



ANNUAL REPORT

Arizona Biomedical Research Centre

2024

ARIZONA
— DEPARTMENT OF —
HEALTH SERVICES
Arizona Biomedical Research Centre



Welcome to Our **ANNUAL REPORT** 2023-2024

Victor Waddell, Ph.D.
ABRC Executive Director
Bureau Chief
Arizona State Laboratory

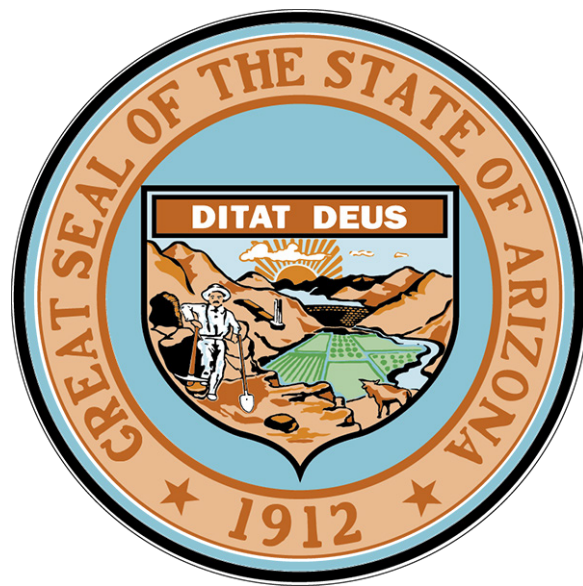
The Arizona Biomedical Research Centre's (ABRC) mission is "accelerating biomedical research, education, and innovation to benefit Arizonans." In FY 2024 we were able to fulfill our mandate to provide the citizens of Arizona with the fruits of our three core programs and continue the ABRC's mission with positivity. Community support is integral to the success of the ABRC core programs of providing grant funding to support biomedical research within the state, award funds to our State Universities to host educational events on innovations in science, and save lives through the efforts of our public cord blood program. Together, we've achieved many program milestones. None of these achievements would be possible without the unwavering support of our valued community partners, agency leadership, the Governor's office, State legislature, and the people of Arizona.

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HEALTH SERVICES

Arizona Biomedical Research Centre



Kathleen M. Hobbs, MSW, Governor
State of Arizona

Jennifer Cunico, MC, Director
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Accelerating Biomedical Research, Education, and Innovation to Benefit Arizonans

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Program Director's **PERSPECTIVE**

During FY 2024, the ABRC established a formal grant cycle which our researchers would find more dependable. The steps taken this past year, allowed us to allocate a large pool of funding for grant awards that could sustain two new three-year grant cohorts each fiscal year. During FY 2024, we awarded grants to two new cohorts, of 25 grants and 28 grants, respectively.

Our three state Universities exceeded our expectations in the number and quality of 28 research-related educational events.

Our Public Cord Blood Program outreach efforts delivered our message of saving lives through cord blood donation to hundreds of Arizonans at awareness events in Phoenix, Tucson, and Flagstaff. The ABRC staff, interns, and partners from the Save the Cord Foundation attended nearly 15 engagements. During FY 2024, we recorded the shipment of the program's 97th unit for use in transplantation.

Overall, FY 2024 was a year of accomplishment and growth as we strive to enhance the health and wellness of all Arizonans.



John S. Garcia, MBA
Program Director

Executive Summary

The Arizona Biomedical Research Centre (ABRC) was created by Arizona citizens who had the foresight to set aside tobacco and lottery revenue to identify and support innovative biomedical research to improve the health of all Arizonans. The ABRC is part of the Arizona Department of Health Services Public Health Laboratory Bureau (ASPHL) within the Division of Public Health Preparedness. The ASPHL Bureau Chief serves as Executive Director for ABRC and day to day operations are overseen by the ABRC Office Chief with support of a Deputy Program Director who manages the operations of the activities of the program. A grant program coordinator and grant project specialist oversee the grant contract, finances, and activity reporting. Two Cord Blood Program interns assist with cord blood education and awareness activities.

The ABRC provides approximately \$9 million dollars each year in direct grants to biomedical researchers. The ABRC also provides about \$1.2 million in grants to state universities so that researchers can become successful and globally competitive, through workshops, conferences, and other educational activities. Finally, ABRC supports approximately \$1.3 million in grants to qualifying hospitals for the collection and public banking of donated umbilical cord blood and other birth tissue for use in research and life-saving treatments.

Funding comes from two sources: Tobacco Taxes and Lottery Revenue. Approximately \$7.7 million in tobacco tax revenue flows, in accordance with Arizona Revised Statute §36-275, into the Health Research Fund to support the biomedical research grant program. Nearly \$4.5 million in Lottery revenue, in accordance with Arizona Revised Statute §36-274, is deposited each year into the Disease Control Research Fund to support the Research Education and Cord Blood Programs.

The research supported by the ABRC funds seeks to identify the causes, epidemiology, and diagnosis of diseases affecting Arizonans. It also is used to support the translation of research to formulate cures for diseases, develop medically accepted treatments, prevent diseases, discover and develop new drugs, and invent biomedical devices. All this is accomplished through the close collaboration with researchers, scientists, physicians, and educational institutions. Additionally, the cord blood collection program collaborates closely with hospitals, nurses, and medical directors, to enhance the development of cures and treatments for over 80 diseases.





ABOUT US

The Arizona Biomedical Research Centre (ABRC) supports innovative biomedical research to improve the health of all Arizonans. The ABRC provides direct grants to biomedical researchers and institutions in support of their efforts to develop cures and treatments for disease and illness. Additionally, the ABRC provides grants to Arizona's three universities to enable them to become successful and

globally competitive, through workshops, conferences, and other educational activities. Finally, ABRC supports the collection and public banking of donated umbilical cord blood and other birth tissue for use in research and life-saving treatments.

-Accelerating Biomedical Research, Education, and Innovation to Benefit Arizonans

WHAT WE DO

The Arizona Biomedical Research Centre (ABRC) provides approximately \$9 million dollars each year in direct grants to biomedical researchers. ABRC also provides about \$1.2 million in grants to state universities so that researchers can become successful and globally competitive, through workshops, conferences, and other educational activities. ABRC also supports approximately \$1.3 million in grants to qualifying hospitals for the collection and public banking of donated umbilical cord blood and other birth tissue for use in research and life-saving treatments. Additionally, ABRC provides grants and financial support to the Arizona Alzheimer's Consortium (\$4.125 million), Translational Genomics Research Institute (\$2 million), Marijuana Research (\$2.65 million), and Psilocybin Clinical trials (\$3.72 million).



Research Grants

Grants totaling \$9 million annually help identify the causes, epidemiology, and diagnosis of diseases affecting Arizonans. The funds awarded support the translation of research to formulate cures, medically accepted treatments, prevent disease, and invent biomedical devices.



Research Education

ABRC is committed to enhancing and furthering bioscience and clinical research supporting local researchers and clinical professionals by bringing national and local experts together to cover emerging topics at little or no cost to the Arizona research community.



Arizona Public Cord Blood Program

This program was created to advance the collection of and increase the number of umbilical cord blood units available for transplantation. Stem cells in cord blood can be collected, stored, and made available for transplant to treat over 80 diseases such as leukemia, lymphoma, sickle cell, SCIDS, Hurler Syndrome, Parkinson's, and ALS.



Special Research Programs

The ABRC administers special funding for the study of Alzheimer's, various biomedical and genetic research, clinical studies and research on the safety of an efficacy of Marijuana as a medical treatment, and for clinical trials to test the efficacy of Psilocybin whole mushrooms for treatment of various psychological or emotional conditions.

Support for ABRC programs is provided to accelerate promising research toward clinical testing and breakthroughs designed to improve the health of Arizonans. While ABRC's strong emphasis is on funding basic and translational research projects to generate preliminary data, ABRC continues to seek innovative projects that leverage all of Arizona's resources and strengthen collaboration.



JOHN GARCIA, MBA
Program Director



VICTOR WADDELL, Ph.D.
Executive Director



KEALYN MCCOOL, MS
Deputy Program Director



TERESA CARO
Grant Contract
Administrator



NATASHA NEWSOM
Grant Project
Coordinator



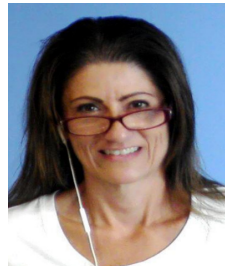
SHANDRE NIAMEOGO
Cord Blood Program
Intern



KYLEE COOK
Cord Blood Program
Intern



LAURA SAENZ-SERNA
Finance Manager



GINA DACQUISTA
Financial Analyst



KAITLIN BURRESON
Senior Procurement
Specialist

Meet the **ABRC Team**

The ABRC is an Office of the Arizona State Public Health Laboratory (ASPHL) bureau. It receives its direction principally through the ABRC Executive Director (Chief of the Bureau). Responsibility for the strategic direction falls on the ABRC Program Director (Office Chief). Daily operation of the programs is overseen by the Deputy Program Director. The ABRC is staffed by a Grant Contract Administrator, Grant Project Coordinator, and two Cord Blood Program Interns. Supporting the ABRC are the efforts of a Finance Manager, Financial Analyst, and Senior Procurement Specialist.

2024 HIGHLIGHTS

\$ 2,569,298*

Supporting continuing grants for diverse biomedical research in Arizona

\$ 6,561,448

Supporting TGen, Alzheimer's disease research, HIV, Marijuana, and Psilocybin research

\$ 1,596,072**

Supporting Research Education and the AZ Public Cord Blood Program

* This amount includes minimal operating costs of approximately 11 percent.

** Operating expenses include operating costs, promotional items used by participating hospitals, and outreach services of about 13 percent.

Research Grants

- 42 continued and 27 new research projects supported
- 16 publications from research supported by ABRC
- 11 Arizona institutions supported, including NAU, ASU, UA Tucson, & Phoenix, Mayo Clinic, VaxSyna, Critical Path Institute, AZ Veterans' Research Foundation, Banner U of A, Southwest Autism Research and Resource Center, St. Joseph's Hospital, and Translational Genomics Research Institute (TGen)

Research Education

- 5,200+ Arizonans participated in educational programs
- 51 free events including workshops, conferences, webinars, and training modules, were held
- Events were held in Flagstaff, Phoenix, Tucson, Yuma, in-person and virtually-online

Arizona Public Cord Blood Program

- 97th cord blood unit was used in a life-saving treatment for Acute Bilineage Leukemia
- The 9th Annual Cord Blood Conference was a hybrid conference and attended by 225 doctors, nurses, practitioners, and the general public from 20 states and 27 countries.

Arizona Biomedical Research Centre

CORE PROGRAMS



01

RESEARCH GRANTS

02

RESEARCH EDUCATION

03

ARIZONA PUBLIC CORD BLOOD PROGRAM

04

ALSO SUPPORT

- Arizona Alzheimer's Consortium
- Translational Genomics Research Institute (TGen)
- HIV
- Psilocybin Clinical Trials
- Marijuana Clinical Trials and Research

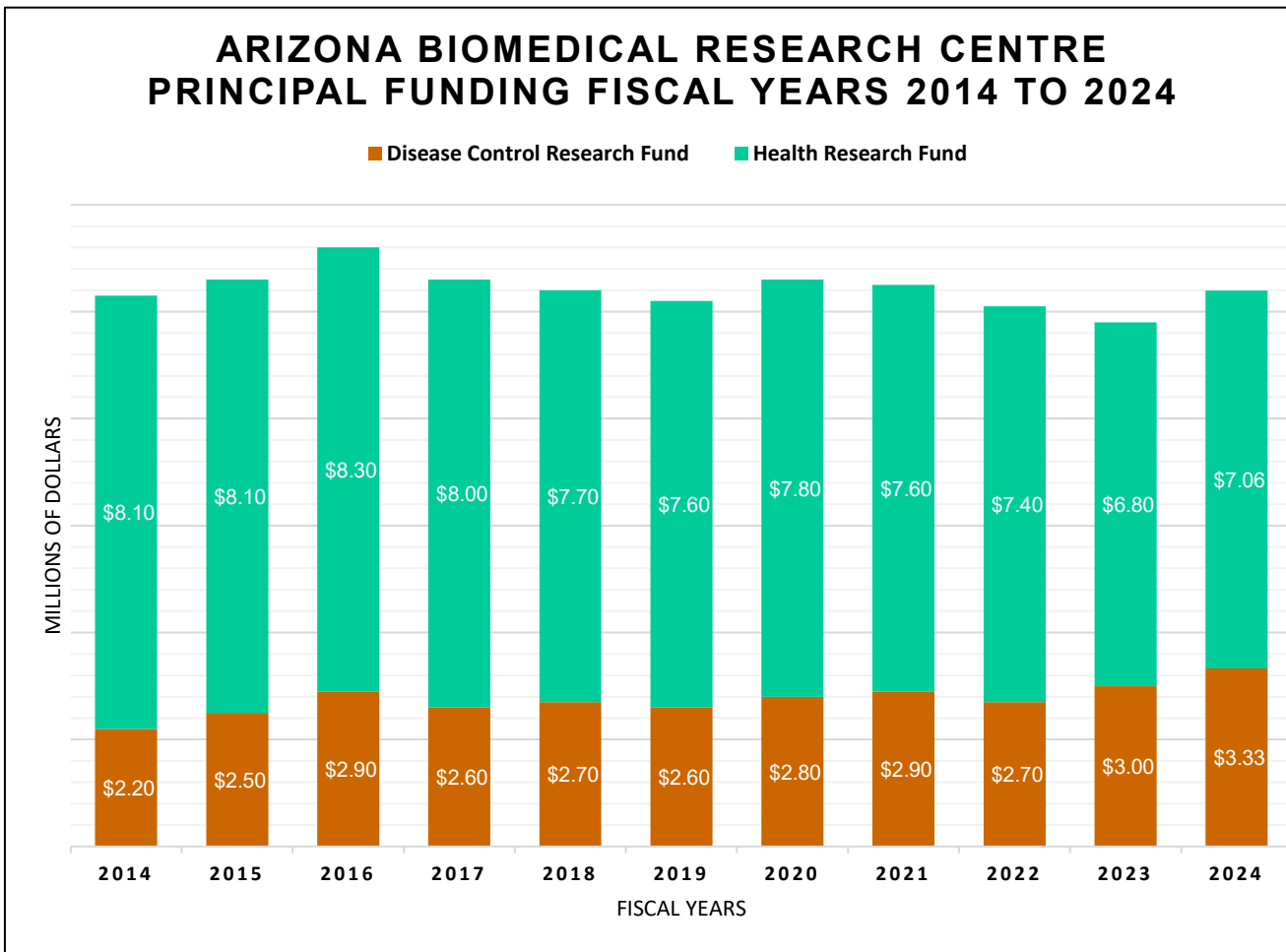
FINANCIAL SUMMARY

REVENUE

ABRC's revenue in FY 2024 totaled **\$25,821,504**

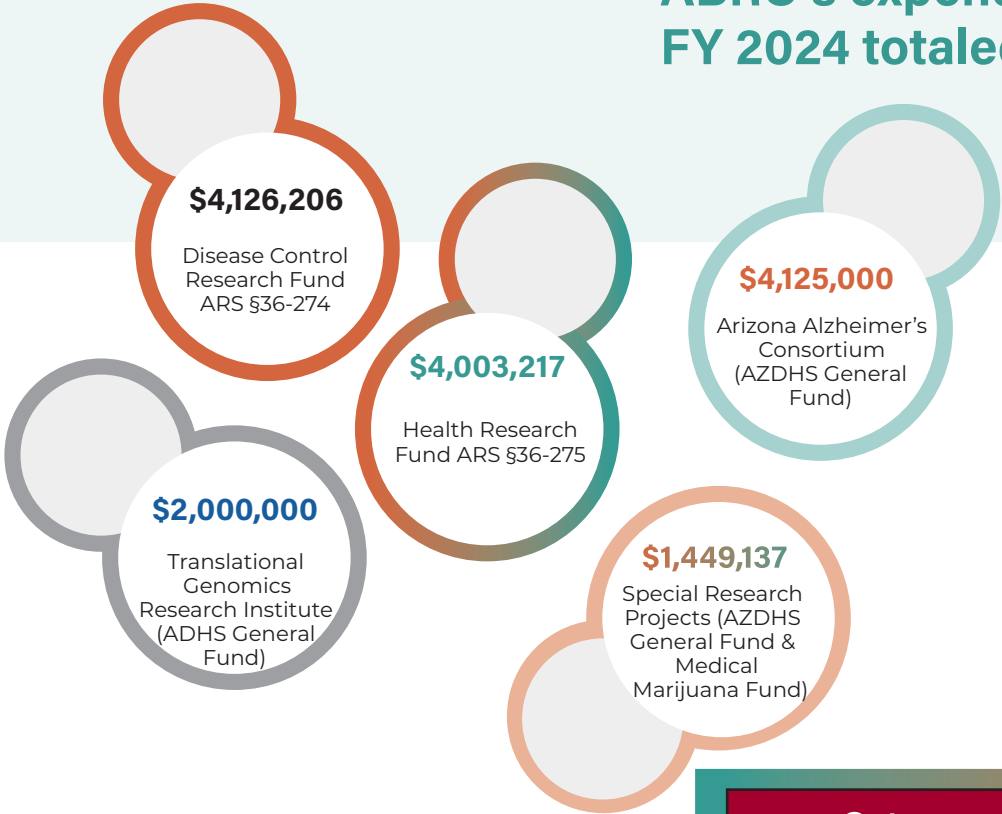
- Disease Control Research Fund ARS §36-274 (Lottery Revenue) **\$3,331,334**
- Health Research Fund ARS §36-275 (Tobacco Tax) **\$7,061,999**
- Other Appropriated Revenue (General Fund, Medical Marijuana Fund) **\$15,428,171***

*Not included in the chart below.



EXPENDITURES

ABRC's expenditures in
FY 2024 totaled **\$15,703,560**



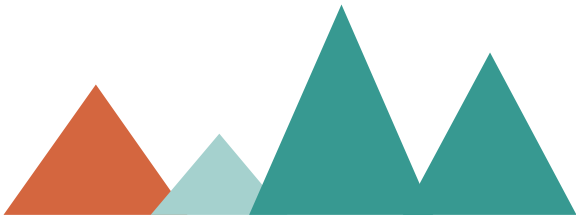
Psilocybin Clinical Trials program added to special research project lineup

The Psilocybin Research Program was established pursuant to the provisions of Laws 2023, Chapter 133 (56 th Leg 1 st Reg), SB 1720, Sec. 44. The program was enabled through the provisions of Laws 2023, Chapter 139 (56 th Leg 1 st Reg), SB 1726, Sec. 6; granting \$5,000,000 for clinical trials to determine the efficacy of whole mushroom Psilocybin in treating several conditions, disorders, or illnesses. Two grants totaling \$3,724,853 were awarded in FY2024.

Category	Expenditure
Research Grants	\$3,638,841
Arizona Alzheimer's Consortium	\$4,125,000
Translational Genomics Research Institute (TGen)	\$2,000,000
Arizona Public Cord Blood Program	\$690,100
HIV	\$1,095,365
Research Education	\$680,942
Operating	\$2,024,175
Marijuana Research	\$215,006
Psilocybin Research	\$1,234,131
TOTAL	\$15,703,560

ARIZONA PUBLIC CORD BLOOD PROGRAM

FY 2024 Highlights



Overview

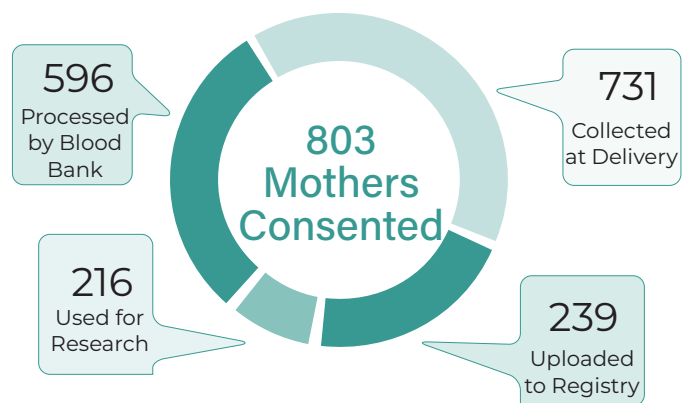
Umbilical cord blood is blood that remains in the blood vessels of the placenta and the umbilical cord, and is collected after the baby is born and the cord has been clamped and cut. Donating umbilical cord blood is free, painless and neither mother nor child is harmed in the collection.

Cord blood stem cells can be used much the same way that bone marrow stem cells are used for life-saving transplants. For many patients in need, a cord blood transplant is the best, or only hope for a cure. Cord blood can be used to treat or cure over 80 diseases, such as blood cancers (e.g. leukemia) and bone marrow disorders, (e.g. aplastic anemia).

Cord blood used in transplants must have a high Total Nucleated Cell count (TNC). In order to ensure a collected unit has enough cells, the provider collects as much cord blood as possible. Cord blood units over 90 ml are sent to the cord blood bank for processing. Most cord blood units used in transplants have more than 1.75×10^9 TNC.

