manipulation of epigenetic modifications affects health, longevity, and the progression of various human diseases (e.g. Alzheimer’s Disease). By studying these questions, our goal is to develop strategies to help reduce disease and disability in humans as they age. We employ a variety of techniques, including next-generation sequencing and bioinformatic analysis, genetic engineering, and population longevity experiments.

Most recently, we discovered that increasing levels of the epigenetic-modifier gene Sirt6 extends lifespan and preserves physical activity with age in flies. This pro-longevity effect of increased Sirt6 levels is mediated through epigenetic repression of ribosome biogenesis genes. These genes normally promote protein synthesis, and their repression in turn leads to decreased protein synthesis – a phenotype associated with slowed aging. Currently our lab is focused on identifying additional molecular and tissue-specific mechanisms by which Sirt6 regulates aging, and exploring the potential role of Sirt6 in Alzheimer’s Disease. We are also performing screens to identify new epigenetic modifiers of aging.



(Left) Transgenic fruit fly engineered to express GFP when epigenetic perturbations occur. (Right) Summary mechanism for lifespan extension by Sirt6 overexpression. Sirt6 overexpression epigenetically represses Myc target genes involved in ribosome biogenesis, by removing the activating epigenetic mark H3K9ac in the TSS/proximal promoter region, leading to reduced protein synthesis and lifespan extension.

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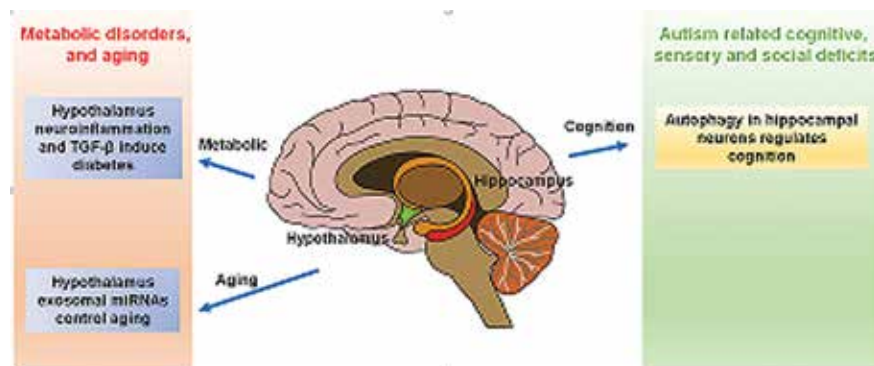
JINGQI YAN, PH.D., ASSISTANT PROFESSOR



RESEARCH INTERESTS: Autism and Metabolic diseases

Our research interest is to understand the pathophysiology of autism and metabolic disorders, and develop novel therapeutic strategies. The major research methods we are using include molecular biology, brain surgeries (virus and drug brain injection, and neural stem cell transplantation), cognitive and social behavioral tests of mice, histology and microscopy, chemogenetic method, induced pluripotent stem cells, and genetic and disease mouse models.

To date, our research has revealed that: 1) hypothalamic astrocytes secrete TGF- β to induce neuroinflammation and diabetes; 2) hypothalamus neural stem cells control aging and extend the life span of mice through secreting extracellular vesicles (exosomes); 3) autophagy in hippocampal neurons regulates synaptic plasticity and cognition in autism. Autism spectrum disorders (ASDs) are a group of developmental disorders. In 2020, approximately 1 in 54 children in the U.S. was diagnosed with autism. Patients with autism exhibit complex and debilitating neurological phenotypes, including impaired cognition, hyperactivity to sensory stimuli, and social deficits. Fragile X syndrome (FXS) is the leading genetic cause of autism and the most common form of heritable intellectual disabilities. Currently, one of our projects is focused on investigating how autophagy and exosomes regulate brain synaptic transmission and neural circuits controlling sensory, cognition, and social behaviors in the healthy condition and pathology of autism. Findings from our research are expected to develop novel therapeutic strategies for cognitive and social deficits associated with autism spectrum disorders.



