Kansas City University 2024 Research Symposium

Distinguished Speakers

Keynote Speaker:

Brad A. Amendt, MS, PhD

Professor of Anatomy and Cell Biology and Orthodontics
Director, Craniofacial Anomalies Research Center Carver College of Medicine/College of Dentistry
University of Iowa

New Advances in Gene Therapy to Repair and Regenerate Craniofacial and Dental Tissues

Abstract: Bone formation in the craniofacial complex is regulated by cranial neural crest (CNC) and mesoderm-derived cells. Different elements of the developing skull, face, mandible, maxilla (jaws) and nasal bones are regulated by an array of transcription factors, signaling molecules and microRNAs (miRs). miRs are molecular modulators of these factors and act to restrict their expression in a temporal-spatial mechanism. Molecules and microRNAs control the different genetic pathways that form the craniofacial complex. By understanding how miRs function in vivo during development they can be adapted to regenerate and repair craniofacial genetic anomalies as well as bone diseases and defects due to traumatic injuries. We will highlight some of the new miR technologies and functions that form new bone or inhibit bone regeneration.

Bio: Research in the Amendt group focuses on four major areas, 1) studying the expression and regulation of genes and co-factors involved in mammalian development, 2) the molecular basis of selected human genetic disorders, 3) the role of stem cells and microRNAs (miRs) in regulating craniofacial and bone development and regenerative medicine and 4) therapeutic applications of miRs and PMIS miR inhibitors in disease, cancer, and tissue repair. The overall goal of the laboratory is to elucidate the combinatorial code of transcription factors and mechanisms required for normal development of craniofacial structures, including bone and teeth. We are currently using miRs to control stem cell development and to regenerate tissues. miRs control stemness properties of craniofacial tissue progenitor cells and we are using miRs to program embryonic stem cells and reprogram dental/craniofacial progenitor cells. The function and interaction of miRs with transcription factors play a major role in the timing and development bone and tissues. We have developed the Plasmid-Based microRNA Inhibitor System (PMIS) to determine the roles of miRs during craniofacial development. The PMIS effectively knocks down the activity of miR clusters to

allow for the analyses of multiple miRs on separate chromosomes. This is the first demonstration of an in vitro system to knock down miR clusters and we make mice expressing miR inhibitors to understand the functional role of miRs during development. The laboratory strives to provide the basic framework for the development of technologies towards treating human genetic defects. Preparing and training graduate students and postdoctoral associates for a career in research is an extremely important aspect of my career and required to advance knowledge. The Amendt Laboratory is supported by grants from the National Institutes of Health.

Scientific Address:

Brian Clark, PhD

Professor of Physiology
Executive Director, Ohio Musculoskeletal and Neurological Institute
Ohio University
Osteopathic Heritage Foundation Harold E. Clybourne, DO, Endowed Research Chair

Aging Well in the 21st Century: Preventing Frailty and Fractures

Abstract: This talk will describe research aimed at addressing two of the most significant challenges associated with aging: sarcopenia and osteoporosis. Sarcopenia, a condition characterized by the loss of skeletal muscle mass and strength, is a key contributor to frailty and an increased risk of fractures in the elderly. Our research investigates the neuromuscular mechanisms underlying sarcopenia, offering insights into how aging affects muscle and nerve function and proposing targeted interventions to mitigate its impact. In parallel, we explore the advancement of Cortical Bone Mechanics Technology, a groundbreaking approach designed to enhance the diagnosis and understanding of osteoporosis. By providing a more nuanced assessment of bone strength and fracture risk, this technology represents a significant leap forward in our ability to prevent fractures and improve quality of life for the aging population. Through a comprehensive examination of these areas, our work contributes to the broader goal of aging well in the 21st century, emphasizing prevention, early diagnosis, and effective intervention strategies for frailty and fractures.

Bio: Brian Clark, PhD is a professor of Physiology and Neuroscience in the Department of Biomedical Sciences at Ohio University where he also serves as the executive director of the Ohio Musculoskeletal and Neurological Institute (OMNI) and is the Harold E. Clybourne, DO,Endowed Research Chair. Dr. Clark has held continuous funding since he was a graduate student, and over the past two decades he has secured and managed ~$30M as principal investigator or project director from federal agencies (namely NIH), private foundations, and industry. He has published more than 180 peer-reviewed articles and chapters (total citations >13,000) in high-impact clinical journals and basic/applied physiology and neuroscience journals. He has also been invited to write numerous prestigious review articles and books chapters, such as a chapter for 'Sarcopenia' (Wiley-Blackwell), the first book published specifically on sarcopenia, and a chapter for the 7th edition of Hazzard's Geriatric Medicine and Gerontology (McGraw-Hill), which is largely considered the most complete, authoritative guide available on the diagnosis and treatment of disorders affecting the elderly. Based on career-long citation metrics he is ranked in the 99th percentile of scientists in his discipline and was in the 99.5th percentile based on citation metrics from 2022 (Ioannidis et al, PLoS Biology, 2019). He has served on more than 60 federal grant review panels, and has served on numerous expert boards (e.g., Global Leadership Initiative in Sarcopenia (GLIS) Steering Committee), has delivered dozens of major national and international lectures and keynotes, and has received major national and international awards (e.g., 2010 New Investigator Award from the American College of Sports Medicine).