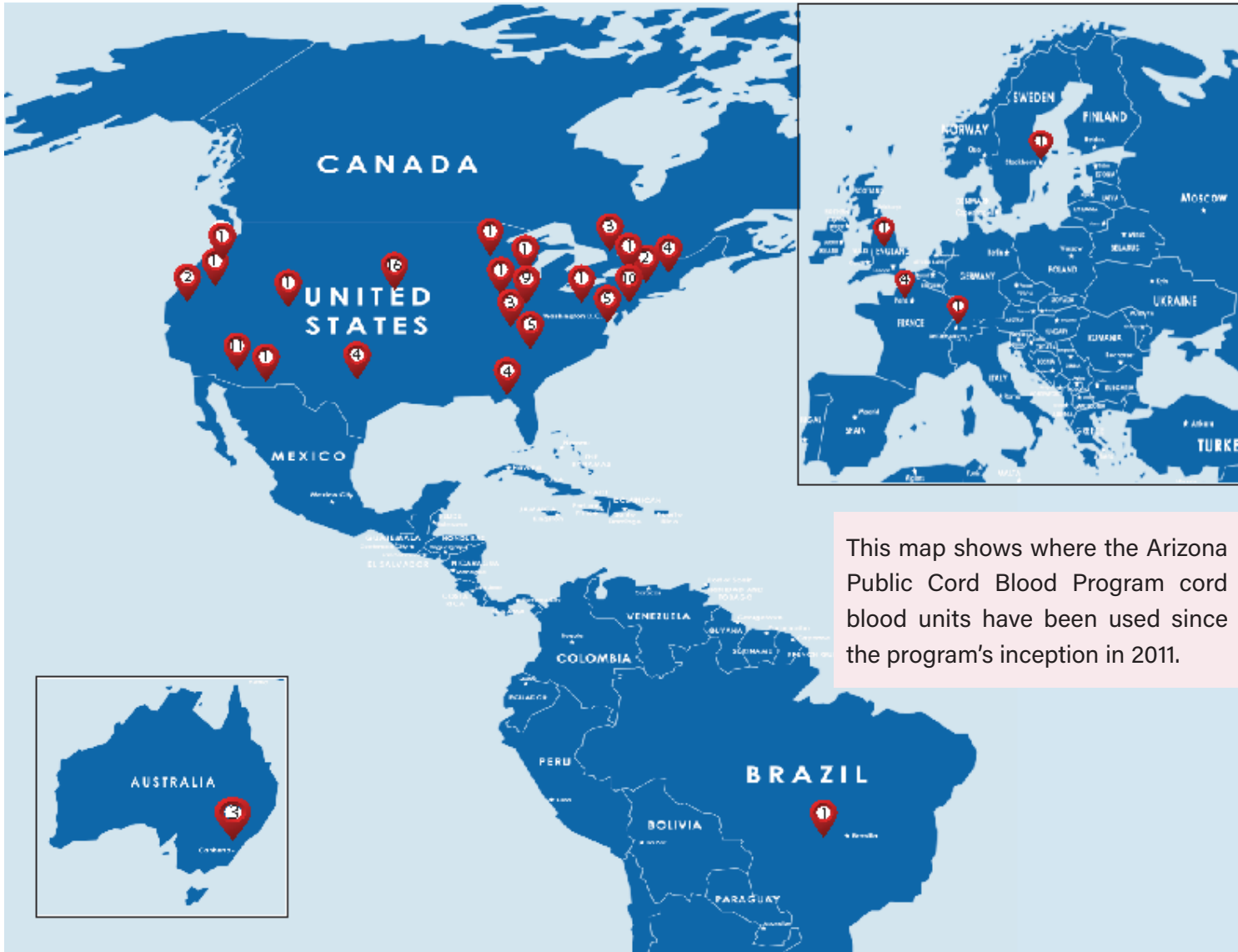
- **9th** AZ Cord Blood Conference was held both **virtually & in-person** on April 18, 2024 with **225** attendees
- **731** cord blood units were **collected** at **5** AZ hospitals
- **596** were **processed** by the cord blood bank
- **239** were **uploaded** to the national registry
- **216** were used by **researchers** with the mother's consent
- **263** ml was the **largest** cord blood unit collected
- **3** cord blood units were used in **transplants**

FY 2024 Highlights



Transplants

97 cord blood units collected by the Arizona Public Cord Blood Program have been used in transplants around the world.



High-quality, Genetically Diverse Units, were Added to the National Registries During FY 2024

Cord blood units donated to the Arizona Public Cord Blood Program, meeting requirements for banking, are listed on national and international registries. The National Marrow Donor Program (NMDP), (formerly Be the Match), is the national registry that lists bone marrow donors as well as available cord blood units. The NMDP has noted that many patients, particularly **Arizona Biomedical Research Centre**

non-white patients, have a harder time finding a suitable match. In response, the Arizona Public Cord Blood Program focuses on the effective collection of large volume, high-quality, genetically diverse units, to the registries. As of June 30, 2024, ninety-seven cord blood units were matched and used for life-saving transplants throughout the U.S. and around the world.

Education and Awareness

The level of public awareness and educational engagement increased during FY2024. The Arizona Public Cord Blood Program added two interns to assist with representing the program at various events and perform outreach to nursing schools, hospitals, and obstetricians. They visited several community college campuses to let nursing students know about umbilical cord blood donations and how stem cells contained in the cord blood is used for the treatment and research of various illnesses. The cord blood program team also provided information to nurses, expectant mothers, and medical professionals during the fiscal year, including the Arizona Perinatal Nurses Conference; Cord Blood Connect Conference; 36th Annual Nurse Practitioner Symposium; Arizona Nurses Association Conference; World Cord Blood Day; 6th Annual reimagine Health Symposium; 9th Annual ABRC-Flinn Research Conference; and 31st Annual Arizona Immunization Conference. The executive director for Save the Cord Foundation attended nearly every event with the cord blood team members.



Contracted Partners

Hospitals

- Dignity Health Chandler Regional Medical Center
- Dignity Health St. Joseph's Hospital and Medical Center
- Dignity Health Mercy Gilbert Medical Center
- Valleywise Health Medical Center
- Tucson Medical Center

Research

Mothers can elect to donate their cord blood unit to research if it doesn't qualify for banking for transplant. Cord blood used in transplant needs to meet strict criteria, such as a minimum dose of stem cells. If the unit does not meet these criteria, it may still be valuable for researchers, who can request units directly from the cord blood bank. In FY 2024, over 216 cords collected by the Arizona Public Cord Blood Program were used in research.

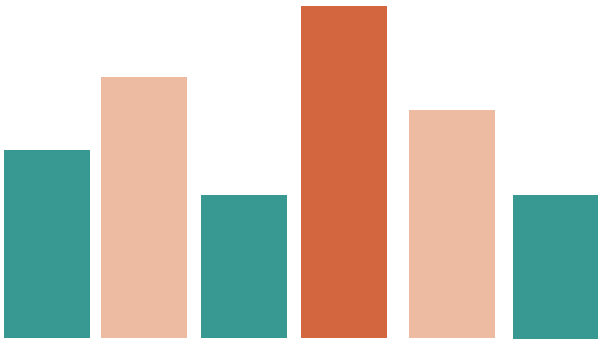


Education

- Save the Cord Foundation, Tucson

Cord Blood Bank

- MD Anderson Cancer Center, University of Texas, Houston



Collection Highlights

The Arizona Public Cord Blood Program could not accomplish its mission or goals without the dedicated efforts of its partners from around the state. The following are some of the highlights the program has experienced during FY 2024.

A special thanks goes to...

Luciana Cordeiro-Araujo, MD (Chandler Regional Medical Center), for collecting the largest cord blood unit - 263 ml; **Marta Clarke**, Cord Blood Technician.

William Chaviri, MD (St. Joseph's Hospital and Medical Center) for collecting the largest number of cord blood units - 16.

Charis Ober, Rachel Manley, Melanie Hall, (Save the Cord Foundation), **Barbara Torrey** (Gilbert Public Schools), and **Dr. Megan Capitano** (Indiana University School of Medicine), for their tireless work in developing the Cord Blood in the Classroom program.

Jeffrey Wilson, Erin Eaton, and Kristine Urrutia (MD Anderson Cord Blood Bank), for their invaluable assistance throughout the year in working with all the collectors and providing exceptional support and education to them throughout the year.

Kylee Cook, BS, CNA, ABRC Cord Blood Intern for selfless support and leadership of the interns at the University of Arizona in Tucson and for her invaluable work in preparing the Save the Cord Foundation's Cord Blood in the Classroom program for implementation.

Finally, but most importantly, **all the parents** who voluntarily gave their baby's umbilical cord blood to help save lives and support finding cures and treatments for today's diseases.

Cord Blood Units Banked by Race and Ethnicity

Race/Ethnicity	Total Banked	Percentage
American Indian / Alaskan Native	6	2.5%
Asian	1	0.4%
Black/ African American	4	1.7%
Caucasian	54	22.6%
Hispanic	123	51.5%
Multiple	51	21.3%
Undisclosed	0	0%
TOTAL	239	100%

Dignity Health, Chandler Regional Medical Center

- Largest cord blood unit collected (263 ml) by Luciana Cordeiro-Araujo, MD
- Most cord blood units collected by Mariana Amaya, MD (15)

Dignity Health, St. Joseph's Hospital and Medical Center

- Largest cord blood unit collected (345 ml) by Joana Danci, MD
- Most cord blood units collected by William Chaviria, MD (16)

Valleywise Health Medical Center

- Largest cord blood unit collected (184 ml) by Jessica Worthington, MD
- Most cord blood units collected by Jessica Worthington, MD (8)

Tucson Medical Center

- Largest cord blood unit collected (273 ml) by Lydia Wester, MD
- Most cord blood units collected by Lydia Wester, MD (13)

RESEARCH EDUCATION PROGRAM

FY 2024 Highlights

WORKSHOPS AND TRAININGS

Arizona State University

- 9th Annual Arizona Cord Blood Conference
- 2024 Arizona Business & Health Summit
- 5 Competitively Selected Events

Northern Arizona University

- Institutional models for Retaining Healthcare Workforce
- Nutritional Health Messaging
- Culturally Centered Addictions Research
- Yuma, 6th Annual Review of Community Engagement & Collective Approach to Action
- Water Rights, Access and Public Health

University of Arizona, College of Medicine, Tucson

- Clinical Trials Development Workshop V
- Research Day
- Translational Research Workshop
- Medical Scientist Training Retreat
- Friday Frontiers in Biomedical Science Series of 9 Events
- Mini Medical School: Community Education Events
- Children's Post-infectious Autoimmune Encephalopathy (CPAE) Consortium Conference



University of Arizona, College of Medicine, Phoenix

- 6th Annual Reimagine Health Research Symposium: Health and Disease over the Lifespan
- 9th Annual ABRC-Flinn Research Conference with grant awardees from the Arizona Biomedical Research Centre, Flinn Foundation, and the Valley Research Partnership
- PCM as a Tool for Clinician Communication with Patients and Peers in Healthcare Settings
- Achieving Diversity, Equity, and Inclusion in Medical Education Employing Generative Artificial Intelligence like ChatGPT
- Clinical Outcomes Evaluation and Research Workshop
- Arizona Perinatal Improvement Summit 2024: Research and Health Initiatives
- Pharmacogenomics: Propelling Practice and Proof in Populations Symposium
- APEX Bio2 Introduction to Aerospace Medicine and Surgery Course



RESEARCH GRANTS PROGRAM

FY 2024 Highlights

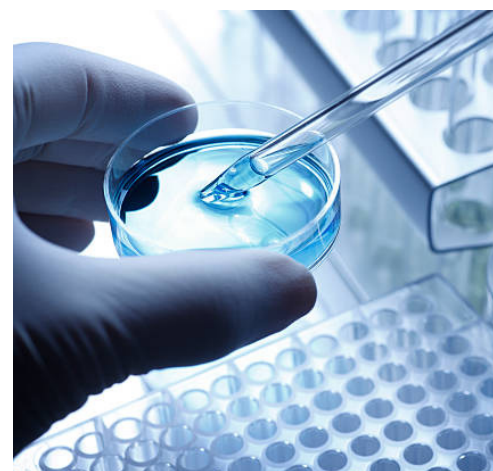
42 continued projects (which includes carry-forward funds)

- » 14 Investigator Grants (\$250,000 / year X 3 years)
- » 28 New Investigator Awards (\$75,000 / year X 3 years)

27 new projects

- » 7 Investigator Grants (\$250,000 / year X 3 years)
- » 20 New Investigator Grants (\$75,000 / year X 3 years)

11 institutions supported, including NAU, ASU, UofA Tucson, & Phoenix, Mayo Clinic, VaxSyna, AZ Veterans' Research Foundation, Banner UofA, Southwest Autism Research and Resource Center, St. Joseph's Hospital, Translation Genomics Research Institute (TGen), and Critical Path Institute



Abstracts of the funded projects are provided in Appendices A, B and C.

Overview



ABRC funding opportunities aim to accelerate promising research toward clinical testing and breakthroughs designed to improve the health of Arizonans. While ABRC's strong emphasis is on funding basic and translational research projects to generate preliminary data, ABRC continues to seek innovative projects that leverage Arizona's resources and strengthen collaboration.

The Arizona New Investigator Award (AZ NIA) helps new investigators conduct research aimed at testing basic hypotheses to generate preliminary data necessary to apply for larger funding opportunities. The Arizona Investigator Grant (AZ IG) funds more senior researchers who conduct on-going basic or translational research with a goal of seeking larger federal grant funding, moving into clinical trials/device studies, or commercializing their research.

ABRC funds research projects that are aimed at the causes, epidemiology, and diagnosis of human diseases; public health and community-based participatory research; the formulation of cures and medically accepted treatments; prevention of human diseases, including new drug discovery and development; advancing the prevention and treatment of tobacco-related disease and addiction; and/or behavioral studies and attitude assessments.

Funded Projects

2022 Cohort

Grantee	Grantee Organization	Technology and Significance
New Investigator Awards (up to \$75,000 / year for 3 years)		
Eleana O. DeFilippis	Mayo Clinic	<u>Therapeutic</u> : determine the association between liver eosinophil (EOS) and fibrosis of obese NASH patients; GLP-1RA could slow the progression of fibrosis by decreasing liver EOS activation.
Tara Furstenau	Northern Arizona University (Flagstaff)	<u>Diagnostic</u> : developing a multiplexed PCR amplicon sequencing (AmpSeq) assay which will offer fast, sensitive, and high-resolution typing at a low cost. Designing these assays can be a computational challenge that requires (1) selecting targets that will provide strain-level resolution and AMR typing and (2) designing large primer sets that will perform well.
Julianne Holloway	Arizona State University (Phoenix)	<u>Diagnostic</u> : to develop new tissue-engineered scaffolds that are capable of spatially controlling cellular behavior to regenerate the complex, heterogeneous tendon to bone interface. 1) Design a biomimetic fibrous scaffold with dual gradients in fiber alignment and mineralization, and 2) Investigate the impact of mineralization and fiber alignment gradients on a) in vitro cell behavior and b) in vivo tissue repair.
Keehoon Lee (formerly Jolene Bowers)	Translational Genomics Research Institute (Phoenix)	<u>Intervention</u> : determine spatial and temporal distribution of <i>Coccidioides</i> in ambient air in endemic areas and what factors are influencing the distribution would help us better understand risk of inhalation of fungal spores and coccidioidomycosis.
Hyunglae Lee	Arizona State University (Phoenix)	<u>Device and Prevention</u> : utilize a patent-pending robotic balance platform and an innovative robotic balance 5-week training approach that effectively identifies altered ankle mechanics following stroke and benefit the overall lower extremity function including postural balance and walking in stroke survivor.
Koenraad Van Doorslaer	University of Arizona (Tucson)	<u>Diagnostic</u> : determine the heterogeneous interactions between HPV and their host cells and if it dictates the outcome of the infection. By using single-cell transcriptomics to determine how evolutionarily related HPVs, with different oncogenic risk, interact with the individual host cell will characterize both the viral and cellular transcriptome.

Funded Projects

2022 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Faith Walker	Northern Arizona University (Flagstaff)	<u>Diagnostic</u> : develop and test an environmental screening system for less invasive detection of rabies virus (RABV) from multiple sample types, using the highly sensitive LN34 real time RT-PCR assay on samples . Develop and test a whole genome sequencing approach using tiled amplicons that will lead to a comprehensive phylogeographic analysis of RABV in Arizona.
Noel Warfel	University of Arizona (Tucson)	<u>Therapeutic</u> : determine of how hypoxia promotes lung cancer metastasis and identify the role of hypoxia and PIM in driving lung cancer progression while testing a new strategy to prevent metastasis and treat patients with metastatic disease.
Jessica Weaver	Arizona State University (Phoenix)	<u>Device</u> : design microencapsulation devices for nutrient and insulin transport and utilize computational methods to predict molecular transport within devices of varied geometry, to design an optimal device prior to fabrication. 3D printed injection molds will be used to rapidly prototype and iterate device designs in vitro. Determine device impact on primary islet cells' viability and function in vitro and in vivo.
Craig Weinkauff	University of Arizona (Tucson)	<u>Diagnostic</u> : determine the molecular mechanisms underlying the transition from stable to unstable carotid atherosclerosis resulting in stroke and identify how VCAM-1 contributes to carotid plaque instability in humans.
Justin Wilson	University of Arizona (Tucson)	<u>Therapeutic</u> : understand how inflammation impacts key tumor-promoting factors regulated by AIM2 in response to the intestinal microbiota and determine the dynamic relationship between inflammation and tumorigenesis in response to microbial recognition by AIM2 may lead to novel immune- and microbiota for improved cancer therapy.

Funded Projects

2022 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Investigator Grants (up to \$250,000 / year for 3 years)		
Charles Adler	Mayo Clinic	<u>Therapeutic</u> : determine 1) the magnitude of SMG and skin a-syn density change over time, 2) the improvement in adequate tissue acquisition doing bilateral SMG biopsies, 3) any laterality differences between SMG gland a-syn density, 4) correlate a-syn density and changes in density between SMG and skin biopsies.
Maria Altbach	University of Arizona (Tucson)	<u>Diagnostic</u> : transform the current paradigm for CAD management through a novel MRI technology combined with artificial intelligence to assess the risk of plaques to rupture based on plaque composition, hemodynamic burden, and the presence of subclinical events.
Michael Daines	University of Arizona (Tucson)	<u>Diagnostic</u> : understanding the effects of IVIG therapy or other treatments targeting inflammation and behavior on the airway and gut microbiome and the associated immune responses may open new avenues for research into the mechanisms of immunomodulatory role of these treatments in CPAE patients specifically, and in autoimmune diseases in general.
Rongguang Liang	University of Arizona (Tucson)	<u>Device and Diagnostic</u> : develop a multimodal, label-free three-photon microscope for high-resolution and deep skin imaging. Three-photon imaging will be able to achieve higher resolution over deeper imaging depths, improving sensitivity and specificity for skin lesion detection and diagnosis.
Kaushal Rege	Arizona State University (Phoenix)	<u>Therapeutic</u> : investigate the synergy of APE1 inhibitors in combination with heat shock protein 90 (HSP90) inhibitors and checkpoint inhibitor immunotherapy as free drugs and nanoparticle formulations. HSP90 and immune checkpoints, which aid melanoma cell survival and escape from immune surveillance, respectively, are clinically relevant targets.

Funded Projects

2023 Cohort

Grantee	Grantee Organization	Technology and Significance
New Investigator Awards (up to \$75,000 / year for 3 years)		
Madeline Andrews	Arizona State University (Phoenix)	<u>Therapeutic</u> : determine how metabolic state corresponds to cortical cell type specification through the characterization of e cortical cell type specification in the novel mouse transplantation model and the identification of glycolysis gene expression in cortical cells across development in multiple models. Also, determine whether changes in glycolysis affect cortical specification decisions by identifying glucose uptake and glycolysis metabolite output in living cortical progenitors & neurons and determining whether inhibiting glycolysis alters cell type specification.
Scott Beeman	Arizona State University (Phoenix)	<u>Diagnostic</u> : transform management of glioblastoma patients by developing an MRI method to measure tumoral amino acid uptake and metabolism by demonstrating the efficacy of amino acid MRI in preclinical models of GBM and optimizing amino acid MRI, that may lead to discovery of amino acid metabolic pathways that guide GBM treatment and stage GBM based on amino acid metabolism.
Erik Blackwood	University of Arizona (Phoenix)	<u>Therapeutic</u> : using hiPSC-derived cardiomyocytes and a novel mouse model of HFpEF to determine the effects of depleting endogenous ATF6, specifically in either atrial or ventricular cardiomyocytes, on cardiac structure, function, and gene expression during HFpEF, and evaluate the potential therapeutic effects of novel small molecule activators of ATF6 in mouse and hiPSC models of HFpEF.
Zhyiu Dai	University of Arizona (Phoenix)	<u>Therapeutic</u> : determine if a deficiency of YAP/TEAD signaling leads to loss of AT1 cells and deficiency of VEGF-A signaling, resulting, in impairment of endothelial repair after tobacco smoke-induced injury and COPD-PH development. This will help understand the pathogenesis of cigarette smoke-induced PH that may reveal a novel therapeutic target to treat patients with PH-COPD.

Funded Projects

2023 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Tyler Gallo	Banner Health Foundation (Phoenix)	<u>Diagnostic</u> : implement Heparin-induced thrombocytopenia (HIT)-related clinical decision support to improve timely and accurate diagnosis in patients identified to be at risk of HIT. Appropriate diagnosis of HIT can improve patient outcomes by decreasing their risk of potentially fatal thrombotic events.
Tobias Jakobi	University of Arizona (Phoenix)	<u>Therapeutic</u> : decipher critical cell to cell communication components which contribute to pathological cardiac hypertrophy and may lead to development of new ways to diagnose and treat CVD earlier for a positive impact on the health of Arizonans.
Jelena Eremija (Formerly Peter Klinger)	University of Arizona (Tucson)	<u>Diagnostic</u> : develop a focused panel of protein targets that can serve to differentiate children who suffer from PANS from those who have non-PANS OCD, autism spectrum disorder (ASD), and healthy control subjects. Ultimately the project's goal is to develop and validate a laboratory test that can verify clinically diagnosed PANS and contribute to personalized treatment through the prediction of clinical outcomes.
Won Hee Lee	University of Arizona	<u>Diagnostic</u> : using a combination of human iPSC-ECs, derived from healthy and T2D patients, a diabetic mouse model, and an endothelial-specific histone deacetylase 9 knockout mouse model, to delineate novel molecular mechanisms responsible for health risks posed by electronic cigarettes in accelerating onset and severity of obesity or diabetes.
Pawel Lanieweski	University of Arizona	<u>Therapeutic</u> : determine if Sneathia promotes pathophysiological changes in the cervix, such as chronic inflammation and epithelial barrier disruption, leading to adverse health outcomes throughout female reproductive tract, by investigating the pathogenesis of two key species of the Sneathia to contribute key insights to understanding the function and impact of these bacteria on host defense, physiology, and metabolism, revealing further research avenues and potential prophylactic and/or therapeutic strategies.

