UAMS SHOWCASE OF MEDICAL DISCOVERIES

BioVentures: UAMS Intellectual Property and Innovations

Oct. 22, 2025

A Research & Innovation event featuring UAMS investigators showcasing their research and discoveries.

UAMS
Research & Innovation

Welcome Message

Daniel Voth
Vice Chancellor for Research & Innovation

Welcome to the UAMS Showcase of Medical Discoveries. This edition features BioVentures, the technology transfer office of UAMS, which serves as the bridge between university innovation and the biomedical industry. BioVentures plays a vital ole in helping our researchers transform their discoveries into real-world healthcare solutions that improve lives and strengthen Arkansas's biomedical economy.

We are proud to highlight the groundbreaking work of UAMS innovators who exemplify how research can move from the lab to meaningful impact through collaboration, entrepreneurship, and scientific excellence.

Thank you for joining us in celebrating the discoveries that advance health, drive innovation, and demonstrate the power of research at UAMS.

Eric C. Peterson, Ph.D.
Professor
Department of Pharmacology & Toxicology, UAMS
President, BioVentures

BioVentures

BioVentures, the technology transfer office of UAMS, serves as the bridge between university innovation and the biomedical industry. Established to translate UAMS research into real-world healthcare solutions, BioVentures supports faculty, staff, and trainees in protecting and commercializing their discoveries while helping to build Arkansas's biomedical technology economy.

Our mission is to foster commercial investment in biomedical inventions emerging from UAMS, advancing human health and driving statewide economic growth. BioVentures manages intellectual property, facilitates licensing and startup formation, and connects UAMS

innovators with industry partners, entrepreneurs, and investors.

Beyond IP management, BioVentures offers educational programs, including workshops and one-on-one guidance on intellectual property, commercialization, and entrepreneurship. The organization also provides incubation space, helping turn early ideas into viable companies.

By providing resources, expertise, and connections, BioVentures enables UAMS researchers to see their innovations reach patients and markets. Through this work, BioVentures strengthens the university's impact, fuels economic development, and showcases how discoveries made at UAMS can improve health and transform lives across Arkansas and beyond.

BioVentures

Mitch McGill, Ph.D., NRCC(CC)
Associate Professor
Department of Environmental
Health Sciences

About the Investigator: I am a toxicologist and clinical chemist with specific expertise in drug-induced liver injury (DILI). I conceived the invention and have overseen the validation studies to date.

The problem: Suspected liver injury is one of the most common reasons for termination of new drugs during clinical trials. However, there is concern that many drugs terminated due to potential liver damage are actually safe, costing pharmaceutical companies and potentially depriving patients of effective treatments. Currently, liver injury detection is based on monitoring of the enzyme alanine aminotransferase (ALT) in blood. Typically, ALT is released from dying cells and therefore reflects tissue injury. However, it is well-established that ALT elevations can occur in the absence of liver damage too. In other words, ALT can yield false positives. Thus, new biomarkers with greater specificity for liver damage are needed.

The solution: We have identified a promising new marker of liver injury that is more specific than ALT and we are developing an immunoassay system to measure it. This marker is based on the fact that cell damage causes dysregulation of proteases such that the proteases can come into contact with and cleave proteins that are not normally cleaved in healthy cells. The presence of these cleaved proteins in blood should be a specific indication of actual liver cell damage.

Brian Koss, Ph.D.
Assistant Professor
Department of Biochemistry and
Molecular Biology

Targeting ATF6 activation to promote ICB response

Jacob L Edmondson, Daniel Fil, Alan J Tackett, and Brian Koss

About the Investigator: I am an Assistant Professor in the Biochemistry and Molecular Biology Department and experienced cancer immunology researcher with a primary interest in understanding how the immune system controls cancer progression. My expertise includes cancer biology, adaptive immunity, mouse models of cancer, and proteomics.

Problem: Unleashing the immune anti-tumor response against metastatic melanoma through immune checkpoint blockade (ICB), and advancements in tumor-infiltrating lymphocyte (TIL), therapies have redefined clinical care. However, approximately half of metastatic melanoma patients exhibit primary resistance to ICB and many patients showing initial response eventually acquire resistance. ICB resistance is multifactorial, involving tumor cell-intrinsic and -extrinsic mechanisms and dynamic interactions within the tumor microenvironment (TME)[1,2]. Many tumor-specific pathways are associated with ICB resistance, including those

induced by TME stress and impacting release of immunomodulatory signaling biomolecules.