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AMIN ZHOU, PH.D., PROFESSOR

**RESEARCH INTERESTS: Interferon, RNase L signaling and cancer**

There are two major research projects in Dr. Amin Zhou's laboratory. The first one is to study RNase L, one of the key enzymes in the interferon functions against viral infection and in the control of cell proliferation. Tissue distribution has revealed that RNase L is highly expressed in the spleen, thymus, and all types of immune cells. However, the physiological role of RNase L in immunity is largely unknown. The preliminary results suggest that RNase L may be a potential target for proinflammatory diseases such as diabetes and atherosclerosis. The RNase gene disrupted mouse model and cells are used to investigate the effect of RNase L on the function of immune cells such as macrophages. Another project is to elucidate the role of TMCO1, an endoplasmic reticulum (ER)-associated protein. Homozygous frameshift mutation in TMCO1 causes distinctive craniofacial dysmorphism, skeletal anomalies, and mental retardation. TMCO1 also functions as an ER Ca²⁺ load-activated Ca²⁺ channel. Recently, TMCO1 has been found in the laboratory to contribute to cancer progression and metastasis. The project goal is to determine the molecular mechanism by which TMCO1 is involved in cancer biology. The information gained from the studies may suggest TMCO1 as a potential target and a prognostic biomarker for cancer treatment.

Selected references:

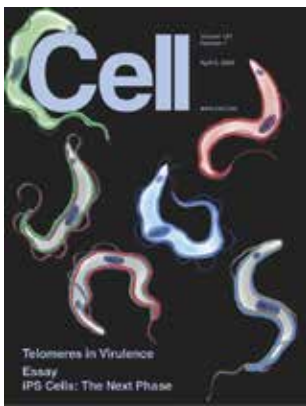
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NATIONAL AND INTERNATIONAL VISIBILITY

Over the past 15 years, GRHD researchers have published nearly 400 manuscripts in high-profile, peer-reviewed journals including *Science*, *Nature*, *Nature Communications*, *Cell*, *Molecular Cell*, *Proceedings of the National Academy of Sciences USA* and others. These publications have been collectively cited nearly 10,000 times (according to Web of Science). Based on the amount of funding and the quality and quantity of publications, GRHD ranks in the top 10 gene research centers in the country, among notables, the Plant Gene Expression Center at the University of California at

Berkeley and the Center for Eukaryotic Gene Regulation at the Pennsylvania State University. With this recognition, GRHD was selected out of the ~ top 20 Genetic Centers across the globe, and featured in a video produced for the American Society of Human Genetics (ASHG) Annual Meeting 2015, by WebsEdge, a global leader in web-based and conference TV.

GRHD faculty are in high demand as both speakers at national and international conferences and workshops and as organizers of many prestigious meetings in their respective fields of research.



iScience

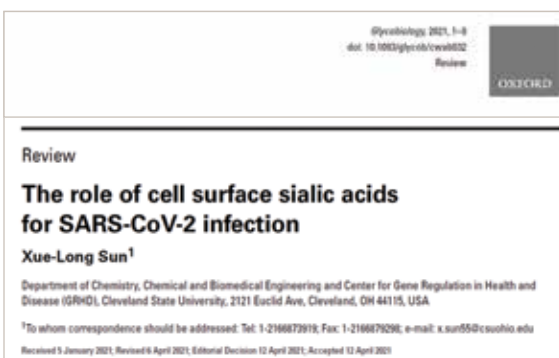
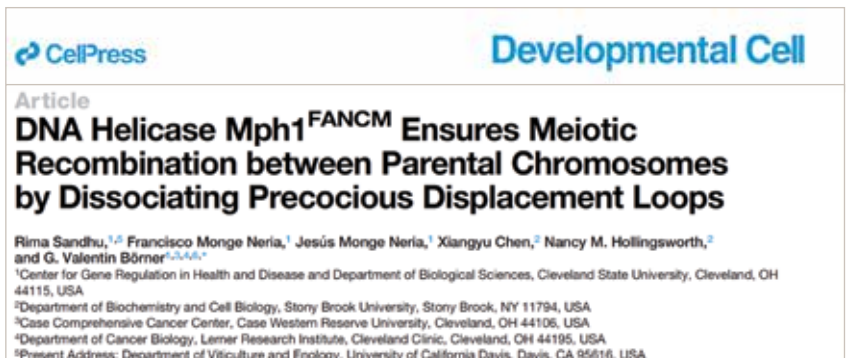
Article