Funded Projects

2023 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Mary Pardhe	VaxSyna, Inc. (Phoenix)	<u>Therapeutic</u> : develop a low-cost HPV vaccine that is broadly protective and had a targeted two-dose schedule. Verify the vaccine formulation is nontoxic, using standard toxicology methods and a rabbit model. The successful completion of this project is critical to initiate GMP manufacturing and an IND application with the FDA.
Kristen Pogreba-Brown	University of Arizona (Tucson)	<u>Diagnostic</u> : determine the relationship between pre-existing chronic conditions and the development of PASC, impacts of PASC on the development of new chronic conditions, and the influence of PASC on the management of existing conditions, through the identification of population-level disparities (rural/urban, county, etc.) in the incidence and prevalence of PASC across Arizona and the biomedical and social risk factors for the development of PASC and factors that facilitate resilience and recovery from PASC.
Jong Seto	Arizona State University (Phoenix)	<u>Diagnostic</u> : develop new clinical methods for the measurement of fluorosis that are reliable and feasible for surveillance at the community level by testing the severity of hypomineralization to correlations of changes in tooth structure measured using nondestructive optical imaging methods to demonstrate that these imaging methods can be clinically efficient and effective in the surveillance of fluorosis on Arizona's population.
Shalini Sharma	University of Arizona (Phoenix)	<u>Therapeutic</u> : isolate a UAP56 specific RNA aptamer(s) that can be developed as a pharmacological inhibitor of splicing and test its therapeutic potential by identifying and characterizing high affinity UAP56-aptamers and determining their splicing inhibitory activity, and develop a modified UAP56-aptamer that exhibits high stability and selective cellular toxicity.
Kenan Song	Arizona State University (Phoenix)	<u>Therapeutic</u> : develop an implantable pelvic mesh using biocompatible polymers (e.g., polyvinyl alcohol (PVA), chitosan) with controlled bonding strength and tunable lifetime by leveraging 3D printing for tunable scaffold structures beneficial for cell attachment, nutrition transmission, and personalized medicine.

Funded Projects

2023 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Jennifer Stern	University of Arizona (Tucson)	<u>Therapeutic</u> : determine if the use of dietary manipulation (caloric restriction, chow control, and high fat diet), a genetic glucagon receptor knockout, and a viral-induced constitutively active or dominant negative AMPK expression, can isolate the role of liver glucagon receptors and downstream AMPK signaling lifespan and health span.
Jordon Yaron	Arizona State University (Phoenix)	<u>Therapeutic</u> : test that impaired SerpinB3 signaling would contribute to diabetic wound impairment by defining the role of SerpinB3 in diabetic wound impairment, and evaluating SerpinB3 as a wound healing therapeutic.
Wenlong Zhang	Arizona State University (Phoenix)	<u>Device Rehabilitation</u> : design novel soft robotic hip-knee exosuit and evaluate its effectiveness for stroke rehabilitation in clinical and community settings. The device would be a reliable, affordable, and autonomous robotic solution to meet the growing need of neurorehabilitation by enabling patients in both clinics and local fitness centers.
Investigator Grants (up to \$250,000 / year for 3 years)		
Deveroux Ferguson	University of Arizona (Phoenix)	<u>Therapeutic</u> : determine if cocaine addiction results from neuron specific mal-adaptations in corticolimbic circuits, and that SIRT1 epigenetic mechanisms contribute to these mal-adaptations and regulate cocaine reward in a cell and circuit-specific manner. This will be accomplished by investigating molecular and circuit mechanisms underlying cocaine addiction, including the cell-type specific role of corticolimbic circuits and their maladaptation during cocaine addiction. Also, test potential epigenetic mechanisms involving SIRT1 gene.

Funded Projects

2023 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Melissa M. Herbst-Kralovetz	University of Arizona (Phoenix)	<u>Diagnostic</u> : identify predictive biomarkers as non-invasive diagnostics to improve endometrial cancer detection and patient disease stratification to decrease morbidity and mortality associated with this cancer in women, by testing cervicovaginal metabolic profiles and local cancer biomarker levels altered in EMC relative to healthy controls and benign conditions, and demonstration that these lipidomic and proteomic profiles possess high predictive accuracy and sensitivity/specificity as novel biomarkers for early EMC diagnosis.
Pawel Kiela	University of Arizona (Tucson)	<u>Therapeutic</u> : determine if gut microbiome and metabolome in CPAE is altered prior to treatments when compared with controls and that systemic and intestinal markers of inflammation correlate with patterns in the microbiome.
Joshua LaBaer	Arizona State University (Tempe)	<u>Diagnostic</u> : develop a noninvasive blood test specifically for LSA-CRC to improve compliance with screening, reduce the burdens of an invasive annual procedure, and lead to early detection of colorectal cancer and improved survival in this high-risk population (people in their mid-twenties with Lynch Syndrome).
Raymond Migrino	Arizona Veterans Research and Education Foundation	<u>Therapeutic</u> : determine if NLGM1 could improve acute and chronic neurologic function in mice subjected to cerebral arterial occlusion and if NLGM1, in doses used for stroke, is biologically safe. A multi-institutional collaboration model will be used to further the development of a novel Arizona-formulated nanotherapeutic for translational use to favorably impact stroke outcomes.
Masmudur Rahman	Arizona State University (Tempe)	<u>Therapeutic</u> : test oncolytic virus-based immunotherapy combined with clinically approved Selinexor to enhance tumor killing by OV, resulting in enhanced anti-tumor immune responses and long-term tumor clearance. Determine if this combination therapy is effective against metastatic tumors in the lungs and immunologically "cold" tumors in patients.

Funded Projects

2023 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Christopher Smith (Formerly Richard Frye)	Southwest Autism Research & Resource Center (Formerly University of Arizona)	<u>Awareness and Prevention</u> : improve understanding of folate metabolism abnormalities, define biomarkers of folate abnormalities in mothers and children with Autism Spectrum Disorder (ASD), develop them into risk equations which can be integrated into a clinical decision support tool, and provide insight to improve the health of the mother, fetus, and child using safe folate compounds designed to bypass folate pathway abnormalities, leading to reductions in the risk of ASD, birth defects and pregnancy complications.
Ashley Stokes	St. Joseph's Hospital and Medical Center	<u>Diagnostic</u> : develop an advanced magnetic resonance imaging (MRI) method to investigate neurovascular changes associated with Alzheimer's disease. Compared to existing methods, this advanced method increases sensitivity to brain activity and informs on microvascular function. By coupling this method with functional MRI and cerebrovascular reactivity, complementary functional and vascular changes can be quantified across distinct vascular scales, from large vessels to capillaries.

Funded Projects

2024 Cohort

Grantee	Grantee Organization	Technology and Significance
New Investigator Awards (up to \$75,000 / year for 3 years)		
Casey Ager	Mayo Clinic	<u>Therapeutic:</u> develop a new approach for the treatment of multiple cancer types. The project aims to create novel TRPS1 antagonists that target Tumor-infiltrating regulatory T cells, which are known to suppress the body's antitumor immune response and orchestrate resistance to cancer immunotherapies. This research will utilize genetically engineered mouse models and CRISPR/Cas9 editing in human cells to understand how the TRPS1 transcription factor works in TI-Treg function.
Claudio Barnardazzi de Miranda Azevedo	University of Arizona	<u>Therapeutic:</u> explore the relationship between gut microbiota, postnatal gut maturation, and NHE3 (Na ⁺ /H ⁺ exchanger 3), which is a key protein involved in sodium absorption and pH regulation in the intestines. This study proposes that the interplay between gut bacteria and NHE3 is critical for the development of a healthy gut microbiome and the prevention of enteric infections in early development. The goal of the research is to investigate this complex interaction as a potential therapeutic target for improving gut health and reducing susceptibility to infections.
Rabail Chaudhry	University of Arizona (Tucson)	<u>Therapeutic:</u> investigate the pharmacodynamics of Tranexamic acid (TXA), an antifibrinolytic agent commonly used in surgery to reduce transfusion needs. This project aims to improve therapeutic outcomes by using rotational thromboelastometry and the standardized tissue plasminogen activator (TPA)-based viscoelastometric assay to determine TXA's effects on fibrinolysis in patients undergoing orthopedic, cardiac, and trauma surgery. The goal of the study is to better understand the duration of TXA's effects, which could lead to more effective dosing strategies and improved patient outcomes.
Ralph Fregosi (Formerly Lila Buls Wollman)	University of Arizona (Tucson)	<u>Therapeutic:</u> investigate the impact of nicotine withdrawal on cardiovascular and respiratory function, specifically focusing on the body's response to hypoxia. This research has significant clinical implications because it aims to understand how nicotine withdrawal, a common occurrence in hospitalized patients, may impair the body's natural, life-saving responses to hypoxia, a frequent medical complication. This understanding could lead to improved treatment strategies for hospitalized patients experiencing nicotine withdrawal.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Christopher Glembotski (Formerly Erik Blackwood)	University of Arizona (Phoenix)	<u>Therapeutic</u> : investigate the role of the serum glucocorticoid kinase 1 (SGK1) protein in cardiometabolic heart failure with preserved ejection fraction (cMet HFpEF) using a cardiac-specific SGK1 targeting mouse model to assess cardiac function and metabolism. The goal is to evaluate the therapeutic efficacy of a novel SGK1 inhibitory peptide for preserving cardiac function and systemic metabolism during cMet HFpEF.
Alexei Gonzalez-Estrada	Mayo Clinic	<u>Diagnostic</u> : establish novel drug allergy testing approaches, including a mast cell activation test as an in vitro platform and the use of sterile water as a diluent for in vivo skin tests. These new approaches aim to improve the accuracy of drug allergy testing, which is critical for identifying the causes of perioperative anaphylaxis, a life-threatening allergic reaction with high morbidity and mortality.
Nick Henscheid	Critical Path Institute	<u>Diagnostic</u> : use AI/ML model architectures to develop an advanced predictive model for Alzheimer's Disease using multi-cohort data from the Critical Path Institute's Critical Path for Alzheimer's Disease. The goal is to create a Drug Development Tool that will accurately predict clinically useful variables and be generalizable across cohorts to inform future trial designs.
Lifeng Lin	University of Arizona (Tucson)	<u>Diagnostic</u> : enhance the accuracy of treatment effect estimations in meta-analyses, a crucial aspect of comparative effectiveness research that synthesizes evidence from multiple studies to inform treatment decisions. The project will focus on developing novel methods, including deriving evidence-based informative priors for Bayesian meta-analyses and creating a user-friendly open-source software package for clinicians to implement these methods.
Chen-wei Liu	University of Arizona (Phoenix)	<u>Therapeutic</u> : use CRISPR technology to investigate the impact of e-cigarette exposure on vascular function and its potential link to atherosclerosis. The goal is to understand the effects of e-cigarettes on endothelial cells, particularly in individuals with pre-existing conditions like atherosclerosis, and to identify potential therapeutic targets for mitigating e-cigarette-related health risks.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Hamidreza Marvi	Arizona State University (Tempe)	<u>Device and Diagnostic</u> : develop a robotic system to improve the precision and accessibility of endoscopic resection for gastrointestinal neoplasms. This system will utilize an endoscopic anchoring magnet, controlled by an external robotic arm, to enhance surgical maneuverability and potentially reduce the need for colectomies in the treatment of colorectal cancer.
Heather Mead	Translational Genomics Research Institute (Phoenix)	<u>Diagnostic</u> : utilize innovative antibody analysis tools, NAPPA and PepSeq, to identify new diagnostic targets for Valley Fever. The goal is to develop a multi-target diagnostic test based on the ELISA,, a common and accessible platform used in clinical diagnostics, to improve diagnostic accuracy and reduce the significant health and economic impacts associated with delayed or misdiagnosed cases.
Sampath Rangasamy	Translational Genomics Research Institute (Phoenix)	<u>Therapeutic</u> : utilize patient-derived fibroblasts, human-induced pluripotent stem cell (hiPSC) models, and "humanized" Mtfmt mouse models to investigate the mechanisms and consequences of mitochondrial translation defects caused by MTFMT mutations. The goal is to identify potential therapeutic targets for mitochondrial disorders by elucidating the role of MTFMT in mitochondrial translation and its implications for various diseases, including Leigh syndrome, COXPD15, and neurodegenerative disorders.
Chandler Roe	Northern Arizona University	<u>Diagnostic</u> : develop a rapid, cost-effective point-of-care diagnostic for <i>Onchocerca lupi</i> , a neglected parasite that causes blindness in dogs and has been increasingly reported in humans. The project will use PepSeq technology to identify immunogenic peptides indicative of acute canine infection and develop a serological lateral flow immunoassay prototype for detecting <i>O. lupi</i> infections in dogs.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Travis Sawyer	University of Arizona (Tucson)	<u>Diagnostic</u> : advance multispectral and polarization-sensitive endoscopic technology for the early detection of gastric cancer in underserved Arizona communities, including Hispanic and Native American patients who experience higher incidence and mortality rates. The goal is to identify optimal early detection imaging biomarkers and develop a novel transnasal endoscope for accessible delivery of care, ultimately reducing gastric cancer disparities and improving management of the disease.
Shang Song	University of Arizona (Tucson)	<u>Device and Diagnostic</u> : use 3D-printing technology to create customizable conductive nerve guides to address the growing challenge of peripheral nerve injuries (PNI), particularly in Arizona's aging population. The goal is to enhance stem cell therapy and promote nerve regeneration, leading to improved functional recovery, better quality of life for individuals affected by PNI, and reduced healthcare costs.
Juliana VanderPluym	Mayo Clinic	<u>Awareness and Prevention</u> : investigate the link between social determinants of health (SDoH) and migraine/headache diagnosis and treatment among Arizona Medicaid recipients. The study will use Arizona Medicaid (AHCCCS) claims data and analyze the influence of SDoH, using Z codes, on the diagnosis and treatment of migraine. The research aims to determine if exposure to negative SDoH contributes to disparities in receiving a specific "migraine" diagnosis and guideline-recommended treatments.
Navish Wadhwa	Arizona State University (Tempe)	<u>Therapeutic</u> : explore how bacteria detect and respond to the flow of urine, a key process in the development of UTIs. Understanding this mechanism could lead to new therapeutic targets that disrupt bacterial movement and colonization of the urinary tract, potentially leading to innovative preventative strategies and improved patient outcomes.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Faith Walker	Northern Arizona University	<u>Diagnostic</u> : develop and test an environmental screening system for the detection of rabies virus (RABV) using fecal samples and a highly sensitive real time RT-PCR assay. This will allow researchers to determine the distribution and dispersal of the virus in Arizona, a state with high rates of rabies in wildlife, in anticipation of the northward movement of vampire bats.
Sui Yang	Arizona State University (Tempe)	<u>Device and Diagnostic</u> : design and develop a new class of fiber optic catheters using a metamaterials lens concept to create a high-resolution, miniaturized endoscopic optical imaging technique. This super-resolution optical endoscope, if successful, will enhance the diagnosis and treatment of cardiovascular disease, which is a leading cause of death in both the U.S. and Arizona.
Qiyun Zhu	Arizona State University (Tempe)	<u>Diagnostic</u> : revolutionize pathogen identification by developing innovative computational methods tailored for microbiome data. The project will address the challenge of false microbial identification by curating databases to match specific diagnostic goals and combining read mapping with assembly techniques. These user-friendly, open-source software tools will lead to heightened accuracy in pathogen detection.
Investigator Grants (up to \$250,000 / year for 3 years)		
Heather Bean	Arizona State University (Tempe)	<u>Diagnostic</u> : develop a rapid and non-invasive breath test to diagnose Valley Fever (VF) using volatile organic compound biomarkers. The goal is to reduce the time to diagnosis for VF and improve upon current serology testing, which is not sensitive enough to detect early VF infections. This can lead to misdiagnosis, delayed treatment with antifungal medications, and the potential misuse of antibiotics.
Carlos Caulin	University of Arizona (Tucson)	<u>Therapeutic</u> : determine if inhibiting Cdk4/6 can enhance the effectiveness of anti-PD-1 therapy in treating p53-mutated oral squamous cell carcinoma (OSCC). OSCC is a common and deadly cancer, and a large percentage of OSCC cases involve p53 mutations that make the tumors resistant to anti-PD-1 therapy. The identification of new therapeutic targets like Cdk4/6 could lead to better treatment strategies and improve outcomes for OSCC patients.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Setsuko Chambers	University of Arizona (Tucson)	<u>Diagnostic</u> : develop and validate a non-invasive blood test that uses a panel of circulating miRNA biomarkers to identify women at high risk of developing ovarian cancer. Ovarian cancer is often diagnosed late, leading to poor outcomes, and there are currently no tools to objectively assess the risk in women who have a family history of ovarian cancer but lack identifiable genetic risk factors. A readily available and accurate risk stratification tool could facilitate earlier detection and improved survival rates.
Nan-kuei Chen	University of Arizona (Tucson)	<u>Device and Diagnostic</u> : develop a non-invasive and radiation-free quantitative lung MRI technology to improve the diagnosis of lung cancer, Valley Fever, and COPD. Current imaging methods, such as X-rays and CT scans, expose patients to undesirable radiation and often lead to false positives, resulting in unnecessary and risky lung biopsies.
Zhiqiang Li	St. Joseph's Hospital and Medical Center	<u>Device and Diagnostic</u> : develop a novel MRI technique that allows for fast, high-quality diffusion MRI of the spinal cord near metals. Current MRI methods are inadequate for evaluating surgical outcomes in a timely manner in patients with cervical spondylotic myelopathy (CSM) who have metal implants, leading to delayed decision-making and increased risk of long-term disability.
Neal Woodbury and Vel Murugan (Formerly Efrem Lim)	Arizona State University (Tempe)	<u>Therapeutic</u> : evaluate the effectiveness of current RSV vaccines against circulating RSV strains in the Maricopa community by analyzing the immune response in vaccinated individuals and identifying mutations in the virus. This study will utilize sequencing and phylogenetic studies of RSV samples, RSV neutralization assays, and peptide array-based deep mutational scanning to achieve this. The findings will be used to inform the development of improved vaccines with broader protection against current and future RSV variants.

Funded Projects

2024 Cohort (Continued)

Grantee	Grantee Organization	Technology and Significance
Jason Sahl	Northern Arizona University	<u>Diagnostic</u> : develop a rapid, point-of-care diagnostic test for syphilis that uses saliva instead of blood. This new test will utilize a lateral flow immunoassay paired with nucleotide amplification to directly detect <i>Treponema pallidum</i> , the bacterium that causes syphilis. Current antibody-based tests cannot always distinguish between active and historical infection, highlighting the need for more sensitive and efficient diagnostic tools for improved public health outcomes.

Translational Genomics Research Institute (TGen)

FY 2024 Highlights

ABRC funds, through a state legislative initiative, continued support for the Translational Genomics Research Institute (TGen):

- » **\$ 2 million** from the ADHS General Fund 72 research projects.
- » TGen participated in **161 peer-reviewed research publications** and presented **32 presentations** at leading national & international conferences, supported by AZDHS funding.
- » Personnel (**0.55 FTE**)
- » Other associated costs related to Collaborative Project Support, Proteomics, Next-Generation Sequencing, Tissue Processing, Faculty Start-Up, Informatics, High-Performance Computing, and Technical Maintenance and Support as outlined in the contract agreement.
- » **7 New U. S. Patents** were issued.
- » TGen provided genomic epidemiology and outbreak analyses to the Arizona Department of Health Services, the Arizona State Laboratory, county and tribal health departments, and multiple healthcare systems. These contributions have bolstered the state's public health response and improved healthcare outcomes through cutting-edge molecular and genomics-based research.
- » At this time, the TGen North Clinical Laboratory (TNCL) is no longer offering virology testing. TNCL has assisted remaining partners with the transition to point-of-care

Overview

Translational Genomics Research Institute (TGen) is a Phoenix, Arizona-based non-profit organization dedicated to conducting groundbreaking research with life changing results. TGen is focused on helping patients with neurological disorders, cancer, and diabetes, through cutting edge translational research (the process of rapidly moving research towards patient benefit). TGen physicians and scientists work to unravel the genetic components of both common and rare complex diseases in adults and children. Working with collaborators in the scientific and medical communities literally worldwide, TGen makes a substantial contribution to help our patients through efficiency and effectiveness of the translational process." (www.tgen.org)



Marijuana Research and Clinical Trials

FY 2024 Highlights



Arizona State University

At the end of FY 2024 researchers on this project reported that 60% of the project was complete. This included submitting a paper for peer review on trends in cannabis-related hospital visits and cannabis-related risk of hospital visits for mental health problems from 2016-2021. By the end of the fiscal year, the research team had submitted three manuscripts for publication.

Northern Arizona University

At the end of FY 2024 researchers on this project reported completing 15% of the project goals. The focus of the project is to estimate the prevalence and characteristics of the use of recreational and medicinal marijuana users over time and with seasonality. The researchers contacted several entities and dispensaries to establish relationships to gain access to various purchase records.