Solution: Activation of ATF6 is used here to increase cancer cell sensitivity to immune-mediated killing, particularly by CD8+ T cells, and to enhance the efficacy of immune checkpoint blockade. Experiments demonstrated that both pharmacological activation using AA147 and genetic modifications to express a constitutively active form of ATF6 resulted in significant improvements in immune-mediated tumor suppression, including reduced tumor growth in a mouse melanoma model and long-term immunity as evidenced by the resistance to tumor recurrence upon re-challenge. The invention outlines several implementation methods, such as genetic modification, nanoparticle delivery systems, and pharmacological activation, providing a versatile framework that can be integrated with existing immunotherapy regimens to improve treatment outcomes.

Christopher Wardell, Ph.D.
Assistant Professor
Department of Biomedical Informatics

Purpose: To construct machine-learning segmentation models to accurately label bones and surgically implanted hardware in whole-body CT images.

Materials and Methods: 90 whole-body CT scans were manually segmented using 60 labels and also subsegmented into cortical and trabecular bone. Segmentations were verified by board-certified radiology and nuclear medicine physicians. The impacts of isotropy, resolution, multiple labeling schemes, and postprocessing were assessed. Models were benchmarked against 362 samples from three datasets and compared against TotalSegmentator, an alternative segmentation model. Performance was assessed using Dice scores (DSC), normalized surface distance (NSD), asymmetric average surface distance (ASSD), Hausdorff distance (HD95), and manual inspection.

Results: Skellytour scored consistently on an internal dataset (DSC: 0.937, NSD: 0.993) and two external datasets; VerSe (DSC: 0.938, NSD: 0.999) and the TotalSegmentator test set (DSC: 0.957, NSD: 1.000), outperforming the TotalSegmentator model on the first two. Subsegmentation into cortical and trabecular bone was similarly accurate (DSC: 0.953, NSD: 0.995). Skellytour segmentation metrics were significantly better and had qualitatively higher resolution than TotalSegmentator, particularly in osteolytic lesions and low-density bone.

Conclusion: Skellytour is a highly accurate and generalizable bone segmentation and subsegmentation solution for CT data which is available as a Python package via GitHub (https://github.com/cpwardell/Skellytour).

Daniel Fil, Ph.D.
Staff Scientist
Department of Biochemistry and Molecular Biology

About the Investigator

I am a molecular biologist with over a decade of experience in translational research, specializing in cancer immunotherapy and T-cell engineering. As an Associate Staff Scientist at the University of Arkansas for Medical Sciences, I focus on developing engineered CAR-T cells with improved persistence in hostile tumor microenvironments.

Abstract

Engineering CAR-T Cells Resistant to EZH2 Inhibition to Enhance Therapeutic Persistence

Daniel Fil, PhD[1+], Megan R. Reed, PhD[2], Katherine Wallis, BS[2], Billie Heflin[2], Sydnye L. Shuttleworth[1], Lora J Rogers, BS[2], Katherine Bronson, PhD[2], Thomas A. Williams, BS[3], Alan J Tackett, PhD[2] and Brian Koss, PhD[4], (1) UAMS, Little Rock, AR, United States, (2) University of Arkansas for Medical Sciences, Little Rock, AR, (3) University of Arkansas for Medical Sciences, Conway, AR, United States, (4) University of Arkansas for Medical Sciences, Little Rock, AR, United States

The Problem

CAR-T cell therapies have shown remarkable promise in treating certain cancers, but their long-term effectiveness is often limited by T-cell exhaustion and loss of persistence. At the same time, EZH2 inhibitors—drugs designed to make tumors more immunogenic—can unintentionally weaken CAR-T cells by destabilizing their epigenetic program. This creates a major therapeutic challenge: while tumors may become easier to target, the CAR-T cells themselves become less durable.

My Solution

This work investigates this therapeutic tradeoff and develops new strategies to overcome it. Specifically, we are engineering CAR-T cells that are resistant to the negative effects of EZH2 inhibition. By protecting CAR-T cell persistence while maintaining the tumor-sensitizing benefits of EZH2 inhibitors, this approach aims to enable powerful combination therapies that expand the success of immunotherapy to more patients with difficult-to-treat cancers.