Featured Speaker:

Cornelius A. Thiels, DO, MBA

Surgical Oncologist & Assistant Professor of Surgery | Practice Chair | Division of Hepatobiliary & Pancreas Surgery
Assistant Professor of Health Services Research | Mayo Clinic College of Medicine
PI of Surgical Outcomes and Oncology Lab & Surgical AI2 Lab at Mayo Clinic

Building a Career as a Surgeon Scientist

Abstract: Dr. Thiels will discuss his journey to become an academic surgeon scientist at Mayo Clinic. Dr. Thiels will share how he built a clinical research lab and provide an overview of his recent work aimed at leveraging artificial intelligence to improve surgical outcomes. The talk will include advice for medical students who are interested in research and a career as a surgeon scientist.

Bio: Cornelius Thiels, DO, MBA, FACS is a surgical oncologist in the Division of Hepatobiliary & Pancreas Surgery at Mayo Clinic. He specializes in the management of retroperitoneal sarcomas, pancreatic cancer, and metastatic colorectal cancer. He runs the Hepatic Artery Infusion Pump program at Mayo Clinic and routinely utilized robotic surgery. He is also an assistant professor of Health Services Research and co-director of a Surgical AI Lab at Mayo Clinic. He has published over 100 peer-reviewed publications and currently serves as the Minnesota State Chair for the Commission on Cancer of the American College of Surgeons.

Featured Speaker:

Shyamanga Borooah, MBBS, MRCP, FRCOphth, PhD

Assistant Professor of Clinical Ophthalmology
Chief of Clinical Ophthalmic Genetics
University of California San Diego

From Bench to Bedside in Macular Degeneration

Abstract: The retina is a complex neurological layer of cells lining the back of the eye. The macula is the area of the retina critical for high acuity, central vision. When the macular is diseased or degenerated, it leads to severe functional vision loss and blindness. Macular degeneration is the commonest cause of vision loss in the developed world and includes age-related macular degeneration (AMD). AMD affects approximately 20% of the population by the age of 80. However, AMD is a complex, multifactorial disease which makes AMD difficult to model which is a barrier to understanding disease mechanism and developing new treatments. One method for understanding complex diseases has been the use of rare, Mendelian inherited forms of disease with similar phenotypes to study specific disease pathways. There are several autosomal dominant inherited macular degenerations which develop subretinal deposits, macular atrophy, macular neovascularization and blindness in a similar manner to AMD. This talk will focus on the use of stem cell modelling and, in particular, the study of pathophysiology in extracellular matrix turnover and complement pathway activation to understand these rare diseases and how greater understanding of his has helped provide insights to disease mechanism in the more common, but complex AMD. The talk will also demonstrate how this new knowledge has helped in the development of novel targeted AMD treatments, to slow disease progression and reduce the burden of blindness resulting from AMD.

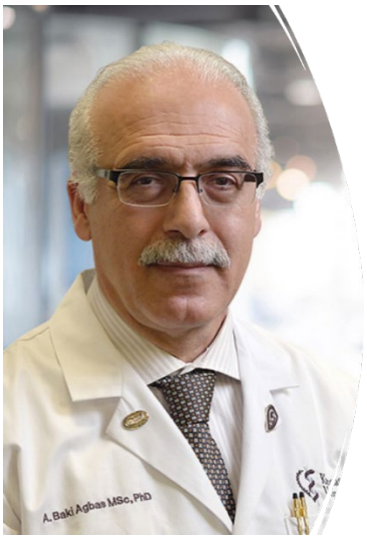
Bio: Shyamanga Borooah, MBBS, MRCP, FRCOphth, PhD, is a physician scientist and currently assistant professor of Clinical Ophthalmology and Chief of Clinical Ophthalmic Genetics at the University of California San Diego. Clinically, he initially qualified from Imperial College London and completed his residency in the UK training in ophthalmology with a sub-specialization in retinal diseases and ophthalmic genetics which included training at the prestigious Moorfield's Eye Hospital in London. Dr. Borooah received a PhD exploring a model of macular degeneration using patient derived stem cells, at the NIH equivalent MRC Center for Regenerative Medicine before being awarded a Fulbright post-doctoral scholarship bringing him to the University of California San Diego to translate some of the findings from his doctoral studies. He currently leads an NIH supported lab focusing on understanding disease mechanism and developing novel treatments for macular degenerations and inherited retinal disease.