Southwest Arizona Autism Research and Resource Center - Marijuana Clinical Trials

During FY 2024 the research team at Southwest Arizona Autism Research and Resource Center completed three of the five aims of their proposal. They prepared a manuscript on their findings from a series of focus groups investigating the use of marijuana as treatment for mental health conditions. The first component investigated changes in attitudes of key stakeholders (caregivers, adults, and healthcare professionals) from the autism community. Next, they received US Food and Drug Administration (FDA) approval for a trial medicinal product to test the safety and efficacy needed to treat anxiety in adults with autism spectrum disorder (ASD). Upon receipt of FDA approval, the researchers have applied for the necessary licenses from the Drug Enforcement Administration and for approval of the Institutional Review Board prior to commencing the clinical trial portion of the project.

Overview

Abstracts of the funded projects are provided in Appendix D.

Through two state legislative measures, the ABRC provided support from the Medical Marijuana Fund for research to evaluate the correlation of marijuana use and mental illness, including psychosis and violent behavior, and to conduct clinical trials to determine the safety and efficacy of marijuana use by humans and the impact of potential interactions with prescription, non-prescription, and illicit drugs.

- » **Marijuana Research** —Laws 2021, (55th Leg 1st Reg) Chapter 398, SB 1847, Sec. 4 ARS §36-2812 as amended), Paragraphs A., B., and F.
 - **\$250,000** of support from the Medical Marijuana Fund for 2 research projects with Arizona State University and Northern Arizona University to evaluate marijuana and psychological disorders.
- » **Marijuana Clinical Trials** — Laws 2021, Chapter 419 (55th Leg 1st Reg), HB 2298, Sec. 1.
 - **\$5,543,324** awarded to Southwestern Autism Research and Resource Center for a five-year investigation into the safety and efficacy of using a marijuana-based investigational therapeutic to treat anxiety in persons with autism spectrum disorder.

Psilocybin Research Clinical Trials

FY 2024 Highlights

- » The Arizona Biomedical Research Centre (ABRC), pursuant to a measure passed by the Arizona Legislature which allocated general funds through the Arizona Department of Health Services (ADHS), supported research on the safety, efficacy, and therapeutic potential of Psilocybin whole mushrooms, focusing on various health conditions such as anxiety, depression, PTSD, and the drug's interactions with other medications.
- » Under Laws 2023, Chapter 139, Section 6, ADHS established the Psilocybin Research Advisory Council (PRAC) to guide the award and oversight of up to \$5 million in grants for US Drug Enforcement Administration (DEA) - licensed and US Food and Drug Administration (FDA) - regulated phase 1, 2, and 3 clinical trials.
- » The PRAC was constituted by the Director of ADHS, which included: the ADHS Director's designee, an Arizona law enforcement officer, a military veteran, and a researcher with experience studying Psilocybin or other psychedelic drugs. The council position of Arizona medical physician with license to study psychedelics could not be filled as the qualifications prevented finding a match. This council vacancy, however, did not hinder the council from conducting its mandated business.
- » Upon the advisory council's recommendations, ADHS awarded \$3,724,853 in February 2024 to two grantees: The University of Arizona (\$975,739) and Scottsdale Research Institute (\$2,749,114) to conduct clinical trials.
- » At the end of FY 2024 and during the FY2025 Arizona Legislative process, the ADHS FY 2025 budget allocation was approved with language to free the funding from lapsing and extend the program through June 30, 2026. This action allows the potential award of the remaining \$1,175,147 for additional applications and awards by February 1, 2025.

Abstracts of the funded projects are provided in Appendix D.



Appendix A

2022 Cohort Research Abstracts

New Investigator Awards (NIA) | \$ 75,000 / year for 3 years

Investigator Grant (IG) Awards | \$ 250,000 / year for 3 years

*Abstracts are included as submitted by the research team



Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years

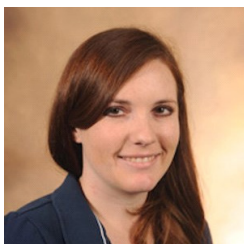


Eleanna O. DeFilippis, MD, PhD

Mayo Clinic

Project Title:
Investigating the Link Between Eosinophils and NASH Fibrosis in Human Liver

Non-Alcoholic Fatty Liver Disease (NAFLD) is the most common liver disease in the world, and 80% of affected patients are obese. In 10% of cases, NAFLD progresses to cirrhosis (NASH) and liver failure requiring transplantation. By 2030, NAFLD/NASH is expected to account for 27 million of Americans. Medical therapies are limited. NAFLD is a complex disease where the role of innate immune system in the development of liver fibrosis is emerging, but not fully understood. Based on our preliminary data, we hypothesize that the liver of obese NASH patients shows elevated numbers of eosinophil (EOS) associated with liver fibrosis; GLP-1RA could slow the progression of fibrosis by decreasing liver EOS activation. We will first evaluate whether gastric bypass surgical candidates with NASH have a greater content of liver eosinophil compared to a group of equally obese subjects with NAFLD without fibrosis. We will also correlate number of EOS in the liver with insulin sensitivity indices. Next, to test the hypothesis that drugs like GLP1-RAs decrease liver EOS-associated proinflammatory processes in the liver, we will select bariatric surgical candidates with NASH to receive Semaglutide for 16 weeks prior to surgery.



Tara Furstenau, PhD

Northern Arizona University

Project Title:
Amplicon Sequencing Panel for Strain-level Identification of MRSA and Associated Antimicrobial Resistance Determinants

Antimicrobial resistant (AMR) pathogens, particularly methicillin resistant *Staphylococcus aureus* (MRSA), have become a major public health concern. Nationally, MRSA was responsible for over 60,000 infections in 2014, and in Arizona, it is the most common cause of serious invasive infections in the state. MRSA strains can vary widely in pathogenicity so it is important to quickly diagnosis infections so that the appropriate treatment can be prescribed. Accurate molecular typing is essential for infection control and surveillance of MRSA, but unfortunately, existing molecular typing techniques are insufficient. We intend to overcome these insufficiencies by developing a multiplexed PCR amplicon sequencing (AmpSeq) assay which will offer fast, sensitive, and high-resolution typing at a low cost. Designing these assays can be a computational challenge that requires (1) selecting targets that will provide strain-level resolution and AMR typing and (2) designing large primer sets that will perform well together in a single reaction. Our AmpSeq assay will be designed for the detection and characterization of MRSA strains and their AMR determinants directly from clinical samples and we validate the performance of the panel using previously collected MRSA+ samples. Our experiences will inform the development of software that will help automate the design of future panels.

Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years



Julianne Holloway, PhD

Arizona State University

Project Title:
Engineering Dual Fiber Alignment and Mineralization Gradient Fibrous Scaffolds to Promote Rotator Cuff Repair

Rotator cuff tears are one of the most common orthopedic injuries in the United States, where current repair techniques report failure rates between 20% to 90%. A major factor contributing to failure is the rotator cuff's limited healing capacity and inadequate regeneration of the tendon to bone interfacial tissue. The use of tissue engineering-based approaches to augment rotator cuff repair is promising; however, current scaffolds do not recapitulate the complexity of the rotator cuff which transitions from highly aligned fibrous tissue (tendon) to mineralized tissue (bone). As a result, there is a clinical need to develop new tissue-engineered scaffolds that are capable of spatially controlling cellular behavior to regenerate the complex, heterogeneous tendon to bone interface. To address this need, we propose combining magnetically-assisted electrospinning with biomolecular photo conjugation to generate fibrous scaffolds with completely independent gradients in fiber alignment and mineralization. Magnetically-assisted electrospinning selectively controls fiber alignment in the presence of a magnetic field. Then, using photoreactive-based polymers, photo conjugation can be performed post-electrospinning to orthogonally and spatially tether biomolecules of interest. By combining magnetically-assisted electrospinning with photo conjugation, we will be able to manufacture fibrous scaffolds that mimic the structural and chemical gradients present in the native tendon to bone interfacial tissue. We hypothesize bioinspired fibrous scaffolds that mimic the natural complexity of the tendon to bone interface will serve as a template for regenerating mechanically functional and organized interfacial tissue.



Hyunglae Lee, PhD

Arizona State University

Project Title:
Patient-adaptive Robotic Balance Training for Lower-extremity Stroke Rehabilitation

Stroke is one of the leading and most lasting causes of long-term disabilities in Arizona. With unprecedented growth in the older population in Arizona, effective and efficient stroke rehabilitation has become important health, social, and economical issues. We propose a paradigm-shifting robotic approach to advance current practices in balance training for stroke rehabilitation. The proposed approach would not only benefit the overall lower extremity function in stroke survivors but also further lead to secondary benefits of improving the quality of daily activities and reducing relevant healthcare cost.

Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years

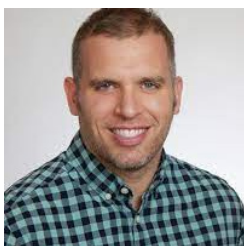


**Keehoon Lee,
PhD (Formerly
Jolene Bowers)**

The Translational
Genomics Institute

Project Title:
Cocci Watch:
Assessing the
Incidence of
Coccidioides in
Ambient Air in
Phoenix, Arizona

Arizona is a main endemic area for *Coccidioides*, and carries the majority of the burden of coccidioidomycosis, or valley fever, with thousands of new human and canine cases each year, causing significant morbidity and millions of dollars in healthcare costs. *Coccidioides* lives in the desert soils, and coccidioidomycosis is contracted by inhalation of the fungal spores, suggesting that people's risk of disease correlates with the aerosolization of the spores. The distribution of fungus in soils is sporadic and unpredictable, and the incidence of new coccidioidomycosis cases is seasonal, implying that a person's risk of contraction of valley fever depends on time and place. We propose to test for *Coccidioides* DNA with a highly sensitive assay on a set of ambient air filters already available, that were collected daily over the course of a year from multiple sites in the Phoenix metropolitan area, which will allow us to map the incidence of airborne fungal spores in space and time. We will also map the incidence of valley fever cases as well as storm events to understand the influences of and on *Coccidioides* in ambient air. Understanding the spatial and temporal distribution of *Coccidioides* in ambient air in endemic areas and what factors are influencing the distribution would help us better understand risk of inhalation of fungal spores and coccidioidomycosis.



**Koenraad Van
Doorslaer, PhD**

University of
Arizona

Project Title:
Comparative
Genomic Insights
into Papillomavirus
Evolution and
Oncogenicity
Determinants

Despite causing ~5% of human cancers, only a small subset of human papillomaviruses (HPVs) are oncogenic. While a dozen HPVs are classified as carcinogenic, the oncogenic potential varies across a broad spectrum; the actual virus ("type"-) specific cancer risk varies by an order of magnitude. Importantly, the molecular basis for these differences is not understood. Understanding host-pathogen interactions requires an understanding of the viral lifecycle; thus, our experiments are performed under conditions that closely mimic a natural infection. Interactions between HPV and their host cells are highly heterogeneous. It is likely that this heterogeneity dictates the outcome of the infection. We will use single-cell transcriptomics to determine how evolutionarily related HPVs, with different oncogenic risk, interact with the individual host cell. We will characterize both the viral and cellular transcriptome. The strength of the proposed work lies in the combination of evolutionary data with the analysis of viral-host interactions at the individual cell level. The pathways differentially affected by oncogenic viruses represent potential targets for therapeutic intervention. The results obtained will serve as preliminary data for federal and foundation awards. Finally, data obtained in this study will be shared widely by publication in several journals.

Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years



Faith Walker, PhD

Northern Arizona
University

Project Title:

Rabies Virus
Surveillance Using
Non-traditional
Sample Types
Collected from the
Human-Wildlife
Interface

Rabies is a zoonotic disease of the central nervous system that invariably results in mortality. In Arizona suburban outbreaks of the disease occur regularly in wildlife populations, and interactions between wildlife and residents results in exposures every year. Despite the proximity and serious nature of this virus, it is not possible to systematically screen the environment for the disease or track its movements. We propose to take advantage of two new genetic approaches to address these weaknesses. First, we will develop and test an environmental screening system for less invasive detection of rabies virus (RABV) from multiple sample types, using the highly sensitive LN34 real time RT-PCR assay on samples that are readily collected in the field. Second, we will develop and test a whole genome sequencing approach using tiled amplicons that will lead to a comprehensive phylogeographic analysis of RABV in Arizona and an understanding of strain movements, hot spots, and important ecosystems for sylvatic transmission. We have RABV positive samples, a large repository of multiple sample types from bats, an established study site in a human-wildlife interface zone, two state-of-the-art genetics facilities, and a team at the interface of wildlife biology, genetics, infectious disease, and public health, all of which points to the success of this project. Our findings will serve as proof-of-concept systems for surveillance and tracking of RABV in Arizona and elsewhere, and will be disseminated to our network of One Health partners.



Noel Warfel, PhD

University of
Arizona

Project Title:

PIM Kinases Alter
Mitochondrial
Dynamics and
Response to
Therapy in Lung
Cancer

The physical state of the mitochondria is emerging as a key factor mediating therapeutic resistance in cancer. Mitochondria constantly undergo fusion (elongation) and fission (fragmentation) processes. Fission is important for cell death, whereas fusion promotes survival. Drp1 is required for mitochondrial fragmentation. As a result, loss of Drp1 in cancer cells increases fused mitochondria and resistance to therapy. Clinical studies indicate that Drp1 levels are decreased in lung cancer and loss of Drp1 is correlated with worse patient prognosis. However, we do not understand how Drp1 is controlled in cancer, and there are no approved drugs that promote mitochondrial fragmentation to improve the response to chemotherapy. Here, we identify that the pro-survival protein, PIM, is increased in lung cancer and suppresses Drp1. Inhibition of PIM increased Drp1 and mitochondrial fragmentation, which can sensitize cancer cells to chemotherapy. Thus, inhibiting PIM represents the first clinically actionable target to increase Drp1 activity and promote mitochondrial fragmentation. The proposed research will determine how PIM controls Drp1 and evaluate PIM inhibitors in combination with chemotherapy in lung cancer. Because we are combining FDA-approved therapies and PIM inhibitors that have been tested in humans, our therapeutic strategy could make an immediate impact on patient care.

Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years



**Jessica Weaver,
PhD**

Arizona State
University

Project Title:
Hydrogel
Macro device
to Deliver and
Immunoselected
Insulin-producing
Cells for the
Treatment of
Insulin-dependent
Diabetes

10.8% of Arizonans have been diagnosed with diabetes; of these patients more than 27% will require insulin to manage their disease. Clinical islet transplantation, a cell therapy-based treatment for insulin-dependent diabetic patients, would eliminate the pain and cost burden of daily insulin injections, as well as the risk of long-term secondary complications, by restoring native insulin signaling. While clinical successes have demonstrated the feasibility of achieving insulin independence via this therapy, the necessity of long-term immunosuppressive drugs limits the widespread applicability of this procedure. As a result, researchers have investigated devices to isolate transplanted cells from the recipient immune system, including macroencapsulation devices which prioritize whole graft containment, retrievability, and safety. To date, these devices have demonstrated limited pre-clinical and clinical efficacy due to islet malfunction from poor oxygen and insulin transport within the device. Therefore, there is a critical need to rationally design macroencapsulation devices for nutrient and insulin transport. Through this proposed work, we will use computational methods to predict molecular transport within devices of varied geometry, to design an optimal device prior to fabrication. To test devices, 3D printed injection molds will be used to rapidly prototype and iterate device designs in vitro; a hydrogel material library for the macroencapsulation device will concurrently be evaluated. Finally, we will evaluate device impact on primary islet cells' viability and function in vitro and in vivo.



**Craig Weinkauf,
PhD**

University of
Arizona

Project Title:
Immune
Mechanisms of
Carotid Plaque
Instability

Unstable carotid atherosclerosis is a major cause of stroke, which is the leading cause of death and disability in the United States. Over 80,000 people in Arizona have a stroke per year. In addition, Native Americans suffer from the highest rate of premature deaths as a result of all forms of cardiovascular disease and the incidence of mortality from stroke is higher in Hispanics than any other ethnic group. Current treatment of carotid atherosclerosis fails to prevent many strokes, yet equally as important, also results in 20 patients treated by surgery to prevent only 1 stroke. This demonstrates our poor understanding of plaque instability and our inadequate patient risk assessment. Our objective is to understand the molecular mechanisms underlying the transition from stable to unstable carotid atherosclerosis resulting in stroke. Our exciting preliminary data indicate that of several promising candidate molecules/pathways, only endothelial Vascular Cell Adhesion Molecule-1 (VCAM-1), an inflammatory receptor important for macrophage and lymphocyte adhesion and migration into tissues, is associated with unstable plaque in humans. This proposal assembles an exceptional team of mentors/collaborators with diverse expertise in vascular surgery, advanced in vivo microscopy, immunology and atherosclerosis biology to understand how VCAM-1 contributes to carotid plaque instability.

Appendix A: 2022 Cohort Research New Investigator

\$75,000 per year for three years



**Justin Wilson,
PhD**

University of
Arizona

Project Title:
Regulation
of Intestinal
Inflammation and
Cancer Signaling
by Innate Immune
Sensors

Colon cancer development is associated with the loss of tumor suppressors, which normally prevent cancer cell growth and spread. Inflammation is tightly linked to colon cancer development through not fully understood mechanisms. The tumor suppressor protein "Absent in Melanoma 2" (or AIM2) is reduced or missing in 67% of colon tumors. AIM2 has at least 3 known functions making it an ideal target for cancer therapy: 1) AIM2 prevents tumor development by limiting excessive cellular growth; 2) AIM2 functions as an intracellular receptor for microbial double-stranded DNA, leading to regulation of inflammatory cytokines; and 3) AIM2 shapes the composition of the trillions of bacteria residing within the colon, collectively referred to as the microbiota. This proposal will assess how inflammation impacts key tumor-promoting factors regulated by AIM2 in response to the intestinal microbiota. The central hypothesis of this proposal is that recognition of intestinal microbiota-derived components (e.g., DNA) by AIM2 restricts inflammation-induced cell signaling in macrophages and intestinal epithelial cells, which leads to tumor suppression. A better understand of the dynamic relationship between inflammation and tumorigenesis in response to microbial recognition by AIM2 may lead to novel immune- and microbiota-targeting strategies for improved cancer therapy.

Appendix A: 2022 Cohort Research Investigator Grants

\$250,000 per year for three years



**Charles Adler,
MD, PhD**

Mayo Clinic

Project Title:
Submandibular
Gland Needle
Core Biopsy as a
Tissue Biomarker,
the Diagnosis
of Parkinson's
Disease and
the Monitoring
of Disease
Progression

Background: We will build on our translational research studying peripheral alpha-synuclein (a-syn) in the submandibular gland (SMG) of patients with Parkinson's disease (PD) and extend the work to REM sleep behavior disorder (RBD), a prodromal stage of PD. SMG and brain a-syn density correlate but it is unknown if density increases over time. **Research Problem:** Determine 1) the magnitude of SMG a-syn density change over time, 2) the improvement in adequate tissue acquisition doing bilateral biopsies, and 3) any laterality differences between glands. **Methods:** Perform bilateral SMG needle core biopsies on 30 clinically diagnosed PD and 10 clinically probable RBD. All will have clinical examinations and bilateral SMG biopsies performed at Mayo Clinic Arizona with tissue sent to Banner Sun Health Research Institute for histological staining and evaluation. All subjects will have a second assessment and biopsy 2 years later. **Projected Outcomes:** We expect to find an increase in a-syn density over time, improved adequate tissue acquisition, and similar left-right a-syn density. **Project Impact:** If SMG a-syn density increases over time this could serve as a tissue biomarker for clinical studies that target a-syn aggregation. We would have powerful preliminary data for planning trials of PD disease-modifying agents and will seek funding and industry partners for these trials in Arizona.



**Maria I Altbach,
PhD**

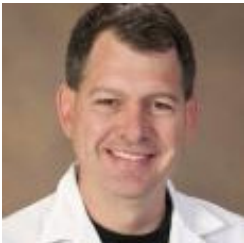
University of
Arizona

Project Title:
Development of
MRI Biomarkers
for Improved
Risk Stratification
of Patients
with Carotid
Atherosclerosis to
Prevent Stroke

Cardiovascular disease and stroke are among the most widespread and costly health problems facing Arizona. Stroke has a cost of \$33 billion/year and is a major cause of death and disability. Stroke disproportionately affects adults 65 and older and the underserved populations in our state. According to the Arizona Health Improvement Plan, reducing stroke is one of our state's priorities. Carotid atherosclerotic disease (CAD) is responsible for 20% of strokes but these events are preventable through surgical intervention. However, with the current paradigm for surgical management of CAD, strokes are being missed because surgical decision is solely based on degree of carotid artery stenosis not on plaque biology. The goal of this project is to transform the current paradigm for CAD management through a novel MRI technology combined with artificial intelligence to assess the risk of plaques to rupture based on plaque composition, hemodynamic burden, and the presence of subclinical events. Our project gathers scientists from academia and industry partnering with a network of vascular surgeons in Southern Arizona with the goal of deploying a technology to assess the likelihood of stroke in our population and the need for surgical intervention. Our state will also benefit from intellectual property originated from the new technology.