Donald J. Johann, Jr., MD, MSc, FACP
Professor, College of Medicine
Director, UAMS Genomics
Sequencing Facility

About the Investigator

Dr. Johann is a research-based physician-scientist (medical oncologist and computer scientist), and an internationally recognized expert on liquid biopsy science for oncology. His background is also focused on developing more effective therapies and molecular diagnostics for patients with cancer.Prior to medical school he worked as an engineer for the Sperry/Unisys Corporation on R&D projects involving advanced avionics.

Abstract & Problem Statement

Background - For the past ~20 yrs there have been several multi-parameter genomics tests developed for subtyping Breast Cancer Tumors, eg, OncoType Dx, PAM50 (Prosigna), EndoPredict, MammaPrint, etc. A **short-coming** of these approaches and all known methods is that they do not work well on archival samples. This is especially true for samples that are old (eg, 20 -30 yrs) and of degraded condition.

Innovation – development of a next-generation *in vitro* dual RNA & DNA based multi-molecular diagnostic assay, which performs well on archival specimens for the identification of a molecular subtype of a tumor, with an application for breast cancer.

Challenge & Opportunities – obtaining clinical utility for a multi-parameter genomic signature requires high levels of evidence.This is usually performed from "*prospective clinical trials*", which are costly and take time. There is a role for using archived specimens from "*previously conducted trials*" that have addressed a clinical question and have long-term follow-up. This invention now allows the ability to conduct virtual clinical trials, where questions may be asked and answered more quickly and with less expense vs conventional clinical trials.

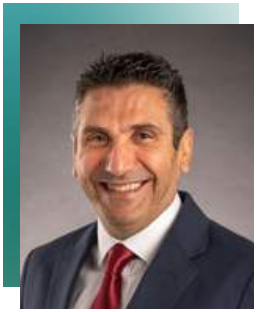
Gresham Richter, M.D.
Professor and Vice Chairman of
Pediatric Services
Otolaryngology, College of Medicine
Chief of Pediatric Otolaryngology

Tracheal Collar with Integrated Sensors

The Smart Tracheal Collar is a novel medical device that hopes to transform routine tracheostomy care into a real-time monitoring platform. By embedding miniaturized sensors and micro-electronics directly into a comfortable neck flange, the collar continuously tracks key physiologic parameters such as temperature, oxygen concentration, respiratory rate, heart rate, caloric consumption, pressure, and tissue health at the tracheostomy site. This enables early detection of airway obstruction, respiratory compromise, tracheostomy dislodgment or occlusion, and stoma/skin health—conditions that often lead to morbidity and costly complications and hospital readmissions.

Designed to integrate seamlessly with all standard tracheostomy tubes, the system wirelessly transmits data to patients, families, and clinicians for proactive airway and physiologic management. This innovation bridges a critical gap between patient safety and digital health, offering hospitals and home-care providers a new level of insight and control. With scalable manufacturing potential and strong patent protection, the Smart Tracheal Collar represents the intelligent airway management and connected respiratory care in children and adults with trachesotomies.

VanGuard Biofilm Team



Mohamed O. Elasri, Ph.D.

Mark S. Smeltzer, Ph.D.

Gyan S. Sahukhal, Ph.D.

Brendan A. Frett, Ph.D.

Nirjal Mainali, Ph.D.

Meenakshisundaram Balasubramaniam, Ph.D.

VanGuard Biofilm LLC

VanGuard Biofilm, LLC is a health-focused startup founded by Dr. Mohamed O. Elasri (PI) and a team of co-inventors with complementary expertise that led to the discovery of novel antibiofilm drug candidates. The scientific team driving this innovation includes:

Team: Drs. Mohamed O. Elasri, Gyan S. Sahukhal, and Mark S. Smeltzer – Experts in biofilm formation and bacterial pathogenesis. **Drs. Meenakshisundaram Balasubramaniam and Nirjal Mainali** – Experts in structural biology and molecular modeling. **Dr. Brendan Frett** – Expert in medicinal chemist with extensive experience in drug development. This interdisciplinary team maintains a dynamic, collaborative environment, with frequent communication and ongoing joint projects

The Problem:
Orthopedic implant-associated infections and chronic wounds represent a serious and costly healthcare challenge in modern medicine. In joint replacement and bone infections, prosthetic joint infections and osteomyelitis affect thousands of patients each year. Biofilms are the underlying culprit, shielding bacteria from antibiotics and the immune system. This leads to

repeated surgeries, months of IV antibiotics, prolonged hospital stays, and in many cases, recurrence or even amputation: making current treatments costly, complex, and often unsuccessful. In chronic wounds, they delay healing, increase amputation risk, and add billions in healthcare costs annually. Conventional approaches: such as systemic antibiotics, silver dressings, and antimicrobial coatings, fall short because they cannot penetrate biofilms or eliminate persister cells.