Myeloid-cell-specific role of Gasdermin D in promoting lung cancer progression in mice

C. Alicia Traugbber,^{1,2,3} Gauravi M. Deshpande,^{4,7} Kalash Neupane,^{1,2,7} Nilam Bhandari,^{1,2,7} Mariam R. Khan,^{1,2} Megan R. McMullen,^{3,5} Shadi Swaidani,³ Emmanuel Opoku,³ Santoshi Muppala,³ Jonathan D. Smith,³ Laura E. Nagy,^{5,6} and Kailash Gulshan^{1,2,3,6,*}

Impavido attenuates inflammation, reduces atherosclerosis, and alters gut microbiota in hyperlipidemic mice

C. Alicia Traugbber,^{1,2,3,5} Amanda J. Iacano,^{3,5} Kalash Neupane,^{1,2,3} Mariam R. Khan,^{1,2} Emmanuel Opoku,³ Tina Nunn,³ Ashutosh Prince,^{1,2} Naseer Sangwan,^{3,4} Stanley L. Hazen,^{3,4} Jonathan D. Smith,³ and Kailash Gulshan^{1,2,3,6,*}



EXTRAMURAL FUNDING

Since its inception in 2008, GRHD has received over \$50 million in extramural funding. For many years in a row, GRHD faculty have routinely generated over 35% of IDCs recouped by CSU as a total. GRHD members have been awarded grants from the National Institutes of Health, the National Science Foundation, the Human Frontiers Science Program, an international program of research support, the American Heart Association, the Department of Defense (DoD) and the Defense Advanced Research Projects Agency (DARPA), the March of Dimes, the Cooley's Anemia Foundation and other foundations and granting agencies. Significantly, funding from the NIH increased more than 4-fold over the years, from ~\$1 million in 2008 to ~\$4.2 million in 2022.

DONOR SUPPORT

GRHD has successfully attracted more than \$3.6 million from private donors, including a substantial \$1 million anonymous gift which funds graduate scholarships, post-doctoral fellowships, pilot and bridge research projects, and equipment needs.

A generous donation from CSU distinguished alumnus, John C. Vitullo, Ph.D., CEO of Omega Laboratories, Inc., Mogadore, Ohio, established the Pilot and Bridge Funding program which seeks to increase the visibility of GRHD as a research center of excellence at CSU. The activities funded will help attract further external support. For example, this fund was recently endowed with a considerable gift from Paul E. DiCorleto, Ph.D., immediate past chair of Cleveland Clinic Lerner Research Institute and member of the GRHD external advisory board. Many anonymous donors also contributed to this fund and we gratefully continue to accept donations.

The John and Patricia Thompson Seminar series was created with a very generous \$100,000 endowment from CSU alumni John and Patricia Thompson. The series sponsors research seminars by nationally and internationally-recognized scientists in the fields of molecular biology and genetics, providing opportunities for GRHD faculty and students to network with leading investigators at the frontiers of biomedical science.

THE ENDOWED JOHN AND PATRICIA THOMPSON SEMINAR SERIES

November 2, 2017: The inaugural seminar, entitled, "The purinosome, an unique metabolon, responsible for cellular de novo purine biosynthesis," was delivered by Stephen J. Benkovic, Ph.D., the Evan Pugh Professor and Eberly Chair in Chemistry, The Pennsylvania State University, and a member of the US National Academy of Sciences.