Appendix A: 2022 Cohort Research Investigator Grants

\$250,000 per year for three years



**Michael Daines,
MD**

University of
Arizona

Project Title:
Impact of IVIG
Therapy and
Upper Airway
Microbiome and
the Associated
Immune Response
in Children's
Post-infectious
Autoimmune
Encephalopathy
(CPAE)

Childhood post-infectious autoimmune encephalopathies (CPAE) are diseases that impact mood, movement, and behavior in children and are being treated in the CPAE Center of Excellence at the University of Arizona. One treatment for these conditions is intravenous immunoglobulin, or IVIG, which impacts immunity and inflammation. Understanding mechanisms behind the effects of IVIG therapy on the airway and gut microbiome and the associated immune responses may open new avenues for research into the mechanisms of immunomodulatory role of IVIG in CPAE patients specifically, and in autoimmune diseases in general. This research proposal addresses these questions in 3 aims, (1) to examine dysbiosis and dysregulation in the nasal, oral, and fecal microbiome using next generation sequencing (16S profiling and metagenomics), with particular focus on IgG-coated population of gut bacteria; (2) to examine adaptive immune responses, including pathogenic Th17 response implicated in the breakdown of the blood-brain barrier and infiltration of the relevant areas of the central nervous system by the immune cells and autoantibodies; (3) 2 pilot studies aimed to correlate IVIG-driven changes in microbiome and clinical response and a translational study to reconstitute germ-free mice with elements of the microbiome from children impacted by CPAE before and after they have been treated with IVIG.



**Rongguang
Liang, PhD**

University of
Arizona

Project Title:
Multimodal
Three-Photon
Microscope for
Detection and
Diagnosis of Skin
Lesions

Skin cancer is the most common cancer type in the United States. Arizona has among the highest skin cancer rates in the U.S., early and accurate detection of skin cancer will particularly benefit the health and wellness of Arizonans by reducing morbidity and costs associated with unnecessary biopsies, while maximizing early intervention and decreasing mortality. The goal of this project is to develop a non-invasive imaging technique that can significantly enhance current capabilities to aid in the early detection of skin cancer without surgical biopsy, which will increase early intervention and decreasing mortality. The objective is to develop a multimodal, label-free three-photon microscope for high-resolution and deep skin imaging. We hypothesize that three-photon imaging will be able to achieve higher resolution over deeper imaging depths, improving sensitivity and specificity for skin lesion detection and diagnosis. The multidisciplinary team will develop a mode-locked all-fiber tunable fs laser, build and characterize a multimodal three-photon microscope with adaptive optics and widefield polarized dermo scope, and evaluate

Appendix A: 2022 Cohort Research Investigator Grants

\$250,000 per year for three years

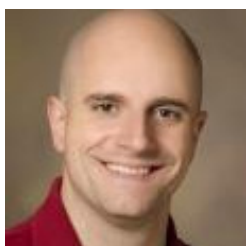


**Kaushal Rege,
PhD**

Arizona State
University

Project Title:
APE1 Inhibition
Combinational
Therapy for
Advanced
Melanoma

Melanoma is diagnosed in five new patients every day in Arizona and results in more than two deaths per week. Sun exposure in AZ drives incidence and a large fraction of children is diagnosed with late-stage disease; the 5-year survival for late-stage melanoma is less than 15% (AZ Melanoma Profile 2017). Several patients undergo relapse, have poor prognosis due to lack of effective treatments, and many do not respond to immunotherapy. Our proposed research will attack the key survival pathways in advanced melanoma cells using combination treatments that target APE1, a master regulator of DNA repair and redox response that promote melanoma cell survival. We will investigate the synergy of APE1 inhibitors in combination with heat shock protein 90 (HSP90) inhibitors and checkpoint inhibitor immunotherapy as free drugs and nanoparticle formulations. HSP90 and immune checkpoints, which aid melanoma cell survival and escape from immune surveillance, respectively, are clinically relevant targets. Mechanistic and in vivo studies will be carried out for tumor recession and survival using APE1-HSP90 inhibitor and APE1-immune checkpoint inhibitor combination treatments. This pre-clinical study will set the stage for melanoma clinical trials in AZ and develop new technologies and treatments. We will initiate a Cancer Technologies Symposium and disseminate melanoma awareness in AZ schools.



**John Streicher,
PhD**

University of
Arizona

Project Title:
Development of a
Selective Mu-Delta
Opioid Receptor
Heterodimer
Antagonist for
Enhancing Opioid
Analgesia while
Reducing Side
Effects

Opioid addiction and overdose is a serious problem for Arizonans, which has increased by 74% since 2012. The mu-delta opioid receptor heterodimer (MDOR) may act to decrease opioid analgesia and increase side effects like addiction, but is difficult to target. We designed a first-in-class bivalent MDOR antagonist (D24M), with >89 fold selectivity and <1 nM potency for the MDOR. We further found that D24M increased oxycodone analgesia in acute and chronic pain by ~50-600%, while strongly decreasing morphine withdrawal. However, D24M does not cross the blood-brain barrier (BBB), decreasing its therapeutic potential. In this proposal, we aim to improve the selectivity, stability, and BBB penetration of our MDOR antagonists, developing them as potential therapeutics to improve the health of Arizonans by increasing opioid efficacy while decreasing side effects. We will do this by 1) optimizing pharmacophore affinity and linker rigidity to generate compounds with >500 fold MDOR selectivity; 2) creating glycosylated and Nano formulated versions of our antagonists for intranasal administration to improve their delivery to the brain; and 3) testing our formulated MDOR antagonists in mouse models of acute and chronic pain, withdrawal, tolerance, and reward/addiction liability to demonstrate that our compounds improve opioid analgesic efficacy while decreasing side effects.

Appendix B

2023 Cohort Research Abstracts

New Investigator Awards (NIA)		\$ 75,000 / year for 3 years
Investigator Grant (IG) Awards		\$ 250,000 / year for 3 years
*Abstracts are included as submitted by the research team		



Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



Madeline G. Andrews, PhD

Arizona State University

Project Title:
Metabolic Regulation of Human Cortical Development

This study will initiate novel exploration into the role of metabolism in human cortical development and implications for neurodevelopmental disorders. Appropriate fate specification and metabolic function are vital for typical neural development, where impairments in these programs during neurogenesis contribute to disorders, like Autism. In preliminary studies, we identified increased glycolytic stress and impaired cell type-defining gene expression programs in current in vitro model systems of human development when compared to primary cells. I hypothesize that increased use of glycolytic programs for cellular energy impairs cortical cell type specification. Through my ABRC studies, I aim to determine how glycolysis influences human cortical progenitor and neuronal fate, which requires innovation of new technical approaches due to current human cell culture limitations. First, I will develop a novel rodent transplantation method to study more endogenous-like human cellular development to characterize the metabolic state of cortical cell types. Second, I will apply bioenergetic approaches to measure the metabolic state of living cortical cell types before directly perturbing glycolysis to determine the impact on cell identity. Together, these studies will provide fundamental insight into the role of metabolism in normal and atypical human cortical development.



Scott Beeman, PhD

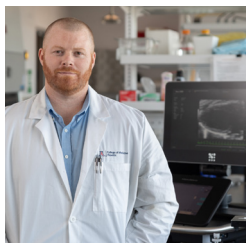
Arizona State University

Project Title:
Mapping Amino Acid Uptake and Metabolism in GBM Using ²H MRI

Glioblastoma (GBM) brain tumors rank among the most lethal of all human cancers. GBM treatment relies on contrast-enhanced (CE) MRI to identify tumor-associated blood brain barrier (BBB) disruption; however, infiltrating tumor extend beyond the boundaries of BBB disruption, leaving the tumor periphery invisible on CE-MRI. This leads to under-treatment and greater incidence of recurrence. GBM cells up-regulate amino acid (AA) transporter expression and can thus be detected with positron emission tomography (PET) based on their high uptake of radio-labelled amino acids. However, AA-PET has two major drawbacks: First, it does not resolve AA metabolism; however, abnormal AA metabolism is a critical biomarker of GBM malignancy. Second, the vast majority of GBM patients in the US do not undergo AA-PET; access to AA-PET is severely limited by geographic location, cost, and FDA approval. A method to map AA uptake and metabolism in GBM that has the accessibility of CE-MRI would be a significant advance. Recent work shows that, by replacing hydrogen with deuterium on glucose, one can quantify its uptake and metabolism with deuterium (²H) MRI. Similarly, we hypothesize that the uptake and metabolism of deuterated AAs in GBM can be measured with ²H MRI. Here, we aim to: (i) demonstrate efficacy of ²H AA-MRI in patient-derived xenograft models of GBM and (ii) optimize ²H AA-MRI.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years

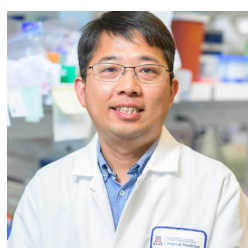


Erik Blackwood, PhD

University of Arizona

Project Title:
Molecular Roles for ATF6 and the Unfolded Protein Response in Pathogenesis of Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction (HFpEF) is associated with high morbidity and mortality with a 5-year survival after hospitalization worse than most cancers of ~35%, and, currently, there are no evidence-based therapies for HFpEF. HFpEF is associated with perturbations in protein folding that occur during pathological cardiac remodeling causing the accumulation of cytotoxic misfolded proteins. I have recently discovered that in various models of HF, a primary adaptive responder, ATF6 induces an adaptive gene profile and I recently identified and characterized a novel small molecule activator of ATF6 that enhances cellular proteostasis in the heart. In this proposal, I will focus on ATF6 in HFpEF, with the hypothesis that the accumulation of cytotoxic misfolded proteins in HFpEF triggers activation of ATF6, which is required for mitigating proteotoxicity in atrial and ventricular cardiomyocytes. I will address this hypothesis using hiPSC-derived cardiomyocytes and a novel mouse model of HFpEF in two specific aims, which are to: (1) Determine the effects of depleting endogenous ATF6, specifically in either atrial or ventricular cardiomyocytes, on cardiac structure, function, and gene expression during HFpEF, and (2) evaluate the potential therapeutic effects of novel small molecule activators of ATF6 in mouse and hiPSC models of HFpEF.



Zhiyu Dai PhD

University of Arizona

Project Title:
Role of Alveolar Epithelium and Endothelium Interaction in Tobacco Smoke-induced Pulmonary Hypertension

Chronic Obstructive Lung Disease (COPD) is a major health problem in Arizona and is the third leading cause of death in our state. An estimated 30% -70% of patients with COPD also have pulmonary hypertension (PH), called PH-COPD. The survival of PH-COPD is worse compared to PH or COPD. 3-years survival for COPD-PH patients is around 33%. Understanding the pathogenesis of tobacco smoke-induced PH-COPD will lead to novel therapeutic approach. Cigarette smoke increases apoptosis of alveolar type 1 epithelial cells (AT1) and is involved in the pathogenesis of COPD. To date, no studies have evaluated the AT1 cells in PH and PH-COPD. We hypothesize that deficiency of YAP/TEAD signaling leads to loss of AT1 cells and deficiency of VEGF-A signaling, which results in impairment of endothelial repair after tobacco smoke-induced injury and COPD-PH development. Our proposed studies will have a significant impact on understanding the pathogenesis of cigarette smoke-induced PH. This study may reveal a novel therapeutic target to treat patients with PH-COPD.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



**Tyler Gallo,
PharmD**

University of
Arizona

Project Title:
Heparin-induced
Thrombocytopenia
Clinical Decision
Support
Development and
Implementation

Heparin-induced thrombocytopenia (HIT) is a life-threatening immune reaction to heparin products. More than 30% of hospitalized patients receive heparin products and are potentially at risk of HIT, but diagnosis of HIT can be challenging due to non-specific clinical factors and the limited experience most clinicians have with the disorder. Clinical decision support (CDS) for HIT that includes the HIT-computerized risk (HIT-CR) score could potentially improve clinician recognition and management of HIT to improve patient outcomes. The objective of this project is to implement HIT-related CDS to improve timely and accurate diagnosis in patients identified to be at risk of HIT. Appropriate diagnosis of HIT can improve patient outcomes by decreasing their risk of potentially fatal thrombotic events. The goals of this project will be met by pursuing these specific aims: Aim 1: Implement CDS based on the HIT-CR score to help identify HIT in a major health system that encompasses urban and rural inpatient facilities including critical access hospitals. Aim 2: Evaluate the impact of a CDS advisory for HIT including changes in ordering diagnostic testing for HIT and clinical outcomes of patients. Aim 3: Procure other support to create and deliver an educational program on HIT to inform clinicians of the CDS implementation and serve as an educational resource available to all clinicians.



**Tobias Jakobi,
PhD**

University of
Arizona

Project Title: The
RNA Secretome of
the Heart

Cardiovascular disease (CVD), the leading cause of death in Arizona, accounts for over 12,000 deaths per year. This New Investigator Award proposal aims to decipher a critical cell-cell communication component contributing to pathological cardiac hypertrophy. Paracrine cell-cell communication in the heart is important for maintaining robust cardiac function, and maladaptive changes in the repertoire of secreted communicator substances, such as RNAs, can contribute to cardiac dysfunction and pathology. Some RNAs are exported from cells in specialized extracellular vesicles (EV). However, most published studies focus on micro RNAs isolated from biofluids rather than from tissues, the latter of which have been shown to contribute adaptively and maladaptively to cardiac structure and function. While EV-mediated secretion of microRNAs has been characterized, the majority of EV RNAs secreted from cardiac myocytes remains largely uncharacterized. This comprises a major limitation in our understanding of the functional importance of such EV RNAs in CVD, such as cardiomyopathies, a precipitating component of which is pathological cardiac myocyte hypertrophic growth, as data on other RNAs in EVs are not readily available. The knowledge obtained in this study will lead to developing new ways to diagnose and treat CVD earlier, which will have a positive impact on the health of Arizonans.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years

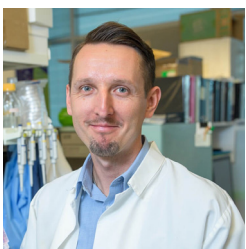


**Jelena Eremija,
PhD (Formerly
Peter Klinger,
MD)**

University of
Arizona

Project Title:
Development of
novel serological
diagnostic tool
for Children's
Post-infectious
Autoimmune
Encephalopathy
(CPAE)

Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS) and Pediatric acute-onset neuropsychiatric syndrome (PANS) and are childhood disorders that involve a sudden onset of obsessive-compulsive disorder (OCD) and neuropsychiatric symptoms. Despite the need for a biomarker to inform diagnosis and guide personalized treatment, PANDAS and PANS are clinical diagnoses which lack a biomarker. The only available biomarker for a disorder with overlapping symptoms, Sydenham Chorea (SC), is a test of 4 neuronal antibodies. This set of biomarkers, however, cannot differentiate PANDAS and PANS from SC or healthy controls. Our project utilizes an unbiased, Nucleic Acid-Programmable Protein Array (NAPPA) of >17,000 full length human proteins. Collaborating with the ASU Biodesign Institute, bio banked blood samples from children with PANS criteria will be analyzed for binding of circulating antibodies to determine candidate autoantigens. Subsequently, a customized array of 1200 candidate autoantigens will be used to screen for differential antibody binding in PANS cases compared to those with OCD, ASD, and neurotypical controls. This innovative translational project aims to develop the foundation for a diagnostic serological test for PANS, containing an array of approximately 50 target proteins that will be used to verify PANS with high specificity.



**Pawel Laniewski,
PhD**

University of
Arizona

Project Title:
Investigating
Sneathia Species
as Drivers of
Gynecologic and
Reproductive
Disorders Using
3D Models of the
Human Cervix

Sneathia is an emerging pathogen of the female reproductive tract linked to adverse gynecologic, obstetric, and reproductive outcomes, including preterm birth, miscarriage, intra-amniotic and postpartum infections, chronic pelvic pain and increased risk of HPV infection and cervical cancer. Intriguingly, in Arizona, Latinas more often carry these bacteria in their genital tract. Although, these common microorganisms are strongly associated with serious conditions with a significant impact on public health, the host defense mechanisms to Sneathia infection are still poorly understood. We hypothesize that Sneathia promotes pathophysiological changes in the cervix, such as chronic inflammation and epithelial barrier disruption, consequently leading to adverse health outcomes throughout female reproductive tract. In the proposed project we will utilize our well-characterized bioreactor-derived three-dimensional model of the human cervical epithelium to investigate the pathogenesis of two key species belonging to the Sneathia genus (*S. amnii*/ *vaginalis* and *S. sanguinegens*). The proposed studies will contribute key insights to understanding the function and impact of these bacteria on host defense, physiology, and metabolism, revealing further research avenues and potential prophylactic and/or therapeutic strategies that may enhance women's health outcomes in Arizona.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



**Won Hee Lee,
PhD**

University of
Arizona

Project Title:
E-Cigarette-
Induced
Epigenetic
Reprogramming
leading to
Endothelial
Dysfunction in
Diabetes

Considering one-third of young adults are at risk of developing diabetes and are among one of the age groups most likely to be using e-cigarettes (e-cigs), it is unknown whether e-cig use represents an independent risk factor in promoting the development and worsening of obesity and its associated vascular diseases. New data from our lab raise additional health concerns demonstrating that (i) e-cig induces vascular toxicity and dysfunction; (ii) e-cig worsens the detrimental phenotype of induced pluripotent stem cell-derived endothelial cells (iPSC-ECs) from type II diabetes (T2D) patients; and (iii) endothelial dysfunction caused by e-cig is associated with increased endothelial-to-mesenchymal transition (EndMT), a form of endothelial dysfunction contributing to the pathogenesis of many diseases including diabetes and cardiovascular diseases. However, neither the molecular cues regulating End MT signaling nor the functional significance of this pathway is established in the onset of obesity or diabetes following e-cig exposure. Using a combination of human iPSC-ECs derived from healthy and T2D patients, a diabetic mouse model, and an endothelial-specific histone deacetylase 9 knockout mouse model, this research proposal aims to delineate novel molecular mechanisms responsible for health risks posed by e-cigs in terms of accelerating the onset and severity of obesity/diabetes.



**Mary Pardhe,
PhD**

VaxSyna, Inc.

Project Title:
Developing
a Broadly
Protective Human
Papillomavirus
Vaccine and
Vaccine Platform

Human papillomavirus (HPV), the most common sexually transmitted disease, is responsible for 4.5% of all new cancer cases worldwide. The most broadly protective vaccine on the market and the only HPV vaccine offered in the US, Merck's Gardasil-9, only protects against nine HPV strains, is costly to manufacture, and requires 2-3 doses. VaxSyna is developing an HPV vaccine that is low-cost, more broadly protective, and has a targeted two-dose schedule. Our vaccine candidate displays the highly conserved HPV L2 antigen on our patented platform that uses virus like particles (VLP) and recombinant immune complexes (RIC). The L2 antigen protects against up to 22 types of HPV in mice and rabbits and has been evaluated in human phase I trials. Our vaccine is produced using an optimized plant expression system with a manufacturing cost estimated at less than \$0.5/dose. Preclinical mouse studies show our vaccine produces high antibody titers and viral neutralization in two doses, without adjuvant. The goal of this project is to verify our vaccine formulation is nontoxic, using standard toxicology methods and a rabbit model. The successful completion of this project is critical to initiate GMP manufacturing and an IND application with the FDA. Upon approval of VaxSyna's HPV vaccine, our advantages of low costs and broad protection will permit us to prevent HPV-caused cancers equitably.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



Kristen Pogreba-Brown, PhD, MPH

University of Arizona

Project Title:
Post-Acute
Sequelae of SARS-
CoV-2 infection

Arizona has been profoundly impacted by the COVID-19 pandemic, recording more than two million cases. An estimated 30% of those infected, across the severity spectrum, develop post-acute sequelae of SARS-CoV-2 (PASC), or "long-COVID". The impacts of PASC can lead to increased healthcare costs, exacerbation of chronic conditions, and an increase in disability claims and unemployment. The Arizona CoVHORT is uniquely positioned to answer a multitude of PASC-related questions with over 8,000 participants followed prospectively since May 2020. The current and future burden to the healthcare system is still unknown, but likely to be profound. Three critical next steps to reduce disease burdens include: identifying risk factors leading to PASC, determining populations at highest risk, and enhancing resilience to PASC thereby improving a patient's ability to recover.

CoVHORT has already served as a model cohort for several important ancillary studies launching in the future. We are well-suited to utilize data already collected, in order to engage collaborating scientists and public health practitioners in future research. Six manuscripts have been published with several more currently under review. The Arizona CoVHORT has the ability to contribute significantly to our understanding of PASC, as well as the broader impacts of the pandemic, helping serve the people of Arizona.



Jong Seto, PhD

Arizona State University

Project Title:
Enhancing Clinical
Assessment of
Fluorosis with
Near-Infrared
Imaging Methods

The objective of this proposal is to develop new clinical methods for the measurement of fluorosis that are reliable and feasible for surveillance at the community level. Methods are needed for the quantitative assessment of fluorosis in vivo. Current methods rely on indices such as the Dean's index based on visual examination, highly subjective, and use an ordinal scale that is poorly suited for identifying differences in the severity of mild fluorosis between communities. The central hypothesis underlying this proposal is that fluorosis manifests as diffuse porosities in the tooth and those porosities increase the magnitude of light scattering that can be measured and quantified non-destructively. The severity of fluorosis is represented by the degree of hypo-mineralization that can be measured with X-ray, polarized-light microscopy, and microradiography. However, such quantitative methods cannot be employed in vivo. Visible and fluorescence based optical measurements suffer from interference of extrinsic stain, specular reflection, variations in enamel thickness and low contrast. Light scattering in hypo-mineralized enamel closely resembles that of demineralized enamel and we postulate that OCT imaging methods will also yield high contrast images of fluorosis. This work is expected to lead to innovative new technology that is more quantitative and reliable for the clinic.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



Shalini Sharma, PhD

University of Arizona

Project Title:
Development of a DEAD Box Helicase UAP56 Specific RNA Aptamer for Cancer Therapy

According to the Arizona Cancer Registry, an estimated 30,638 individuals are diagnosed with invasive cancer yearly and an average of 11,336 Arizonans die from cancer each year. Patients with leukemias and solid tumors have poor outcomes; the 5-year survival rate ranges from ~18% for lung cancer to ~46% for leukemia. Due to the aged population, care of patients with cancer is predicted to be a significant burden on the Arizona healthcare system, underscoring the need for new treatments. Next generation sequencing has revealed the high incidence of splicing gene mutations in hematological malignancies, and solid tumors. This association has made the core splicing machinery a target for therapy. This proposal will validate the targetability of the RNA helicase UAP56 and develop UAP56 specific RNA aptamers with therapeutic potential. UAP56 is an essential component of the spliceosome. We have shown that, interaction of UAP56 with the stem-loop 3 of the 5'-splice site bound U1 snRNA is vital for spliceosome assembly and hypothesize that inhibition of UAP56 function by an RNA aptamer will inhibit pre-mRNA splicing and induce death in cancer cells. Our specific aims are - 1) To identify and characterize high affinity UAP56-aptamers and determine their splicing inhibitory activity, and 2) To develop a modified UAP56-aptamer that exhibits high stability and selective cellular toxicity.