The burden is enormous: chronic wounds affect 2.5% of the U.S. population, including over 10 million Medicare patients, with costs estimated at $28-97 billion annually. Skin and soft-tissue infections add another $3.3 billion and over a million inpatient days each year. Chronic bone infections, such as osteomyelitis and prosthetic joint infections, affect ~1 in 1,000 U.S. adults and are rising with aging populations and increased orthopedic procedures. The global market for anti-biofilm therapies in bone and joint infections alone is projected to grow from $2.1 billion in 2024 to nearly $4 billion by 2035.

Our Solution:
StaphGuard is a first-in-class small molecule that directly targets the global regulators MsaB and SarA, which

control biofilm formation and persistence in *Staphylococcus aureus*. Unlike antibiotics, which struggle against biofilm defenses, StaphGuard prevents biofilm formation, disrupts established biofilms, and prevents persister cell development. In preclinical studies, StaphGuard demonstrated potent anti-biofilm activity, synergy with vancomycin and gentamicin, and no cytotoxicity at up to 20× IC_{50}.

StaphGuard is designed for seamless integration into implant coatings, bone fillers, and wound care formulations, enabling localized, highly effective infection prevention without adding surgical complexity.

Impact:
By addressing the root cause of treatment failure, StaphGuard has the potential to reduce infection rates, improve recovery, and prevent costly revision surgeries. For patients, this means better healing and fewer amputations; for hospitals, it means significant cost savings; and for healthcare systems worldwide, it means a real solution to a long-standing unmet need.

John Arthur, M.D., Ph.D.
Professor
Internal Medicine, College of Medicine
Division Director, Nephrology
Associate Director, TRI
Director, KL2

Development of an assay that can distinguish patients that will develop severe acute kidney injury

Nephsmart, LLC

The only Food and Drug Administration-approved biomarker for prediction of acute kidney injury (AKI) in adults has a false positive rate (FPR) of 50%. Moreover, it predicts moderate to severe AKI, but a biomarker that can distinguish patients that will progress to severe disease from those that will have less severe disease would be more useful. We identified insulin-like growth factor-binding protein 1 (IGFBP-1) as a good but not great predictor of severe AKI. IGFBP-1 was cleaved by an enzyme in the urine. We tested the ability of IGFBP-1 cleavage to predict progression to dialysis. Urine from all 12 patients with stage 1 AKI that progressed to require dialysis cleaved the protein (100% sensitivity). FPR

was 0% among healthy controls. FPRs among patients with stage 1 AKI at the time of collection were 11% for patients who did not progress beyond stage 1, 15% for patients who progressed to stage 2, and 50% for patients who progressed to stage 3 but did not require dialysis. The sensitivity of a test with these characteristics would be 100% in a typical intensive care unit (ICU) population, and the FPR would be 6%. Addition of other protein biomarkers to the assay could improve the accuracy further. We are developing an assay that can measure the cleavage product as well as other AKI biomarkers. Initial use of the assay will be to enrich patients for a clinical trial of AKI drugs.

Marie Burdine, Ph.D.
Associate Professor
Department of Surgery
Director, Division of Surgical Research

Novel Therapy for Prevention of Delayed Graft Function following Kidney Transplantation

The estimated number of kidney transplants in the United States this year is 30,000. Patients will face significant barriers to the survival of their donated organs, including delayed graft function (DGF), which affects 30% of patients and lacks any FDA-approved prevention strategy.1 Defined as requiring dialysis within the first week post-transplant, DGF negatively impacts both short- and long-term graft survival. Ischemia/reperfusion injury (IRI) to the kidney is a major cause of DGF.2 IRI occurs when blood flow is restored to the kidney after a period of ischemia. Prolonged ischemia time worsens IRI increasing the risk of DGF after transplant. Unfortunately, recent changes in transplant allocation protocols have forced an increase in ischemia times, making it crucial to identify therapies that protect grafts from IRI during the peri-transplant