Dr. Stephen Benkovic



The Inaugural John and Patricia Thompson Seminar

October 24, 2018: Douglas Koshland, Ph.D., the Richard and Rhoda Goldman Distinguished Chair in the Biological Sciences and Professor of Genetics, Genomics and Development, UC Berkeley, delivered the keynote, “The good, the bad and the ugly of chromosome dynamics,” as part of GRHD’s 10-year anniversary mini-symposium. Dr. Koshland is a member of the US National Academy of Sciences and a Lifetime Recognition Fellow of the American Society for Cell Biology.



Douglas Koshland, Ph.D.

October 24, 2019: Carlos J. Bustamante, Ph.D., presented the seminar, “Dissecting ribosome translation by co-tempered single molecule fluorescence and force measurements.” Dr. Bustamante is the Howard Hughes Medical Institute Investigator, Professor of Molecular and Cell Biology, Physics and Chemistry, and The Raymond and Beverly Sackler Chair of Biophysics, University of California, Berkeley. He is also a member of the US National Academy of Sciences.



Carlos J. Bustamante, Ph.D.

November 4, 2021: George R. Stark, Ph.D., Staff, Distinguished Scientist of the Cleveland Clinic Lerner Research Institute, member of the US National Academy of Sciences, and a Royal Society UK member, presented the seminar entitled “Complex roles of interferon in cancer.”



George R. Stark, Ph.D.

November 3, 2022: Alan G. Hinnebusch, Ph.D., delivered the seminar “Mechanism of scanning and start codon selection in translation initiation.” Dr. Hinnebusch is a NIH Distinguished Investigator, member of the US National Academy of Sciences, and Head of the Cell Regulation and Development Group at the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) at the National Institute of Health (NIH), Bethesda, MD.



Alan G. Hinnebusch, Ph.D.

EXCERPT FROM EAB REPORTS 2014-2022 AND TESTIMONIALS FROM EAB MEMBERS

“It is extraordinary that CSU has put together such a strong research center only a few years after its inception.”

“The GRHD members carry out a wide range of scientific investigations at a very high level. Despite the diversity of their individual projects, they nevertheless interact with each other extraordinarily well, so that the scope of their collective expertise becomes a great cumulative strength. In this setting, trainees participate in superb science, learning how to think critically and how best to take what is valuable and innovative for their own projects from the broad expertise and experience of their colleagues. Thus, GRHD provides a superb environment that produces groundbreaking research, while simultaneously educating students in how best to be productive in their future independent careers.”

George Stark, PhD, Chair, GRHD advisory board; Staff, Department of Cancer Biology, Cleveland Clinic Lerner Research Institute, Cleveland, OH; Distinguished Scientist, Lerner Research Institute; Member, National Academy of Sciences; Fellow, Royal Society of London

“The spirit and collaborative interactions among the GRHD faculty and between the GRHD faculty and scientists elsewhere in Cleveland are remarkable.”

“What stands out about this group is their cohesiveness, their enthusiasm. This is a group that will bring a lot of acclaim to the university.”

Stephen Benkovic, PhD, Member, GRHD advisory board; Evan Pugh Professor and Eberly Chair in Chemistry, Department of Chemistry, The Pennsylvania State University, University Park, PA; Member, National Academy of Sciences

“GRHD is well on the way to becoming one of the jewels in the university’s crown.”

“The Center for Gene Regulation in Health and Disease (GRHD) has achieved a milestone – it is celebrating its 15th anniversary. What an accomplishment! Fifteen years old, and GRHD continues to grow from strength to strength: with over a 60% increase in GRHD research expenditures over the past 5 years alone. The basis of GRHD’s success – the secret sauce, if you will - is the cohesive union forged among its high achieving junior and senior faculty, spiced with the hard work of its exceptional undergraduate and graduate students, each of whom has benefited from the dedicated mentorship that a GRHD lab provides. I urge you to take a look at our analysis of career outcomes of these students. It is really impressive. We are very pleased to announce that this year, in acknowledgment of the major impact that GRHD has on CSU’s upward research trajectory, GRHD has been elevated to be the first CSU Strategic Research Center. GRHD most assuredly punches above its weight!”