Sui Yang, PhD

Arizona State University

Project Title: 3D Printing-Enabled Regenerative Medicine for Pelvic Organ Prolapse (POP) Treatment

Nearly 1 in 4 women undergo surgery for pelvic organ prolapse (POP) or urinary incontinence in the US. The weakened pelvic floor, which could be caused by childbirth injury, aging, or obesity, fails to support the pelvic organs, resulting in urinary incontinence, sexual difficulties, and POP. Polypropylene (PP) meshes are often used in reconstructive surgeries as a reinforcement to provide long-term, durable support. However, commercial PP meshes risk complications, such as pain, mesh erosion, and infection, being re-classified as a high-risk device by FDA. Dr. Lancaster, Dr. Cornella, Dr. Lott, Dr. Yi (Mayo Clinic), and Prof. Song (ASU) aim to develop a new implantable mesh using biocompatible polymers (e.g., polyvinyl alcohol (PVA), chitosan) with controlled bonding strength and tunable lifetime. The PI Song was a Mayo residency faculty and has initiated collaborations with these Mayo teams in addition to some ongoing student exchanging experience. The Song group will leverage 3D printing for tunable scaffold structures beneficial for cell attachment, nutrition transmission, and personalized medicine to be examined by the Mayo groups. Our POP mesh will have high compatibility and controlled biodegradability. The cooperation shows high research synergy between (i) ASU's strength in bio-manufacturing/ material science and (ii) Mayo's advantage in clinical/biomedical expertise.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



**Jennifer Stern,
PhD**

University of
Arizona

Project Title:
Investigating the
Role of Hepatic
Glucagon
Receptor Signaling
in Healthspan and
Aging

Nearly 1 in 5 Arizonans older than 65 years have Type 2 Diabetes Mellitus (T2DM). T2DM accelerates aging, leading to a rapid decline in physical function. Current treatment strategies for T2DM do not address the accelerated aging caused by T2DM. We have established a key role for glucagon in the accelerated aging in obesity and the slowed aging resulting from calorie restriction. 5'AMP kinase (AMPK) activity, increased by glucagon, has also been implicated in calorie restriction's extension of healthspan. We propose that liver glucagon receptor signaling, which increases with both calorie restriction and obesity, slows aging by causing a rise in AMPK activity. We will use dietary manipulation (calorie restriction, chow control, and high fat diet), genetic glucagon receptor knockout, and viral induced constitutively active or dominant negative AMPK expression to isolate the role of liver glucagon receptor and downstream AMPK signaling in lifespan and healthspan.

The studies proposed herein will test the potential negative consequences of lower liver AMPK signaling in the accelerated aging in response to obesity or glucagon receptor deletion. The existence of glucagon receptor agonists that are already in clinical trials to address the obesity epidemic, provides an excellent opportunity to translate this research into the clinic.



**Jordon R. Yaron,
PhD**

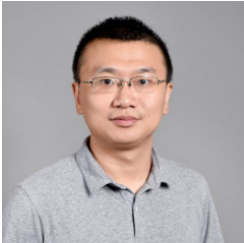
Arizona State
University

Project Title:
Fundamental
and Translational
Investigations
of an Epidermal
Serpine in Diabetic
Wounds

Wounds are a major medical burden. Over 6 million chronic wounds cost >\$20 billion/year in the USA - nearly 5% of the cost of Medicare/Medicaid. Delay in any stage of repair impairs healing and commonly occurs in diabetes. Over 600,000 adults in AZ (1 in 10) live with diabetes, and another 2 million Arizonans (1 in 3) are pre-diabetic, with rates 2x among American Indians. Diabetic wounds are thus a current and imminent health risk to Arizonans. Delayed re-epithelialization is characteristic of diabetic wounds and treatments to target this process are needed. Our preliminary data show that SerpinB3, a protein canonically associated with cancer, is specifically expressed in skin after wounding. We hypothesize that impaired SerpinB3 signaling contributes to diabetic wound impairment. We will (Aim 1) define the role of SerpinB3 in diabetic wound impairment, and (Aim 2) evaluate SerpinB3 as a wound healing therapeutic. The success of this application is supported by a strong team with extensive, complementary experience and a history of productive collaboration in the areas of serpin biology, wound healing, and drug delivery. This proposal leverages the innovative, scientifically robust environment at Arizona State University, in close proximity to collaborating team members at Mayo Clinic, to investigate a novel mechanism of healing with a strong path to clinical translation.

Appendix B: 2023 Cohort Research New Investigators

\$75,000 per year for three years



**Wenlong Zhang,
PhD**

Arizona State
University

Project Title:
Supporting
community-
based stroke
rehabilitation
with a soft robotic
exosuit

In this project, we will design a novel soft robotic hip-knee exosuit and evaluate its effectiveness for stroke rehabilitation in clinical and community settings. The overall vision is to develop a reliable, affordable, and autonomous robotic solution to meet the growing need of neurorehabilitation by enabling patients to conduct exercises in both clinics and their local fitness centers. Three aims are set towards this vision: 1) novel fabric soft actuator design for fast and bidirectional joint support, 2) adaptive and coordinated control of the exosuit, and 3) a pilot study with healthy participants (N=12) in the lab and stroke patients (N=6) in clinical and community settings. This is a collaborative project between ASU, BNI, and Ability360. This project contributes to the independent living for Arizonians with mobility disorders (12% of the population) by developing low-cost robots for community use to make rehabilitation services more affordable and accessible, especially for those living in rural areas and from low-income families. It helps address the health disparity faced by Arizonians and promotes Health Equity and Rural & Urban Underserved Health, as identified in AZ Health Improvement Plan. This project also addresses fundamental challenges in pneumatic soft robots, leading to new intellectual properties and a great potential for commercialization of the exosuit.

Appendix B: 2023 Cohort Research Investigator Grants

\$250,000 per year for three years



**Deveroux
Ferguson, PhD**

University of
Arizona

Project Title:
Neuronal and
Circuit-Specific
Maladaptations
Contributing to
Cocaine Addiction

The objective of this project is to use mouse models to investigate molecular and circuit mechanisms underlying cocaine addiction, including the cell-type specific roles of corticolimbic circuits and their mal-adaptations during cocaine addiction. Our central hypothesis is that cocaine addiction is resulted from neuron specific maladaptations in corticolimbic circuits at molecular, cellular and circuit connectivity levels. We will creatively use a novel activity reporter mouse model (TRAP2) combined with cocaine addiction to identify the most relevant brain wide neuronal ensembles engaged by cocaine, followed by evaluating transcriptional gene networks disrupted by cocaine in distinct population of corticolimbic neurons and their dependencies on SIRT1, an epigenetic regulator of chromatin state (Aim 1). Inspired by our preliminary data using TRAP2 mice, we will further investigate the molecular, cellular and circuit level changes in an mPFC ensemble activated by cocaine addiction (Aim 2). Lastly, the effects of circuit-specific intervention on cocaine addiction will be tested through optogenetic activation and inhibition to probe causal effects of the identified mPFC ensemble in addiction behavior (Aim 3). The project has translational potential in identifying tractable therapeutic targets at molecular and circuit dimensions for cocaine abuse and other substance use disorders.



**Melissa M.
Herbst-Kralovetz
PhD**

University of
Arizona

Project Title:
Identifying
Immunometabolic
Cervicovaginal
Biomarkers for
Early and Non-
Invasive Diagnosis
of Endometrial
Cancer
In Arizonans

Endometrial cancer (EMC) is the most common gynecologic cancer in the United States and Arizona. In contrast to other cancers, rates of type 1 EMC continue to rise. In Arizona, Hispanic and Native American women have a higher incidence and poorer survival rate from EMC than non-Hispanic Whites. Current diagnosis of EMC is based on endometrial tissue sampling, such as biopsy. These procedures are expensive, invasive, and painful, which ultimately impacts acceptability and accessibility. Alternatively, non-invasive cervicovaginal lavage (CVL) has shown high acceptance from patient volunteers recruited by this team. We hypothesize that, due to continuity of the female reproductive tract, cancer biomarker proteins and metabolites, particularly lipids, will be altered in CVL samples from women with EMC relative to healthy controls and women with benign conditions. In the proposed study, we will utilize a diverse cohort of 250 Arizonan women previously enrolled, state-of-the-art "omics" technologies and machine learning algorithms to identify signatures that demonstrate high accuracy and sensitivity/specificity as novel biomarkers for early EMC diagnosis. The proposed studies will contribute to development of non-invasive diagnostics, which will enable early detection of EMC and, consequently, will reduce morbidity and mortality associated with this common cancer in Arizonan women.

Appendix B: 2023 Cohort Research Investigator Grants

\$250,000 per year for three years



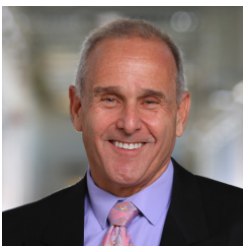
**Pawel R. Kiela,
DVM, PhD**

University of
Arizona

Project Title:

Neuroinflammation-
induced
pediatric
neuropsychiatric
illness: from
mechanism to
translation

Neuroinflammation and severe neuropsychiatric illness following infection is a novel area in clinical care and research. Emerging data point to altered gut microbiota and inflammation leading to impaired blood-brain barrier (BBB) and neuroinflammation. We identified differences in gut microbial composition, and in fecal and systemic metabolome in Children's Post-infectious Autoimmune Encephalopathy (CPAE) as compared to controls. Several taxa associated with autoimmunity were altered in CPAE, and microbiome transplant from CPAE subjects into germ-free (GF) mice led to enhanced inflammatory responses compared to controls. We will explore the mechanisms underlying the role of gut microbial community composition in CPAE using clinical cohorts and murine models. Aim 1 will test the hypothesis that the gut microbiome/metabolome in treatment-naïve CPAE patients are different from controls and those differences correlate with systemic and intestinal inflammatory markers. Altered gut microbiota and inflammatory markers may predict CPAE relapse after cessation of treatments. Aim 2 will test the hypotheses that CPAE patient sera modulate human microglia activation/polarization in vitro and that microbiota from CPAE subjects transplanted into GF mice affect behavioral and local/systemic inflammatory responses, BBB, and neuroinflammation with and without concomitant *S. pyogenes* infection.



**Joshua LaBaer,
PhD**

Arizona State
University

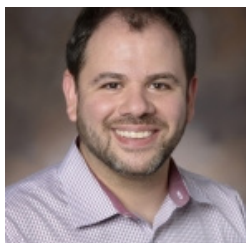
Project Title:

Comprehensive
genomic and
immunological
analysis to
improve
personalized
management of
Lynch Syndrome

Colorectal cancer (CRC) is the 4th most diagnosed cancer and the 2nd highest cause of cancer death in Arizona. There are an estimated 2,600 new cases of CRC diagnosed and around 1,000 deaths due to CRC each year in Arizona. Research aimed at early detection and administration of appropriate treatments to CRC patients saves lives and improves outcomes. Individuals with Lynch syndrome (LS) are more likely to develop colorectal cancer (CRC) at young ages. The current recommendation to initiate annual or biannual CRC screening with colonoscopy at age 25, although effective, is costly and cumbersome and has a low adherence rate. Our overarching goal is to develop a non-invasive blood test that can benefit early detection of LS-associated CRC (LSaCRC). We propose to identify LSaCRC specific antibody biomarkers using a proteome-scale, comprehensive study of the antibody response against tens of thousands of INDIVIDUAL human and gut microbial proteins on an innovative protein array platform. Our project will leverage close collaboration between translational researchers and physician scientists at Arizona State University and Mayo Clinic Arizona to ensure scientific excellence on the bench and subsequent validation of our findings in the clinic. Our proposed study may change the landscape of cancer screening in LS individuals.

Appendix B: 2023 Cohort Research Investigator Grants

\$250,000 per year for three years



**Raymond
Migrino, PhD**

Arizona Veterans
Research and
Education
Foundation

Project Title:

Validation and
development of
nanoliposomes for
neuroprotection in
stroke

Stroke is the 4th leading cause of death in Arizona. We still lack neuroprotective agents to augment or take the place of reperfusion therapy for stroke. We showed in a pilot study that nanoliposomes composed of phosphatidylcholine, cholesterol and monosialoganglioside (NLGM1, 70:25:5 % molar ratios) conferred acute neuroprotection in a middle cerebral artery occlusion (MCAO) mouse stroke model through induction of antioxidant protective response. Our goals are to test and validate optimal timing and dosing of NLGM1 for acute and chronic neuroprotection in stroke, and to establish initial pharmacokinetic (PK), biodistribution and safety profile of NLGM1. We hypothesize that (1) NLGM1 could improve acute and chronic neurologic function in mice subjected to cerebral arterial occlusion and (2) NLGM1 in doses used for stroke is biologically safe. In Aim 1, we will determine the optimal therapeutic regimen (timing and dose) of NLGM1 protection in acute mouse MCAO stroke. In Aim 2, we will evaluate NLGM1 efficacy and optimal regimen for chronic neuroprotection following photothrombotic occlusion stroke. In Aim 3 we will perform PK, biodistribution and safety evaluation of NLGM1. The proposal is a multi-institutional collaboration that could lead to further development of a novel Arizona-formulated nanotherapeutic for translational use to favorably impact stroke outcomes.



**Masmudur
Rahman, PhD**

Arizona State
University

Project Title:

novel combination
therapy with
nuclear export
inhibitor selinexor
and oncolytic
virus for lung and
metastatic cancers

Cancer is the second leading cause of death in Arizona and the United States. Most cancer-related deaths are due to metastasis in the lungs at late stages and are challenging to treat with current therapies. Thus, novel therapies and treatment approaches are required. Here we propose exploiting a novel oncolytic immunotherapy approach with oncolytic MYXV plus an FDA-approved nuclear export inhibitor Selinexor. Based on our preliminary observations, Selinexor reduces cancer cell proliferation, enhances virus replication and killing of cancer cells. We will test our central hypothesis and attain our objectives via the following specific aims: Aim 1: Maximizing the delivery of oncolytic MYXV to the metastatic lung sites: using different metastatic cancer models, virus delivery methods, and IVIS imaging system we will optimize the maximum delivery of virus to the metastatic lung sites; Aim 2: Testing the in vivo efficacy of oncolytic MYXV plus Selinexor: Using selected lung metastasis model and optimized delivery method from aim 1, we will explore combination therapy with Selinexor plus armed oncolytic MYXVs; Aim 3: Activating potent, long-lasting anti-tumor immune responses using combination therapy: We will evaluate durable anti-tumor immune responses and clearance of metastatic tumors by combination therapies with MYXV, Selinexor, and immune checkpoint inhibitors (ICIs).

Appendix B: 2023 Cohort Research Investigator Grants

\$250,000 per year for three years



Christopher Smith, PhD

Southwest Autism Research and Resource Center

Project Title:

Biomarkers of Disrupted Folate Metabolism: Risk Factors for Autism and Pregnancy Complications, Identifying Avenues for Prevention

Abnormalities of folate metabolism have been linked to autism spectrum disorder (ASD), birth defects and pregnancy complications. ASD now affects ~2% of children, and pregnancy complications lead to lifelong consequences. These chronic medical conditions are a socioeconomic burden on the state of Arizona. Since abnormalities of folate metabolism effect prenatal development, it may be possible to address them before birth, thus preventing ASD and improving prenatal/postnatal health. Low dose folic acid improves pregnancy outcomes, but folic acid is not directly bioavailable and inhibits metabolism at high doses, so it may not be the optimal form of therapeutic folate. We hypothesize that multiple factors converge to reduce the delivery of folate during critical developmental periods, and that one mechanism by which folate acts is through gene methylation. Our work will improve our understanding of folate metabolism abnormalities. We will also define biomarkers of folate abnormalities in mothers and children with ASD and develop them into risk equations which can be integrated into a clinical decision support tool. This study will provide insight to improve the health of the mother, fetus, and child using safe folate compounds designed to bypass folate pathway abnormalities, leading to reductions in the risk of ASD, birth defects and pregnancy complications.



Ashley M. Stokes, PhD

St. Joseph's Hospital and Medical Center

Project Title:

Assessment of neurovascular factors implicated in mild cognitive impairment and Alzheimer's disease metastatic cancers

Alzheimer's disease is the most common cause of dementia, and its underlying pathological changes can be assessed using imaging biomarkers. Neurovascular changes are increasingly recognized as contributors to Alzheimer's disease. While neurovascular biomarkers are critical to assess these changes, current biomarkers are limited in their ability to assess the multiple interconnected features that compose the neurovascular system. To overcome these limitations, we developed an advanced magnetic resonance imaging (MRI) method to investigate neurovascular changes associated with Alzheimer's disease. Compared to existing methods, our advanced method increases sensitivity to brain activity and informs on microvascular function. By coupling this method with functional MRI and cerebrovascular reactivity, complementary functional and vascular changes can be quantified across distinct vascular scales, from large vessels to capillaries. More specifically, this project aims to a) establish a clinically feasible, reliable protocol for mapping total and microvascular neurovascular changes and b) characterize complementary functional and vascular biomarkers in healthy aging and cognitively impaired cohorts. This integrative approach will provide insight into functional and vascular dysfunction in aging and Alzheimer's disease via clinically feasible and validated neurovascular biomarkers.

Appendix C

2024 Cohort Research Abstracts

New Investigator Awards (NIA) | \$ 75,000 / year for 3 years

Investigator Grant (IG) Awards | \$ 250,000 / year for 3 years

*Abstracts are included as submitted by the research team



Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Casey Ager, PhD

Mayo Clinic

Project Title:

Elucidating
Mechanisms of
a Novel Tumor-
Infiltrating
Regulatory T-Cell
Master Regulator
TRPS1

Tumor-infiltrating regulatory T cells (TI-Tregs) infiltrate most cancer types, potently suppress antitumor immunity, and orchestrate resistance to cancer immunotherapies. Unfortunately, we lack therapeutics that disable TI-Tregs in patients. To address this need, we discovered and validated a new class of potentially targetable vulnerabilities of TI-Tregs, including the transcription factor TRPS1 (Transcriptional Repressor GATA Binding 1). We are the first to describe a role for TRPS1 in immune cells, thus further investigation into the mechanisms by which TRPS1 controls TI-Treg function is needed. We are generating new genetically engineered mouse models to definitively test our hypothesis that TRPS1 is preferentially active in TI-Tregs and is required by TI-Tregs to mediate resistance to cancer immunotherapy. We will also define the molecular mechanisms by which TRPS1 promotes TI-Treg function in cancer, collaborating with colleagues at Mayo Clinic Arizona to perform CRISPR/Cas9 editing of TRPS1 in human Tregs together with single cell proteomics, RNA sequencing, and epigenetic profiling. These studies have potential to significantly impact the scientific community and inform development of novel TRPS1 antagonists for rational targeting of TI-Tregs; a novel immunotherapy approach with the potential for broad activity across multiple cancer types.



**Claudio
Barnardazzi de
Miranda Azevedo,
PhD**

University of Arizona

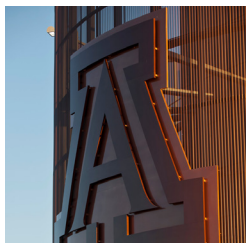
Project Title:

Assessment of
neurovascular
factors implicated
in mild cognitive
impairment and
Alzheimer's disease
metastatic cancers

The period of weaning and solid food introduction is associated with an increase in gut microbial diversity, composition, and metabolic activity. Interruption of this process during this critical window can have profound consequences for immune, respiratory, neurological, and metabolic development, and susceptibility to enteric infections. Postnatal "evolution" of the gut microbiome corresponds with functional GI tract maturation, marked by increased expression of membrane transporters and absorptive capacity. Intestinal Na⁺/H⁺ exchanger 3 (NHE3/SCL9A3) is involved in Na⁺ absorption and intra- and extracellular pH regulation and is upregulated during postnatal development. During this period, gut bacteria are necessary for the high expression of NHE3, as indicated by studies with germ-free (GF) mice. Reciprocally, NHE3 is a critical regulator of the gut microbiota and inactivating mutations in SLC9A3 gene are associated with very early-onset IBD in children. However, the relationship between changes in the gut microbiota, postnatal gut maturation, and NHE3 remains unknown. This proposal will address the hypothesis that reciprocal relationship between the gut commensals and NHE3 represents a key mechanism in microbial-epithelial interactions in the developing gut to shape adult-like microbial community and to reduce susceptibility to enteric infections in early development.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



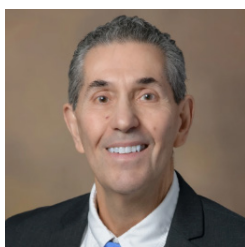
Rabail Chaudhry, MD

University of Arizona

Project Title:

Deciphering
Tranexamic
Acid's Enigma:
Revolutionizing
Surgical Hemostasis
& Thrombosis
Prevention

Tranexamic acid (TXA) serves a critical role in surgery as an antifibrinolytic agent, significantly reducing transfusion necessities. Despite its widespread use in surgeries, there remains limited understanding of its pharmacodynamics in routine doses, primarily due to a lack of precise hemostatic technology for evaluating fibrinolysis changes post-administration. The growing concern is the over-inhibition of fibrinolytic processes post-operatively, termed 'fibrinolytic shutdown,' which could lead to thrombotic complications and, in turn, high mortality rates. This research proposes a systematic exploration of TXA's temporal dynamics after standard dosing across three surgical contexts over three years: orthopedic surgery (Year 1), cardiac surgery (Year 2), and trauma surgery (Year 3). Employing a combination of rotational thromboelastometry (ROTEM) and the standardized tissue plasminogen activator (TPA)-based viscoelastometric assay, this study aims to elucidate TXA's fibrinolytic duration and window post-administration, and to assess associations between TXA pharmacokinetics, hypofibrinolytic and hyperfibrinolytic states, and related clinical outcomes. The anticipated results could guide more effective TXA dosing, thus enhancing postoperative outcomes for Arizonans' and impacting global healthcare positively.