period. Our laboratory determined that inhibition of the kinase DNA-dependent protein kinase catalytic subunit (DNA-PKcs) reduced rejection and extended survival of allogenic skin transplants providing support for the use of DNA-PKcs inhibitors as anti-rejection therapy for kidney transplants.3 To that end, we developed the novel small molecule DNA-PKcs inhibitor DA-143 (provisional patent filed).4 Pharmacokinetic studies determined DA-143 is more soluble and potent than all current DNA-PKcs inhibitors. The generation of DA-143 allows us to adequately assess the impact of DNA-PKcs inhibition on kidney rejection in a clinically relevant, pig kidney transplant model. Interestingly, new studies indicate that DNA-PKcs promotes IRI highlighting an additional potential use for DA-143 in preventing IRI-induced DGF.5 This further elevates the commercialization potential of DA-143 in the kidney transplant market which is currently estimated at $9.52 billion. Given our expertise with the pig kidney transplant model and in-house development of DA-143, we are well positioned to investigate the hypothesis that under prolonged ischemia time, DA-143 added to the organ preservation solution before transplant will reduce IRI and prevent DGF.

Patra Mousumi, Ph.D.
Post Doctoral Research Associate
Department of Radiation Oncology

Targeting GSK3β-Mediated Phosphorylation of 53BP1 at Threonine 334 Enhances T Cell Infiltration and Anti-Tumor Activity in Solid Tumors

About the Investigator:
My name is Mousumi Patra, Ph.D., and I have been working as a Research Associate in Dr. Fen Xia's lab in the Department of Radiation Oncology for the past five years. I am actively involved in multiple research projects, with a particular focus on in vivo studies. My primary role in this invention is performing mouse modeling of solid tumors, including head and neck squamous cell carcinoma (HNSCC) and glioblastoma (GBM), in order to demonstrate improved efficacy in vivo of our enhanced T cell products.

The problem:
Immunotherapy has improved survival in several cancers, particularly hematologic malignancies, but response rates remain low in solid tumors such as HNSCC, where only 11–18% of patients respond at six months. Emerging research highlights the critical role of DNA damage response (DDR)

pathways in regulating immune response. Alterations in DDR can impact lymphocyte activation, immune cell infiltration, and effectiveness of PD-1 checkpoint blockade. In HNSCC, defects in DDR genes are associated with poor prognosis and reduced immunotherapy response. Overall, it is clear that DNA damage is a contributing factor to T cell dysfunction in the context of solid tumors.

Our solution:
We believe that the combination of immunotherapy with the enhancement of DDR activity in cytotoxic immune cells will improve treatment efficacy and help overcome resistance. Our group identified a mutation within the DNA damage protein 53BP1 which serves to promote increased rates of DNA repair. Combining this mutation with CAR T cell therapy results in improved cytotoxicity and persistence against tumor cells. We also find that combination of this mutation with immune checkpoint blockade enhances overall *survival in vivo*. Overall, our findings suggest that targeting 53BP1 phosphorylation enhances response to immunotherapy in solid tumors.

Rami Shahror, Ph.D.
Senior Postdoctoral Fellow
Department of Pharmacology
and Toxicology

Use of CD5l Protein for Treatment of Ischemic Eye Injuries and Retinal Disorders

Rami A. Shahror, Abdelrahman Y. Fouda

Ischemic retinopathies, including diabetic retinopathy (DR), retinopathy of prematurity (ROP), and retinal artery and vein occlusions, are major contributors to visual impairment and impose a substantial financial strain on our healthcare system. Retinal ischemic injury occurs when blood flow to the retina is reduced or blocked, leading to oxygen and nutrient deprivation and potential damage to retinal cells. There are many acute and chronic causes that can lead to retinal ischemic injury. Current treatments exhibit limited efficacy. Accordingly, there is a need to develop novel treatments for ischemic retinopathies.

We recently identified the enzyme histone deacetylase 3 (HDAC3) as a key inhibitor of efferocytosis, a reparative process by which myeloid cells engulf dead cells in the ischemic retinal ischemia. Here, we identified the protein CD5L as a pro-efferocytic molecule that is upregulated in macrophages lacking HDAC3. CD5L's role in retinal ischemic injury was previously unknown. We found that HDAC3 suppresses CD5L transcription in an LXRα-dependent manner. Experiments conducted with mice lacking CD5L and treatment with CD5L recombinant protein demonstrated a protective role for CD5L against retinal ischemic injury. Additionally, we found that CD36, a receptor for CD5L, is upregulated in the retina myeloid cells following ischemic injury. In vitro experiments indicated that CD5L mediates efferocytosis via CD36. We discovered that giving a therapeutic dose of CD5L can protect retinal function after ischemic damage. This shows that CD5L could be an effective treatment for ischemic eye injuries and disorders.