Meredith Bond, Ph.D. Vice President, Research and Innovation, CSU

CLEVELAND SCIENTIFIC COMMUNITY

“The Center for Gene Regulation in Health and Disease (GRHD) at Cleveland State University has become an asset to biomedical science in Cleveland, providing not only cutting edge research and top notch scientists, but access to a pool of uniquely qualified and talented students. At the Lerner Research Institute at Cleveland Clinic, our scientists serve as mentors for outstanding PhD students from GRHD, who bring talent and a strong work ethic to our research laboratories. We are grateful to have the opportunity to interact with both students and faculty from GRHD.”

Christine S. Moravec, PhD, Director, Research Education and Training Center, and Staff, Department of Cardiovascular & Metabolic Sciences, Cleveland Clinic Lerner Research Institute; Assistant Dean for Basic Science Education, Cleveland Clinic Lerner College of Medicine; and Director of Basic Research, Kaufman Center for Heart Failure, Cleveland Clinic, Cleveland, OH

“This group has a tradition of attracting excellent graduate students and vigorous faculty who provide a valuable resource for all of northeast Ohio. They have developed notable research programs and provide an excellent model for undergraduate students, many of whom join these research laboratories.”

Alan M. Tartakoff, PhD, Professor, Department of Pathology, and Co-director, PhD Program in Cell Biology, School of Medicine, Case Western Reserve University, Cleveland, OH

“I have had exciting and productive collaborations with the faculty in GRHD at CSU and I believe the best is still to come. The center has already been very successful – securing highly competitive federal funding for its innovative research while at the same time training and inspiring undergraduate and graduate students at the university.”

Maria Hatzoglou, PhD, Professor, Department of Genetics and Genome Sciences, School of Medicine, Case Western Reserve University, Cleveland, OH



STUDENT TRAINING AND OUTCOMES

Throughout its history, GRHD faculty have mentored nearly 300 students, both undergraduate and graduate, in line with the central mission of CSU, to educate those who might not otherwise have the opportunity, teach them to think constructively, critically, and creatively, and graduate them, fully prepared to succeed. Following graduation, undergraduate students overwhelmingly enrolled in graduate or medical schools (87.25%), whereas the majority of graduate students remained in academia and/or became employed in the biotech/health industry (85.70%). GRHD laboratories, in partnership with Cleveland Clinic's Lerner Research Institute, support CSU's Ph.D. programs in Regulatory Biology and Clinical-Bioanalytical Chemistry, including a specialization in Cellular and Molecular Medicine. While 66% of GRHD trained undergraduates remained in the state, 43.8% of graduate students pursued careers or further education in prestigious institutions such as Harvard, Stanford, and Columbia Universities, the National Institutes of Health, and The Scripps Research Institute.

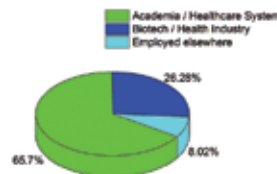


GRHD faculty graduate student training outcomes (2000-2022)

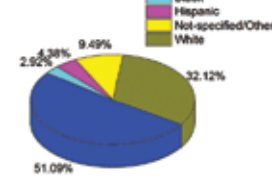
Graduated with PhD or MS



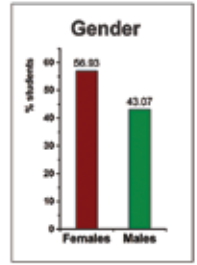
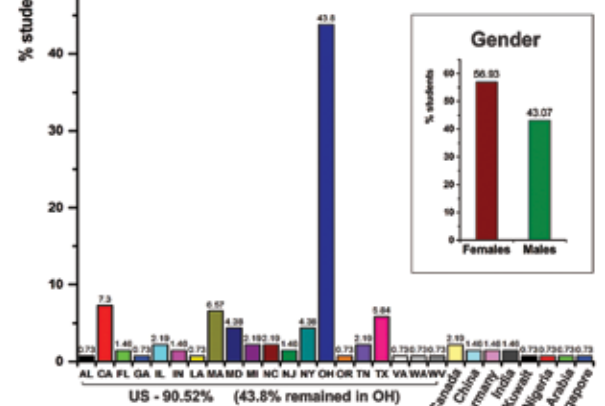
Further employment