Ralph Fregosi, PhD(Previously Lila Buls Wollman, PhD)

University of Arizona

Project Title: The influence of nicotine withdrawal on the control of blood pressure, heart rate, and breathing

In the past 5 years, Arizona has seen a rise in the use of nicotine delivery devices, such as e- cigarettes. E- cigarettes are at least as addictive as traditional tobacco, and there are many adverse signs of nicotine withdrawal, which are associated with adverse outcomes in hospitalized patients. Currently, there is limited published data on the effects of nicotine withdrawal on cardiovascular function and breathing. In experiments studying breathing in rats, I showed that nicotine withdrawal blunts the increase in breathing that should occur in response to low blood oxygen (hypoxia), a reflex that aims to limit arterial blood oxygen desaturation. These data are the first to show that an impairment in this life-saving reflex may be a previously unidentified consequence of nicotine withdrawal. Along with an increase in breathing, the response to hypoxia includes cardiovascular changes to enhance perfusion of blood to critical organs such as the heart and brain. Thus, I will test the hypothesis that nicotine withdrawal blunts the blood pressure, heart rate, and breathing responses to hypoxia. This has important clinical ramifications, as hypoxia is a commonly encountered medical complication, and withdrawal symptoms are often observed in hospitalized patients as it is common for them to abstain from smoking during periods of worsening health or in preparation for surgery.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Christopher Glembotski, PhD (Previously Erik Blackwood, PhD)

University of Arizona

Project Title: The Effects of Serum Glucocorticoid Kinase 1 in Cardiac Pathology and Global Metabolic Dysfunction in Cardiometabolic Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction (HFpEF) has emerged as the greatest unmet medical need in cardiovascular medicine for which there are no evidence-based therapies, with a US prevalence of # million and a 5-year survival after hospitalization worse than most cancers of ~35%. The most prevalent form of HFpEF is characterized by the main co-morbidities of advanced age, obesity, type 2 diabetes, and hypertension. This is of unique concern for Arizona as it has one of the greatest populations above the age of 65 years old and currently more than 35% of its population is obese. Our preliminary data support the notion that the serine-threonine kinase, serum glucocorticoid kinase 1 (SGK1) is a primary regulator of cardiometabolic HFpEF (cMet HFpEF). The hypothesis of this proposal is that SGK1 exacerbates cardiac pathology and subsequent global metabolic dysfunction in cMet HFpEF. I will address this hypothesis using cardiac-specific targeting of SGK1 in a mouse model of cMet HFpEF with a focus on assessments of cardiac function and metabolism in the following Specific Aims: (1) determine the role for cardiac SGK1 in regulating heart function, metabolism and heart directed inter-organ communication during cMet HFpEF; and (2) evaluate the therapeutic efficacy of novel SGK1 inhibitory peptide for preserving cardiac function and systemic metabolism during cMet HFpEF.



Alexei Gonzalaez-Estrada, MD

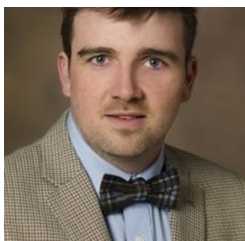
Mayo Clinic

Project Title: Novel Techniques and Technologies for Drug Allergy

Perioperative anaphylaxis is a life-threatening drug allergic reaction that occurs during anesthetic procedures and has a greater morbidity and mortality than other forms of anaphylaxis. The most common identifiable causes of perioperative anaphylaxis in the US include antibiotics (i.e., cefazolin), neuromuscular blocking agents (i.e., rocuronium), and antiseptics (i.e., chlorhexidine). Using currently available testing technology, only 50% of perioperative anaphylaxis cases have a causal agent identified. Both in vivo and in vitro tests have significant limitations. In vivo skin test accuracy is limited by inappropriate diluent conditions and inadequate drug concentrations. In vitro tests (serum specific IgE [sIgE] and basophil activation test [BAT]) for drug allergy have a low sensitivity and other limitations. We hypothesize that a mast cell activation test can be used as a standardized, functional in vitro platform for drug allergy, and that sterile water does not irritate the skin and can be used as a diluent to generate in vivo testing agents with a high concentration, and thereby higher accuracy. This proposal will establish novel drug allergy testing approaches, provide insight to the maximal non-irritating concentrations of chlorhexidine, and validate rocuronium in vivo tests using the reference standard as a model for additional drugs.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



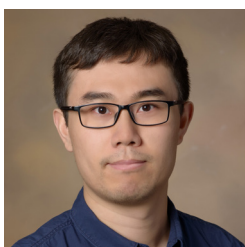
Nick Henscheid, PhD

Critical Path Institute

Project Title:

AI-Based Disease Progression Models for Alzheimer's Disease

Currently, disease progression modeling in Alzheimer's Disease involves using nonlinear mixed effects models or Bayesian progression models to understand longitudinal trajectories of cognitive decline. In such models, patient covariates such as age of onset, a measure of baseline cognitive ability, and presence of genetic risk factors such as ApoE4 genotype are used as predictors of progression of future disease severity. While some modeling successes have been achieved for predicting future disease state within single cohorts, difficulties remain in combining data from multiple cohorts to predicting relevant cognition-based endpoints and pathological aspects of AD as measured by fluid-based biomarkers. For disease progression models to have maximum impact, they must accurately predict clinically useful variables and be generalizable across cohorts. Our objective is to leverage the existing multi-cohort data warehoused at the Critical Path Institute's Critical Path for Alzheimer's Disease (CPAD) to build an advanced predictive model for AD. Our model will be driven by state-of-the-art AI/ML model architectures where appropriate, and we will use the resulting model to build an advanced Drug Development Tool (DDT) that will inform future trial design.



Lifeng Lin, PhD

University of Arizona

Project Title:

Evidence-Based Informative Prior Distributions for Between-Study Heterogeneity in Bayesian Meta-Analyses

Comparative effectiveness research aims to offer high-quality evidence for decision-making about treatment options' benefits and risks. Systematic reviews (SRs) and meta-analyses (MAs) play a key role in building such evidence by combining and contrasting results from multiple studies on the same question. They are highly applicable to many healthcare topics, including those concerning Arizonans. For example, prolonged exposure to high temperatures can cause heat-related illnesses. Different teams have conducted studies to address these health concerns, while Arizona's diverse and underrepresented populations require careful consideration in delivering optimal treatments. SRs and MAs can effectively synthesize evidence for Arizona's diverse populations while respecting their differences. This proposal aims to develop methods that improve the treatment effect estimation in MAs. Specifically, we will: 1) derive evidence-based informative priors for Bayesian MAs using a large dataset from the Cochrane Library; 2) build a user-friendly open-source software package for clinicians to perform the proposed methods accurately; and 3) evaluate the performance of the proposed methods using simulation studies and real-world data (particularly those addressing health concerns among Arizonans). The proposed methods will broadly benefit many fields of healthcare.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



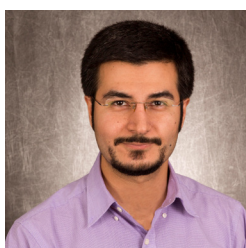
**Chen-wei Liu,
PhD**

University of Arizona

Project Title:

The role of HDAC9 activation in the pathogenesis of e-cigarette-induced atherosclerosis by promoting endothelial-mesenchymal transition

The significant increase in e-cigarettes (e-cigs) usage requires a thorough assessment of its potential health hazards. Endothelial to mesenchymal transition (EndMT) is a type of endothelial dysfunction that is distinguished by the loss of endothelial function, and the acquisition of mesenchymal-like function, a process that is prominent in the pathogenesis of many diseases, including cardiovascular diseases. The key objective of this RFGA-NIA proposal is to study whether e-cigs use may be associated with an increased risk for specific users, such as those with atherosclerosis. The aims that I am trying to achieve for the following aspects: use CRISPR to knockout or overactivate Hdac9 in iPSC-ECs to assess the effects of e-cigs exposure on the vascular function; defining the secretome signature of iPSC-ECs for e-cigs associated EndMT; underlying mechanisms of atherosclerosis to e-cigs in mouse models with genetic deletion (ecHdac9KO) or pharmacological inhibition (ApoE-/- and TMP195, an HDAC9 inhibitor). The proposed aims of this study will have significant appeal in several aspects, including assessing the effects of e-cigs exposure on vascular function using CRISPR, defining the secretome signature of iPSC-ECs for e-cigs-associated EndMT, and elucidating the underlying mechanisms of atherosclerosis in mouse models with genetic deletion or pharmacological inhibition of HDAC9.



**Hamidreza Marvi,
PhD**

Arizona State
University

Project Title:

Robotic Tissue Retraction with Endoscopic Resection of Complex Gastrointestinal Neoplasms

Colorectal cancer is a leading health concern in Arizona and is forecast to be the second primary cause of cancer deaths by 2023. Addressing this, our collaboration between Mayo Clinic and ASU focuses on a robotic system for enhanced endoscopic resection of gastrointestinal neoplasms. The system is composed of an endoscopic anchoring magnet manipulated by an externally-controlled extracorporeal magnet on a robotic arm, acting as a surgeon's "second hand." This innovative approach aims to improve precision during complex resections, broadening access to advanced endoscopic treatments. Despite the efficacy of endoscopic methods like endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) in polyp removal and early-stage cancer treatment, colectomy rates remain high, possibly due to the steep learning curve of these techniques and limited access. Current retraction tools, essential for effective resection, frequently have limited adaptability. Magnet-based solutions have shown potential in addressing this, but optimizing magnet design and control is still challenging. Our solution seeks to bridge this gap, aiming for better patient outcomes and reduced healthcare expenses.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



**Heather Mead,
PhD**

The Translational
Genomics Institute

Project Title:
High throughput
identification of
novel antigens for
the detection of
Valley fever infection

Valley fever (Vf) is caused by *Coccidioides*, a fungal pathogen that is endemic to Arizona, and is diagnosed in an average of 31 Arizonans daily. Delays and misdiagnoses are common, affecting 60-80% of infected people and leading to improper use of antibiotics, increased disease severity, and hospitalization costing an average ~\$55K/primary diagnosis. These health and economic impacts can be reduced by improving the diagnostics available to clinicians. NAPPA and PepSeq are two innovative, high-dimensional antibody analysis tools established at Arizona-based research institutes that have substantial, and complementary, potential to enable the discovery of new diagnostic targets for Vf. In this project, we propose to unlock this potential by 1) using PepSeq to reveal the precise epitope targets of known patient antibody responses across 685 *Coccidioides* proteins that were recently identified by NAPPA and 2) combining the identified targets – both protein-level and epitope-level – to pilot a multitarget diagnostic built around ELISA, a common and accessible platform used in clinical diagnostics. Success in this project will demonstrate the power of integrating the NAPPA and PepSeq technologies and its potential to reveal new diagnostic targets for an understudied pathogen of public health importance in Arizona, and offer improved diagnostic performance over the current standard of care.



**Sampathkumar
Rangasamy, PhD**

The Translational
Genomics Institute

Project Title:
Molecular
mechanisms
underlying
mitochondrial
translation defects
in Neurological
disorders

Mitochondrial translation defects have been identified as contributing factors to many mitochondrial disorders and several neurodegenerative disorders, including Parkinson's. Mitochondrial Methionyl-tRNA Formyltransferase (MTFMT), an enzyme encoded by the nuclear genome, catalyzes the formation of formylated methionine tRNA^{fMet}, which serves as the translation initiation codon for all mitochondrial-encoded proteins. Biallelic mutations in the MTFMT gene lead to autosomal recessive Leigh syndrome (LS), combined oxidative phosphorylation deficiency 15 (COXPD15), and patients display features of neurodegenerative phenotype. The most common loss of function MTFMT mutation is c.626C>T, which generates a splicing suppressor resulting in exon 4 skipping and protein truncation (p.R181SfsX5). To investigate the mechanisms and consequences of mitochondrial translation defects caused by MTFMT mutations, we developed patient-derived fibroblasts and human-induced pluripotent stem cell (hiPSCs) models, as well as novel "humanized" Mtfmt mouse models with either wild-type or mutated Mtfmt. We employ cutting-edge "omics" techniques to elucidate mitochondrial translation and functional defects to achieve our research goals. Our work aims to fill a critical knowledge gap in mitochondrial translational biology, with implications for developing targeted therapies for mitochondrial disorders.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



**Chandler Roe,
PhD**

Northern Arizona
University

Project Title:
Rapid Point of
Care Diagnostic
for the Detection of
Onchocerca Lupi

Onchocerca lupi is a neglected, vector-borne, parasite that causes blindness primarily in dogs but has been described in cats, coyotes, wolves, and humans. Currently, there is no commercial diagnostic, limited treatment, and no cure for this invasive parasite. Over the last decade, reported canine and human incidence has steadily increased in the U.S.. There have been eight confirmed human *O. lupi* cases from U.S., five of which were neuroinvasive cases in children on the Navajo Nation from 2012-2022. We recently reported 9.4% prevalence of *O. lupi* in asymptomatic dogs on the Navajo Nation. These data highlight the need for a rapid, cost-effective point of care diagnostic to aid in detection of asymptomatic animals, that will allow for subsequent treatment to reduce spread and lower the risk of neuroinvasive human infections. Using a novel, powerful, and innovative peptide serological and sequencing technology, PepSeq, our focus is Aim 1: To identify immunogenic peptides indicative of acute canine infection with *O. lupi*, and Aim 2: Develop a serological, lateral flow immunoassay prototype for the detection of *O. lupi* infections in dogs. This proposed work addresses a critical need to identify *O. lupi* infected canids across the state that will inform treatment protocols, identify at-risk human populations, and prevent further pathogen transmission to both animals and humans.



**Travis Sawyer,
PhD**

University of Arizona

Project Title:
Development of an
advanced transnasal
endoscope for
improved early
detection of
gastric cancer in
underserved Arizona
communities

Gastric cancer represents a serious health challenge with significant disparities for underserved groups in Arizona (AZ), such as Hispanic and Native American patients, where incidence and mortality for these groups is up to 5 times higher than average. Early detection of gastric cancer can increase 5-year survival rates from 25% to over 90%, but a minority of cases are detected early due to lack of contrast provided by the standard-of-care white light endoscopy. In our preliminary studies, we demonstrated that multispectral and polarization-sensitive (MAPS) imaging can provide high sensitivity to detect gastrointestinal cancer. In this New Investigator Award project, we propose to advance our MAPS endoscopic technology for early detection of gastric cancer in underserved AZ communities using multispectral and polarization sensitive imaging. In this project, we will identify the optimal early detection imaging biomarkers and develop a novel transnasal endoscope for accessible delivery of care in these communities. Along with collaborators specializing in disparities in underserved AZ communities, we will develop technology translation and community engagement plans. Ultimately, through the proposed work, we will establish the framework to reduce gastric cancer disparities in AZ communities, with significant potential of long-term impact on our management of gastric cancer.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Shang Song, PhD

University of Arizona

Project Title:

3D-Printed
Conductive Nerve
Guides for Peripheral
Nerve Injury

Peripheral nerve injuries (PNI) occur predominately due to trauma and the degree of recovery is inversely related to the age of affected individuals. With unprecedented growth in the older population in Arizona, the medical costs for trauma-induced PNI will continue to increase. The standard clinical treatment for PNI with a sizeable nerve defect is to transplant patients' own nerves from another location to the site of injury. However, the scarcity of donor nerves and surgical morbidity continue to pose significant challenges for PNI treatment. We propose using 3D-printing technology to design conductive nerve guides with customizable sizes and regenerative potential to treat PNI. We hypothesize that 3D-printed conductive nerve guides can electrically enhance stem cell therapy to promote nerve regeneration and functional recovery after PNI. Our approach would directly benefit the affected individuals by improving their quality of life and reduce relevant healthcare cost.



**Julianna
VanderPluym, MD**

Mayo Clinic

Project Title:

Migraine and
Headache and
association with
demographic,
comorbidity, and
social determinants
of health: a
population-based
study of Arizona
Medicaid recipients

Migraine is a common neurological disease and the second overall cause for years lived with disability. There is limited literature pertaining to health disparities and migraine, such as examination of the social determinants of health (SDoH) of communities with disproportionately poor migraine outcomes, which further exacerbates disparities for vulnerable populations. Available through the Center for Health Information and Research (CHiR) at Arizona State University, Arizona Medicaid (AHCCCS) claims data is a unique opportunity to examine the relationship between SDoH, utilizing Z codes, and migraine/headache diagnosis and treatment. Z codes allow for the reporting of factors influencing health status such as education, employment, housing, food security, and problems relating to social environment and psychosocial circumstances. This proposed study will test the hypothesis that increased exposure to negative SDoH are associated with higher rates of receiving the non-specific diagnosis of "headache" over the specific diagnosis of "migraine", and lower rates of guideline recommended treatments. This study will assess the frequency of migraine/headache diagnosis and treatment among pediatric and adult AHCCCS recipients and describe the relationships between migraine/headache diagnoses and treatment with demographic variables, presence of comorbidities and negative SDoH.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Navish Wadhwa, PhD

Arizona State University

Project Title:

Uncovering the role of flow sensing in urinary tract infections

Urinary tract infections (UTIs) are globally prevalent bacterial infections, with around 30,000 emergency room visits in Arizona alone in 2020. Left untreated, UTIs can escalate to severe kidney infections and life-threatening sepsis. To infiltrate the kidneys, bacteria must swim against urinary flow, but the mechanisms governing this interaction remain enigmatic. Our study aims to decipher how bacteria detect and respond to urinary flow, and how these processes contribute to UTI pathogenesis. We hypothesize that flow initiates genetic and behavioral changes in bacteria, allowing them to swim upstream. We will employ cutting-edge biophysical, imaging, and molecular genetics tools to elucidate bacterial flow sensing and its molecular circuitry. Through in vitro flow assays, genetic and molecular analysis, and physiological assays, we will shed light on bacterial swimming adaptations under flow and unveil the molecular mechanisms behind urinary flow sensing. Identifying the molecular underpinnings of flow sensing will offer potential therapeutic targets to disrupt bacterial migration, adhesion, and biofilm formation, curbing urinary tract colonization. Innovative preventative strategies, such as catheter modifications and urinary flow modulation, may arise. As such, this research promises to advance urology and enhance patient outcomes in Arizona.



Faith Walker, PhD

Northern Arizona University

Project Title:

Rabies virus prevalence and dispersal in the AZ-Mexico borderlands region prior to the arrival of the common vampire bat (*Desmodus rotundus*)

Rabies virus causes the highest fatality rate of any infectious disease, with nearly 60,000 human deaths globally each year. In Arizona, one of the leading U.S. states for rabid wildlife, there are regular exposures to humans due to suburban outbreaks of the disease in wildlife. Infection rates, however, are greatly exceeded by those in Latin America due to the common vampire bat (*Desmodus rotundus*). This hematophagous species is moving northward and is projected to cross the U.S.-Mexico border in coming years. Establishing RABV presence and dispersal requires a RABV detection approach based on non-traditional sample types that can be applied broadly. Recently, we used a highly sensitive RT-PCR assay to demonstrate that RABV can be detected from fecal samples of rabid bats. We hypothesize that pairing this assay with fecal samples will enable us to determine distribution and dispersal of the virus in the borderlands area prior to the arrival of vampire bats. Specifically, we aim to Aim 1: Determine presence of RABV in southern Arizona urban and rural (including agricultural) areas by sampling guano from bridges, mines, and caves, and applying the LN34 assay, and Aim 2: Define local dispersal patterns of RABV in the border region by performing whole genome sequencing on rabid animal samples provided by the state as well as positive guano samples from Aim 1.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



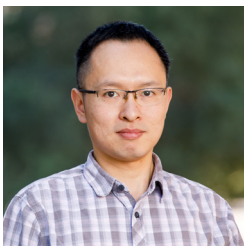
Sui Yang, PhD

Arizona State
University

Project Title:

Super-resolution
Metamaterial based
Optical Endoscopy
for Cardiovascular
Disease Treatment

Cardiovascular disease, led by heart attack and stroke, is the leading cause of death in the U.S. and in Arizona. The development of advanced biomedical imaging capability will not only enable the early disease diagnosis but also can guide the clinical treatments. This project aims to develop a high resolution, miniaturized metamaterials based endoscopic optical imaging technique to serve the pressing clinical needs for intravascular imaging tools. We hypothesize that the optical metamaterials design can be integrated with endoscopic imaging catheter to achieve clinically significant miniaturization, super-resolution imaging technology that surpasses traditional limitations. To achieve this, (1) we will design a new class of fiber optic catheters using metamaterials lens concept that could simultaneously reduce its physical size and reach high resolution beyond diffraction limit. (2) We will test and optimize the imaging capability of the designed metamaterials-based catheters. (3) Integration of metamaterials-based catheters with current fiber optic endoscope to assess cardiovascular imaging in vitro. If successful, the project will enable, for the first time, a super-resolution optical endoscope providing enhanced imaging modality beneficial for clinically treating cardiovascular heart disease, promoting healthy and quality life of Arizonans.