Robert Eoff, Ph.D.
Professor & Vice Chair
Department of Biochemistry and
Molecular Biology

Abstract: The Eoff research group has been studying DNA replication mechanisms for over a decade, uncovering new molecular features of enzymes that assist in bypass of barriers to fork progression. The study of one of these enzymes, human DNA polymerase (pol) kappa, led to the discovery and development of a novel class of inhibitors targeting translesion synthesis (TLS). TLS is a biological response to slowed or stalled DNA replication that is largely conserved from prokaryotes through eurkaryotes, impacting everything from bacterial response to antibiotics, maintenance of difficult-to-replicate parts of the genome, promoting environmental exposure-induced mutagenesis, and causing therapy resistance in multiple types of cancer. Collaborating with researchers in the Department of Pharmaceutical Sciences at UAMS, Dr. Eoff and his team have focused on testing the most selective inhibitor of pol kappa reported to date – UAMS-48 (also called IAG-10).

The Problem: The impetus for our work can be found in studies detailing how higher expression of pol kappa causes resistance to the standard-of-care therapy temozolomide (TMZ; tradename Temodar) in glioblastoma and is a prognostic indicator of shorter survival for patients suffering from this terrible form of cancer. Thus, inhibition of pol kappa in glioblastoma could be used to sensitize patient tumors to standard therapies, likely with little impact on adjacent tissues where this enzyme is not normally expressed at high levels.

Our Solution: Using both cancer cell lines and treatment-naïve primary cultures derived from tumors surgically resected at UAMS, the Eoff lab has demonstrated that UAMS-48 augments the anti-proliferative effects of TMZ in glioblastoma cells and that this effect depends on the presence of the target, pol kappa. Additional experiments revealed that the inhibitor produces a defect in replication gap suppression, a relatively new concept in the DNA replication field and one with important implications for genotoxic therapeutics. In tumors, like glioblastoma, that depend on pol kappa to sustain DNA replication in a way that protects what is already an unstable genome, a defect in gap suppression could prove catastrophic because of exceedingly high levels of single-stranded DNA, which is more vulnerable to damage and cleavage than double-stranded DNA. Indeed, treatment with UAMS-48 produced higher levels of single-stranded DNA in glioblastoma cells, with no observable effect on fork dynamics in normal or non-glioma cells. In summary, pre-clinical studies provide a promising foundation to build towards additional work targeting pol kappa in glioblastoma.

Sydnye Shuttleworth
M.D./Ph.D. Graduate Assistant
Department of Biochemistry and
Molecular Biology

Modulating RNF166 to enhance immune function in cancer

Inventors: Sydnye Shuttleworth and Brian Koss

About the Investigator: I'm a G2 MD/PhD student in the Koss Lab, an NIH/NCI F30 pre-doctoral fellow, and a full member of the Winthrop P. Rockefeller Cancer Institute. I study how T cells survive and function within solid tumors, with an emphasis on developing cellular therapies. I use advanced proteomics to understand proteome turnover in T cells and define how these dynamics influence T-cell function and persistence in solid tumors. My work aims to reveal mechanisms and strategies to enhance adoptive therapies such as CAR-T.

Problem: T cell exhaustion significantly limits the effectiveness of cancer immunotherapies, particularly adoptive T-cell therapies in solid tumors. This dysfunctional state, driven by chronic antigen stimulation and the suppressive tumor microenvironment, leads to T

cells losing their effector functions, impairing their ability to kill cancer cells and produce essential cytokines. While current immunotherapeutic strategies aim to boost or unleash T cell responses, they often fall short because they do not fully address the complex internal cellular changes underlying exhaustion. Specifically, T cell exhaustion involves extensive proteome remodeling, characterized by accelerated protein turnover, destabilization of critical T cell receptor components, and altered protein homeostasis, including shifts in the ubiquitin-proteasome system. Understanding and overcoming these intricate internal protein dynamics and proteostasis collapse remains a significant challenge for developing more durable and effective cancer treatments.