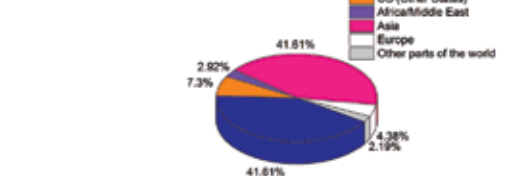
Ethnicity



Geographic patterns after graduation

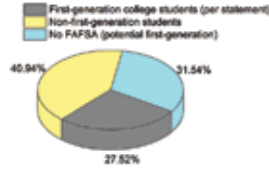


Geographics of enrolled students

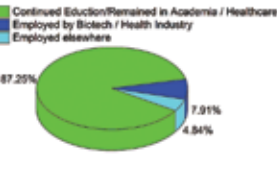


GRHD faculty undergraduate student training outcomes (2000-2022)

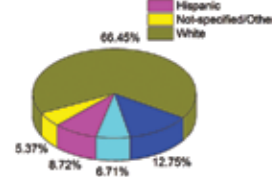
First-generation?



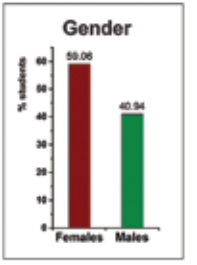
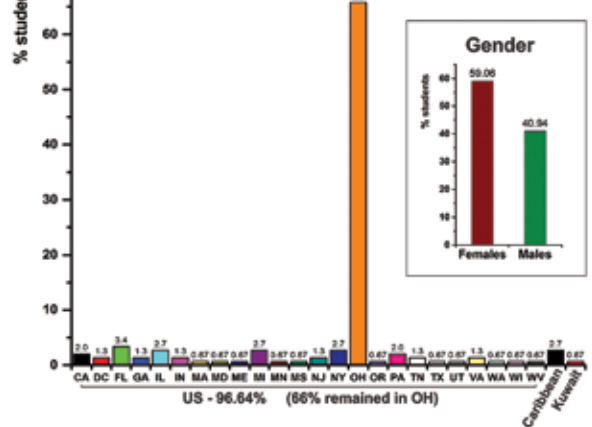
Further career path



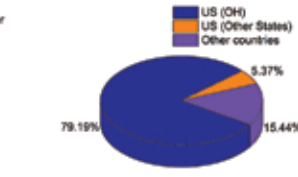
Ethnicity



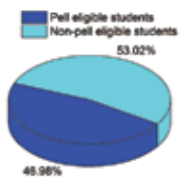
Geographic patterns after graduation



Geographic patterns of enrolled students



Pell eligibility



CLEVELAND STATE UNIVERSITY



Cleveland Clinic
Lerner Research Institute

ENGAGING IN NEW FRONTIERS OF RESEARCH AND DISCOVERY



GRHD is a time-tested, proven model for both the advancement of biomedical science and the training of a diverse community of graduate and undergraduate students at CSU. GRHD accomplishments continue to be very impressive, and are comparable to similar centers and departments within universities in the US with strong cell and molecular biology programs. The spirit and collaborative interactions among the GRHD faculty and between the faculty and scientists elsewhere in Cleveland and around the country continue to be remarkable. As such, we look forward to identifying novel opportunities for research and discovery particularly in partnership with local and national research institutions.

We are truly aware that with achievements and recognition come risks. Though GRHD is especially proud to be part of the growing biomedical research community of the Greater Cleveland area and committed to providing high quality training to the next generation of students at CSU, we know that sustained growth of the Center will not be possible without improvement to the research infrastructure, continued hiring of new dynamic, research active faculty, and expanding appropriate, modern laboratory space. To that end, we deeply appreciate the ongoing efforts by CSU to help solve these issues and continue the growth of the Center for Gene Regulation Health and Disease into a premiere biomedical research center in the US.

WE BELIEVE THE FUTURE OF GRHD IS VERY BRIGHT!

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