KCU Featured Speaker:

A. Baki Agbas, MSc, PhD

Professor of Biosciences

Blood-based biomarker development for ALS: An initiative for the synergistic collaboration between industry and academia



Abstract: The accumulation of aggregated Transactive Response DNA-Binding Protein (TDP-43) is a major contributor to the pathobiology of ALS. This is believed to occur through both protein dyshomeostasis and loss-of-function mechanisms. We have discovered that TDP-43 and phosphorylated TDP-43(pTDP-43) are present in the cytosolic compartment of platelets, and that the pTDP-43 accumulates in platelets in ALS. Here we propose to conduct further analyses of platelets to determine whether they exhibit signs of TDP-43 dysfunction and aggregation similar to those observed in the ALS brain and spinal cord. Objective: To understand the function and accumulation of TDP-43 in platelets and relate this to the role(s) ofTDP-43 in the nervous system in ALS pathobiology. Hypotheses: We postulate that: a) TDP-43 has an important function in platelets; b) understanding TDP-43 biology in platelets can contribute insight into its behavior in neurons and c) the accumulation of specific forms ofTDP-43 in platelets may serve as a surrogate indicator (biomarker) for TDP-43 neuropathology in ALS. Specific Aim 1: To develop and test immunoassays employing ACIU's proprietary antibodies to evaluate the presence of ALS-brain-associated forms of TDP-43 in platelets. Specific Aim 2: To conduct RNA analyses of ALS and control platelet RNA samples to detect differentially expressed and/or differentially spliced RNA transcripts. Specific Aim 3: To validate the most promising TDP-43-related assays from Aims 1 & 2 on ALS and control subject platelet samples. This synergistic collaboration between industrial and academic partners will leverage expertise in ALS-associated biochemistry, gene regulation, cell biology and blood-based biomarker development. We expect our findings to illuminate the function and pathobiology of TDP-43 and identify new ways to target and monitor TDP-43-associated mechanisms of neurodegeneration.

Bio: Dr. Abdulbaki (Baki) Agbas is a professor of Biosciences in the Department of Basic Sciences, Kansas City University. He received his undergraduate degree in chemistry and Master of Science in clinical biochemistry from Ataturk University of Erzurum-Turkey, and a PhD in biochemistry from the University of Szeged-Hungary.

Dr. Agbas received extensive training in the international laboratories in the field of biochemistry, neurobiology, and cell biology. He was awarded an UNESCO-International Training Fellowship program in modern biology in Biological Research Center of Hungarian Academy of Sciences. During his fellowship program, how worked on opioid receptor characterizations in human placenta under the mentorship of Dr. Anna Borsodi. He then continued on the physiology of human placental opioid receptors during his tenure at University of Missouri-Kansas City, Kansas City, Missouri-USA. Dr. Agbas stayed in Kansas City

area, worked in area universities, and broadened his training and expertise in the field of cell biology and neurobiology. Since 2010, Dr. Agbas established his own laboratory and research team to work on developing blood-based biomarkers for Alzheimer's disease and amyotrophic lateral sclerosis (ALS). He has passion on mitochondria biology and developed an interest how mitochondria respiration profile can be used as "organelle-based biomarker" in disease states. He is a founding member of the "Heartland Center for Mitochondria Medicine". Dr. Agbas also teaches various biochemistry subjects for medical and graduate students at KCU.

KCU Featured Speaker:

Nataliya Kibiryeva, MD

Assistant Professor of Biomedical Sciences and Biosciences

Understanding role of long non-coding RNAs during cardiogenesis

Abstract: Recent studies show that long non-coding RNAs (lncRNAs) are widely expressed and play an important role in gene regulation in many biological processes. An important aspect of long non-coding RNA function is the creation of competitive endogenous RNA (ceRNA) networks. The ceRNA networks are large regulatory networks formed by both coding and noncoding RNA transcript interactions. While there are several RNA:RNA interactions that are key to ceRNA network formation, one of the most important interactions is that between lncRNAs and complementary miRNA transcripts. As one lncRNA transcript may be complementary to several different miRNA transcripts, there are many potential lncRNA:miRNA interactions. When these interactions form, the lncRNAs function as miRNA sponges. When lncRNAs act as miRNA sponges, downstream message RNA expression levels are also impacted. Process of lncRNA expression modulating miRNA levels and subsequently regulating gene expression is called a regulatory axis. These axes are frequently denoted as lncRNA/miRNA/protein coding gene axis of regulation and their importance for cardiac development is the focus of this presentation.

Bio: Dr. Nataliya Kibiryeva is an assistant professor of Biomedical Science in the KCU College of Biomedical Sciences. She teaches bioinformatics, scientific methodology and scientific communication. Dr. Kibiryeva received her medical degree from Kharkov State Medical University, Ukraine. After moving to United States, she joined Children's Mercy Hospital (CMH) and worked as a research scientist there for 20 years before joining Kansas City University. During her time at CMH she collaborated with many physician scientists from different specialties helping with analysis of Next Generation Sequencing and incorporating results into their research. Her research interests are focused on the epigenetic regulation of heart development, specifically on the role of non-coding RNAs and alternative splicing in cardiogenesis.