Qiyun Zhu PhD

Arizona State
University

Project Title:

Enhancing infectious
disease detection
in Arizona: novel
computational
approaches
to pathogen
identification in
microbiome data

Infectious diseases pose significant threats to Arizonans, with rising cases like Valley fever underscoring the urgency for enhanced pathogen detection. Traditional diagnostic methods, reliant on specific biomarkers, often fall short in identifying a broad spectrum of pathogens, especially emerging ones. This proposal seeks to revolutionize pathogen identification by developing innovative computational methods tailored for microbiome data. Leveraging high-throughput shotgun sequencing, we aim to address the prevalent challenge of false microbial identifications, a consequence of biased reference databases and the intricacies of short-read mapping. Our dual-pronged approach involves curating databases to match specific diagnostic goals, emphasizing pathogens prevalent in Arizona, and combining read mapping with assembly techniques to bolster pathogen discovery. The anticipated outcomes include user-friendly, open-source software tools that promise heightened accuracy in pathogen detection, directly benefiting Arizona's public health and advancing the broader scientific community's understanding of infectious diseases.

Appendix C: 2024 Cohort Research Investigator Grants

\$250,000 per year for three years



**Heather Bean,
PhD**

Arizona State
University

Project Title:

Breath biomarkers
for diagnosing Valley
fever and monitoring
antifungal treatment

Coccidioidomycosis, or Valley fever (VF), is a highly prevalent fungal pneumonia in Arizona, causing more than 10,000 confirmed cases per year. With growing populations in Arizona, VF cases are expected to climb. VF is currently diagnosed via serology, which lacks sensitivity early in infection, resulting in significant under-diagnosis, delays in diagnosis, and improper treatment with antibiotics. There is a critical need for sensitive and non-invasive diagnostics for identifying VF lung infections. Our goal is to substantially shorten the time-to-diagnosis for VF through the development of sensitive and specific breath tests for VF lung infections. Thus far, we have developed a diagnostic test based on volatile organic compound (VOC) biomarkers that are 86% sensitive and 93% specific for discriminating VF from other forms of community acquired pneumonia. The objective of this application is to evaluate the performance of a VF breath test based upon these VOC biomarkers through the collection and analysis of breath samples from Mayo Clinic Arizona patients diagnosed with community acquired pneumonia. At the end of this project, we will have measured the sensitivity and specificity of a VOC biomarker panel as a rapid test for diagnosing Valley fever via breath testing and will have gathered pilot data on using breath tests to monitor patient responses to antifungal treatment.



**Carlos Caulin,
PhD**

University of Arizona

Project Title:

Targeting p53-
mutated head and
neck squamous cell
carcinoma

Oral squamous cell carcinoma (OSCC) is the sixth most common human cancer worldwide. Despite advances in multimodality therapies, survival rates for OSCC have remained unchanged for decades. Immune checkpoint blockade with antibodies for programmed cell death protein 1 (PD-1) has been shown to improve the survival of patients with advanced OSCC, although only a fraction of the patients responds well. The long-term goal of this application is to uncover cellular mechanisms of resistance to immune checkpoint inhibitors (ICI) and to identify new avenues to sensitize tumors to ICIs. Identifying mechanisms of resistance of anti-PD-1 will guide in patient stratification and help design effective combinatorial therapies. The most frequently mutated gene in OSCC is p53, a gene mutated in >70% of the OSCC. Our previous studies indicate that the p53 mutations promote resistance to anti-PD-1. In this proposal, we will identify mechanisms that contribute to the resistance to anti-PD-1 in p53-mutated OSCC. Our mouse modeling studies, and clinical data suggest that the co-existence of genetic alterations that result in Cdk4/6 activation promotes immunosuppression in p53-mutated tumors. In this application we will determine the potential of Cdk4/6 inactivation to sensitize p53-mutated oral tumors to anti-PD-1.

Appendix C: 2024 Cohort Research Investigator Grants

\$250,000 per year for three years



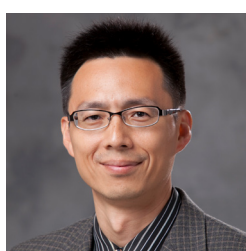
**Setsuko K.
Chambers, MD**

University of Arizona

Project Title:

Developing
Personalized
Ovarian Cancer
Risk Prediction
through Circulating
miRNA Biomarkers
in 'Family-History
High-Risk' Women

Ovarian cancer is the deadliest gynecologic malignancy, largely due to late diagnosis. Identifying women at high risk is critical for prevention and early detection. However, for "family-history high-risk" women -- those with strong family histories but no identified genetic risks -- currently no tools are available to assess their cancer risks and guide clinical decisions objectively. Supported by our preliminary data based on miRNA profiling in blood samples, this study aims to develop and validate a circulating miRNA biomarker panel as a non-invasive tool to stratify ovarian cancer risk in family-history high-risk women. Aim 1 will use an expanded sample size to improve and validate our preliminary circulating miRNA-based machine learning risk model and validate it in a separate cohort. Aim 2 will perform miRNA profiling in ovary and fallopian tube samples (matched to the blood samples) to confirm the model's predictive accuracy at the tissue origin and identify high-risk pathways. Aim 3 will adapt the miRNA biomarker panel into a rapid, cost-effective clinical prototype test using the NanoString nCounter technology. Aim 4 will initiate a longitudinal study to monitor patient risk profiles for further validation. This research could produce the first non-invasive ovarian cancer risk stratification test for family-history high-risk women, addressing an urgent clinical need.



**Nan-kuei Chen
PhD**

University of Arizona

Project Title:

Development of
high-performance,
low cost, low-field
lung magnetic
resonance imaging
(MRI) to improve
care in lung cancer

Lung cancer, coccidioidomycosis (Valley Fever), and Chronic Obstructive Pulmonary Disease (COPD) are lung diseases with major health impact in AZ. Although X-ray and Computed Tomography are used for assessment of these diseases, their ionizing radiation is undesirable. Furthermore, they result in a high rate of false positives, due to high prevalence of Valley Fever granulomas in AZ, leading to risky and costly lung biopsies for differentiating lung cancer from Valley Fever. To address these challenges, we will revolutionize lung imaging by developing non-invasive, non-radiative quantitative lung MRI to achieve differential diagnosis and staging of lung diseases, using a high-performance, low-cost, low-field (0.55T) MRI instrument. This instrument not only improves lung imaging but is easily deployable in small and remote clinics at lower cost than typical MRI. We aim to 1) develop high-resolution quantitative MRI to differentiate cancerous nodules from Valley Fever granulomas; 2) develop oxygen-enhanced functional lung MRI with high temporal resolution for detecting early lung function abnormalities due to COPD; 3) implement artificial intelligent algorithms to reconstruct parameters from MRI data with high precision and accuracy; 4) demonstrate the ability of the new quantitative MRI technology to improve the diagnosis of lung cancer, Valley Fever, and COPD patients.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Zhiqiang Li, PhD

NSt. Joseph's
Hospital and
Medical Center

Project Title:

Establish Novel MRI
Biomarkers for Post-
Surgical Recovery of
Cervical Spondylotic
Myelopathy near
Metal Implants

Cervical spondylotic myelopathy (CSM) is a debilitating disease due to age-related degeneration of the spine. This results in compression of the spinal cord, causing both movement (e.g., difficulty walking, paralysis) and sensation related symptoms (e.g., pain). CSM is more prevalent in older adults. This is important in Arizona, as our senior population has increased by 50% since 2010, with 25% of the population over 60. Surgery is often required to treat CSM, and it is critical to monitor and predict recovery to guide care and rehabilitation. Diffusion MRI provides information on spinal cord health and may serve as a monitoring and/or predictive tool. Unfortunately, current MRI methods are unable to provide high-quality measures near metals implanted during CSM surgeries, forcing neurosurgeons to adopt a "wait and watch" approach. This limits their ability to evaluate surgical outcomes in a timely manner, which delays decision making and increases the likelihood of lifelong disabilities. This project develops a novel MRI technique that allows for fast, high-quality diffusion MRI of the spinal cord near metals and generates measurements that relate to underlying spinal cord health and predict long-term recovery. If successful, this will give neurosurgeons an objective tool to base clinical decisions, improving care and outcomes, and reducing health care costs for Arizonans.



**Neal Woodbury,
PhD (Previously
Efrem Lim PhD)**

Arizona State
University

Project Title:

Assessing and
Predicting Vaccine
Responses for
Respiratory
Syncytial Virus
Variants in Arizona

The objective of this study is to assess how well Respiratory Syncytial Virus (RSV) vaccines protect against RSV infections in the Maricopa community. This will be used to improve the breadth and potency of vaccines against current and future RSV strains. We will perform sequencing and phylogenetic studies of RSV in Maricopa County using 600 RSV positive specimens from Valleywise Health to characterize contemporaneous RSV variants in Arizona (200 specimens per year during project period). and identify F protein mutations. We will enroll a prospective cohort of 50 RSV-vaccinated individuals and 25 health donor controls at Valleywise Health. Using sera collected from this cohort, we will perform RSV neutralization assays to compare functional antibody measurements between pre-vaccination, 4-weeks post-vaccination, and unvaccinated individuals. Additionally, we will perform peptide array-based deep mutational scanning to measure how all possible mutations of the RSV proteome affect antibody binding and enable escape. We will use a combination of neutralization profiles, sequencing datasets and peptide array-based antibody molecular recognition profiles to train a machine learning model to predict the RSV sequences most involved in the immune system's recognition of the virus. This, in turn, will provide insight into the types of sequence changes most likely to take place going forward and the degree to which they will give rise to antibody escape.

Appendix C: 2024 Cohort Research New Investigators

\$75,000 per year for three years



Jason Sahl, PhD

Northern Arizona
University

Project Title:

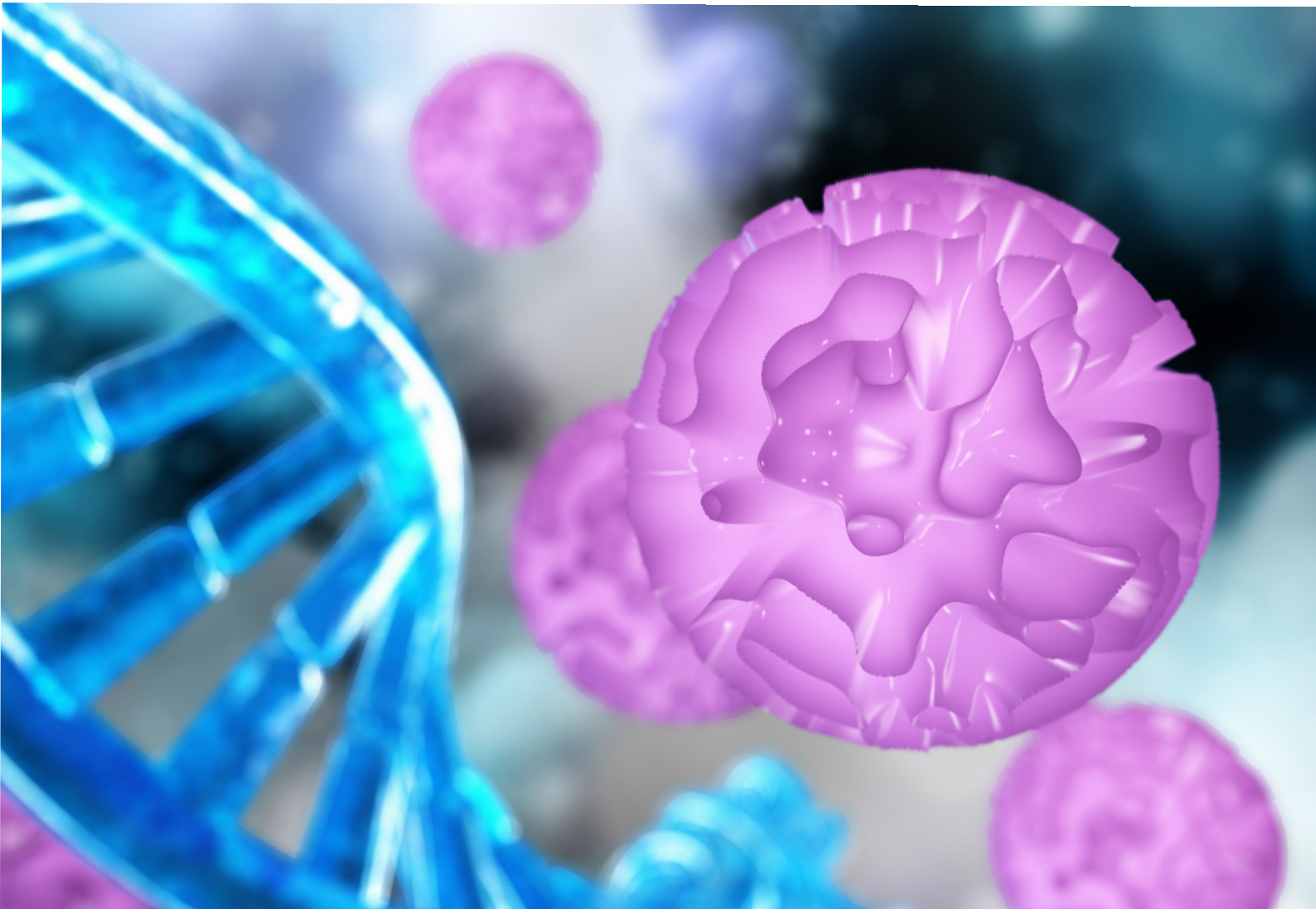
Development of
a Rapid, Point of
Care Diagnostic for
Syphilis

Treponema pallidum is the causative agent of syphilis, a disease associated with sexual and congenital transmission. There has been a recent steep rise in syphilis cases in Arizona suggesting that surveillance methods need to be optimized to track this reemerging disease and focus interventions. Current diagnostics focus on serological detection of patient antibodies, although this technique cannot always distinguish between active and historical infection. Recent studies have demonstrated that saliva is a better clinical matrix for the direct detection of *T. pallidum*, suggesting that a rapid, point of care diagnostic focused on saliva would be more sensitive, faster, and less invasive than current methods. In this study, we propose to develop and validate a lateral flow immunoassay (LFI) to detect *T. pallidum* in saliva. We will pair the LFI with nucleotide amplification to boost the pathogen signal and improve the clinician's ability to identify and treat infections early. We will then screen paired serum/saliva samples collected from confirmed syphilis patients to ensure detection. The outcome of this project will be a validated diagnostic that could be commercialized for routine pathogen surveillance as a tool for improved public health outcomes. Timely detection of active infections is critical for targeted interventions and the improved health of at-risk Arizonans.

Appendix D

2024 Special Research Grants

Marijuana Research		\$ 250,000 / year for 3 years
Marijuana Clinical Trials		\$5,543,324 / year for 5 years
Psilocybin Clinical Trials		\$3,724,853 / for 3 years
*Abstracts are included as submitted by the research team		



Appendix D: 2024 Special Research Marijuana Research

\$79,561 for three years



Madeline Meier, PhD

Arizona State University

Project Title:

Using Electronic Health Record Data to Monitor Cannabis-related Mental Health Emergencies in AZ

The goal of this proposal is to leverage annual emergency department (ED) and inpatient hospital discharge data from all Arizona state-licensed hospitals for the years 2016 through 2023 to answer three main questions. First, is the prevalence of mental illness elevated among ED/inpatient visits related to cannabis compared with ED/inpatient visits unrelated to cannabis? Second, for patients who visit the ED for a cannabis-related reason, what is their risk of a subsequent ED visit for a mental illness-related reason? Third, have ED/inpatient visits related to both cannabis and mental illness increased in recent years, as might be expected given adult cannabis use legalization? ED/inpatient hospital data represent a critical source of information on emerging disease trends and are vital for understanding the magnitude of various public health problems. Further, emergency room visits are among the costliest healthcare visits in the US, and ED presentations themselves are considered a harmful outcome. This project leverages ED/inpatient data to characterize the mental health burden of cannabis use in AZ. The results will be critical for attracting attention and resources within the state for prevention and intervention and for improving the health of Arizonans.

\$170,439 for three years



Kyle Winfree, PhD

Northern Arizona University

Project Title:

Temporal Health Correlates of Cannabis Use Among Arizonans: A Pilot Longitudinal Survey of THC in AZ

In November 2020, the Arizona Smart and Safe Act passed, allowing the legal distribution, possession, and consumption of cannabis in Arizona. With this proposition, the state established a tax revenue for public benefit. In 2021, the state saw roughly \$1.4B in sales, which yielded a tax revenue of \$217M. From this, "\$45[M was allocated] for a variety of different programs and purposes, including the Arizona Teachers Academy, public health, traffic enforcement, education relating to legalizing marijuana, expunging certain criminal records and implementing a social equity ownership program." While the financial benefits to Arizonans are clear and established, the health benefits, or impacts, are not. This project will be the first study to comprehensively examine the temporal pathways of association between cannabis use and both health / disease risk behaviors, and physical / mental health outcomes in Arizona. The inclusion of commodity health wearables will enable us to assess continuous, minute-level physical activity and sleep metrics from a subset of participants, on which innovative multilevel models can be used to analyze the relation with cannabis use over time. Finally, the study design will enable us to examine the mediating / moderating associations between all study variables from which causal inferences between cannabis use, behavior, and outcomes can be determined.

Appendix D: 2024 Special Research Marijuana Clinical Trials

\$5,543,324 for five years



Christopher J. Smith, PhD

Southwest Autism
Research and
Resource Center

Project Title:

Research to Improve
the Health of All
Arizonans Marijuana
Clinical Trials Grant

This project includes two components to investigate the use of marijuana as treatment for mental health conditions. For the first component we will investigate the change in attitudes of key stakeholders (caregivers, adults, and healthcare professionals) from the autism community. For the second component, we will investigate the safety and efficacy of using a marijuana-based investigational medicinal product (MB-IMP) to treat anxiety in adolescents and adults with autism spectrum disorder (ASD). Changes in anxiety is the key endpoint, but changes in core symptoms of ASD and other comorbid symptoms (e.g. irritability) will also be measured. The investigators will collect medical, psychological, and behavioral safety data from all participants at regular study visits (every 1 to 2 weeks) throughout the 8-week double blind, randomized placebo-controlled trial (DB-RPCT). All participants will have the opportunity to continue their participation in 16-week open label study that will allow for the collection of long-term safety and efficacy data. This study will offer valuable information on the health benefits or consequences of using marijuana to treat conditions (anxiety and irritability) that affect a significant number of Arizonans, with or without ASD.

Appendix D: 2024 Special Research Psilocybin Clinical Trials

\$2,749,1141 for three years



**Suzanne Sisley,
MD**

Scottsdale Research
Institute

Project Title:
Psilocybin Whole
Mushroom Research

Indeed, there is literature that suggests that many people are using Psilocybin mushrooms to help with anxiety, depression, and life-threatening illness, and that individuals see Psilocybin mushroom use as a safe and effective way to manage these symptoms (Raisson 2022). Psilocybin is also becoming more available through decriminalization efforts. However, the only clinical trials that have been conducted with high doses of Psilocybin have used synthetic Psilocybin. At present, there is no published data from controlled trials on the safety and tolerability of whole organic Psilocybin mushroom use for individuals with life-threatening illness. Dr. Sisley, learned from veterans/first responders how they were using Psilocybin mushrooms to treat their chronic pain/PTSD and myriad of other ailments. She petitioned DEA to cultivate her own cannabis and Psilocybin mushrooms, and she has successfully maintained this Schedule 1 manufacturer license for three years. Currently, SRI is focused on preparations for submitting a DMF drug master file for FDA approval so that their federally legal Psilocybin mushrooms can be utilized in the very first controlled trials of intact natural mushrooms anywhere in the world. FDA has never evaluated an IND application for whole natural Psilocybin mushrooms so SRI is receiving voluminous inquiries and critiques which must be resolved before FDA authorization can be secured. This Phase 1 trial for whole natural Psilocybin mushrooms has already been submitted to FDA and we are anticipating preliminary approval by March 2024. The Phase 1 application was simultaneously submitted to the IRB committee at Arizona State University. SRI continues to vigorously collaborate with Alira Health CRO on the implementation, management and evaluation of the Phase 1 Open Label Study which should be enrolling patients with life-threatening illness by Spring 2025.

\$975,739 for three years



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Project Title:
Whole Mushroom
Psilocybin for
Treatment of
Obsessive
Compulsive Disorder

This study of Psilocybin whole mushroom aims to 1) advance treatments for obsessive compulsive disorder (OCD) and 2) to understand associated neural mechanism explaining treatment response. This project is a natural extension of our team's clinical research with synthetic Psilocybin for OCD spanning two decades and will advance the field by including mechanistic probes of the neural effects of whole mushroom Psilocybin in OCD patients. We will study tolerability and safety, subjective experience, and efficacy of repeated administration of three different doses of dry Psilocybin whole mushroom. We will enroll 30 medication-free symptomatic OCD-patients from under-served communities as a listed priority. Using a double-masked, dose-controlled approach, 10 participants per group will be randomly assigned to ingest: a) low (10 mg); b) middle (20 mg); or c) high dose (30 mg) of Psilocybin whole mushroom across four dosing sessions each separated by about three weeks. We will use two probes of brain activity including neural network connectivity using functional magnetic resonance imaging (f-MRI), and error-monitoring measurements in electroencephalogram (EEG) to probe pre- and post-study neural changes and explore how these are related to subjective effects, clinical improvement, and dose. Participants will be assessed for twelve months to monitor durability of clinical effects.



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