Solution: The invention enhances T-cell function in cancer immunotherapy by modulating the E3 ubiquitin ligase RNF166 to counteract T-cell exhaustion. T-cell exhaustion, a state of impaired cytotoxicity and increased inhibitory receptor expression, limits the effectiveness of adoptive cell therapies. The technical approach involves genetically engineering immune cells, such as CD8+ T-cells or CAR T-cells, to overexpress RNF166. This overexpression increases the T-cells' resistance to exhaustion, prolonging their cytotoxic function and persistence, and reducing the expression of inhibitory receptors like PD-1, CTLA-4, and LAG-3. RNF166's role was identified through proteomic analyses, which showed its downregulation during exhaustion and its correlation with immunotherapy outcomes, indicating its manipulation targets intracellular protein homeostasis critical for T-cell function.

Tudor Moldoveanu, Ph.D.
Associate Professor
Biochemistry and Molecular Biology

Enable discovery of BCL-2 family inhibitors targeting mode II complexes

Trained in biochemistry, structural and chemical biology, my primary research focus has been in mechanisms of programmed cell death and their targeting in cancer. I spent my postdoctoral and independent career at St. Jude Children's Research Hospital before joining UAMS Winthrop P. Rockefeller Cancer Institute (WPRCI) three years ago. Since joining UAMS, in collaboration with Dr. Darin Jones of Pharmaceutical Sciences, we established a brand-new Screening and Drug Discovery Shared Resource (SDDR), an enterprise sponsored by WPRCI and the College of Pharmacy that enables access of UAMS investigators to the infrastructure and expertise for drug screening and early drug discovery. I am one of the co-leaders of the Cancer Therapeutics Research Program at WPRCI and have helped stir the program to align with WPRCI's mission to develop novel drugs for Arkansan cancer patients.

Our invention addresses an unmet need in developing such drugs to target the cell death pathway known as apoptosis. In many cancers this pathway is blocked through overexpression of the prosurvival guardians BCL-2 family proteins. The guardians block apoptosis by forming a complex, known as mode II, with the pore-forming effector BCL-2 family proteins. Using biochemical, structural, and pharmacological approaches we comprehensively characterized for the first time the mode II complex between MCL-1 guardian and BAK effector. MCL-1 is overexpressed conferring resistance to therapies in many cancers including those of interest to WPRCI catchment area such as multiple myeloma, breast, and lung. Surprisingly, we discovered that existing drugs designed against MCL-1 are poorly active in dissociating BAK from mode II complex with MCL-1.

Our invention is a drug discovery platform that enables characterization of the mechanisms of action of modulators of the mode II complex. Leveraging our platform and SDDR will enable discovery and development of better cell death inducers targeting mode II complex.

Zach Waldrip, Ph.D.
Instructor
Department of Surgery

Dr. Zachary Waldrip is a researcher here at UAMS and Arkansas Children's Research Institute where some of his research focus is on harnessing probiotics as a therapeutic solution to gastrointestinal diseases. Worldwide hundreds of millions of cases of diarrheal diseases, some fatal, are the result of enteric toxin-mediated diseases such as C. *Difficile* infection and shigellosis. Even though many of these are caused by bacterial infections, antibiotics are often ineffective or even exacerbate the problem. Because of the high level of morbidity and mortality caused by these diseases, there is a great need for new, cost-effective solutions. Our team believes there is massive potential in using live biotherapeutic products to address enteric diseases. The probiotic yeast *Saccharomyces boulardii* is generally recognized as safe to consume and is inexpensive to grow, making it the perfect candidate for a cheap, genetically encoded, edible therapeutic. We believe that this organism can be used to express anti-toxin antibodies on the cell surface to act like a molecular sponge that can absorb toxic molecules as they pass through the gastrointestinal tract. This would provide a means of counteracting the deleterious effects of infection while the patient recovers. Toward that end, we are modifying this yeast to express therapeutic antibodies on the cell surface and demonstrating efficacy in the gastrointestinal tract. With funding through Bioventures/ARHVA we are generating antibodies against shiga toxin as an initial target in developing this platform.

BioVentures

UAMS

Research Support Teams

- **Biomed Buildings Research Space & Buildings Management**
- **BioVentures**
- **Division of Laboratory Animal Medicine (DLAM)**
- **Institutional Animal Care and Use Committee (IACUC)**
- **Institutional Review Board (IRB)**
- **Office of Research and Sponsored Programs (ORSP)**
- **Office of Research Regulatory Affairs (ORRA)**
- **Science Communication Group (SciCom)**

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