Arizona Department of Health Services

# Arizona Biomedical Research Commission

## Annual Report 2014–2015

Accelerating Biomedical Research and Innovation in Arizona

## Front Cover and Section Photographs



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# Arizona Biomedical Research Commission

## Annual Report: 2014–2015

**Douglas A. Ducey**
*Governor, State of Arizona*

**Cara Christ, M.D.**
*Director, Arizona Department of Health Services*

### Current Commissioners

General Public

Brandy B. Wells, MS

Medical Community

Peter C. Kelly, M.D.

Mitchell D. Shub, M.D.

Hugo Vargas, M.D.

Scientific Community

George Poste,
D.V.M., Ph.D., D.Sc., L.L.D.

### Commission Staff

Executive Director
Victor Waddell, Ph.D.

Program Manager
Jennifer Botsford, MSPH

Commission Coordinator
Theresa Napoleon

### ADHS Support Staff

Finance Manager
Jeri McAnerny

Administrative Services Officer I
Michelle Cardenas

Procurement Specialist
Ana Shoshtarikj

# Table of Contents

# *Executive Summary*

The Arizona Biomedical Research Commission's (ABRC) mission is "Identifying and supporting innovative biomedical research to improve the health of all Arizonans." In FY 2015, the four core programs accomplished great achievements in working to meet the mission of the ABRC. None of these achievements would be possible without the unwavering support of our valued community partners, Agency leadership, the Governor's Office, and Legislators.

Community support is an integral part of our successes. Our partners worked tirelessly to discuss ways in which existing programs could be leveraged, collaborated on campaigns to increase program awareness, and generously gave their time and resources. Together, we've achieved many program milestones.

## Key Highlights for 2015:

- 20 Cord Blood Units have been released for transplantation to treat or cure life threatening illnesses
- ABRC supported 29 research projects
- Over 675 biospecimens were distributed by the Arizona Biospecimen Locator Program for research
- Three contracts signed with Arizona universities to provide 16 conferences and workshops for local researchers

We look forward to serving Arizona in the years to come and will continue to work towards supporting research, by stewarding the funds wisely, and continuing to leverage community partnerships productively.

# Introduction

The Arizona Disease Control Research Commission was established by the Arizona Legislature and signed into law by Governor Bruce Babbitt in 1984. The mission of the commission was to fund investigators focused on disease problems important to Arizona residents. In the fiscal year 1985-1986, the fund started at $900,000. In 2005, the Arizona Disease Control Research Commission changed its name to the Arizona Biomedical Research Commission, and in 2011, under Senate Bill 1615, ABRC was placed under the direction of the Arizona Department of Health Services.

Today, the ABRC is made up of nine commissioners: three public members, three medical community members, and three scientific community members. The ABRC also includes three program staff: the Executive Director, the Program Manager, and the Commission Coordinator, as well as supporting finance and procurement staff. The ABRC is funded through two funds: the Health Research Fund, a tobacco tax (§ 36-773), and the Disease Control Research Fund, a lottery tax (§ 36-774). Arizona Revised Statutes § 36-271, 36-272, 36-273, 36-274, 26-275 govern the role and duties of the Arizona Department of Health Services and the Arizona Biomedical Research Commission.

The mission and goals of the ABRC are carried out through four key programs: the Research Grants Program, the Research Education Program, the Arizona Biospecimen Locator Program, and the Arizona Public Cord Blood Program. In addition the ABRC supports translational genomics research through a contract with the Translational Genomics Research Institute (TGen), and Alzheimer's research through a contract with the Arizona Alzheimer's Consortium.

## Our Mission

**Identify and support innovative biomedical research to improve the health of all Arizonans.**

## Strategic Map: 2015–2018

The ABRC Strategic Map was developed through a collaborative process between ABRC Commissioners and staff, and updated in 2015. The ABRC Strategic Map is in alignment with the ADHS Strategic Map, and focuses on identifying, funding, and supporting biomedical research; building a strong Arizona presence; and maximizing efficiency and effectiveness of ADHS partnership.

## The Commissioners' Role

The Commission has nine members appointed by the Governor and confirmed by the Senate. The Commission is an integration of three communities: General Public, Medical, and Scientific Research. Each community is represented by three Commissioners appointed for three-year terms.

In accordance with A.R.S. §36-272, the Commission shall advise the department regarding ways to advance research relating to:

1. The causes, epidemiology, and diagnosis of diseases.
2. The formulation of cures for diseases.
3. The development of medically accepted treatment and prevention of diseases, including the discovery and development of new drugs.

The Commissioners guide the work of ABRC by establishing research priorities and identifying key challenges and potential solutions to biomedical research in Arizona. Priorities could range from regional diseases (such as valley fever) to ubiquitous conditions (such as targeted diagnosis or treatment for cancer). Challenges to research may range from increasing availability and access of biospecimens to increasing communication between researchers within fields.

## Commissioner Bios—General Public

**Toni J. Eberhardt, M.B.A.**
Public Relations Director
Banner Medical Group

Commissioner Toni J. Eberhardt is the Director of Public Relations for Banner Medical Group (BMG), Banner Health's employed physician group. In this role, she manages the public relations, marketing, and internal and executive communications for BMG which includes over 1,000 employed physicians across seven states.

Commissioner Eberhardt began her career in the healthcare industry with McKesson, the largest healthcare solutions company in North America. At McKesson, she was the Director of Marketing Communications for McKesson Specialty. As part of her responsibilities, she developed and executed the communications strategies for the Centers for Disease Control and Prevention's (CDC) Vaccines for Children and H1N1 national distributions. In addition, Commissioner Eberhardt worked with bio-tech manufacturers of specialty pharmaceuticals in oncology, rheumatology and other complex disease states to develop patient education and adherence programs.

Commissioner Eberhardt is a fellow from Class IV of the Flinn-Brown Arizona Center for Civic Leadership. She received her Bachelor of Science in Marketing from Arizona State University and also earned her Master of Business Administration.

Commissioner Eberhardt's term ended on April 2, 2015. Her service was greatly appreciated.

### Jeanette K. Shea, M.S.W., L.C.S.W.

Chief Executive Officer
Jeanette Shea & Associates, L.L.C.

Commissioner Jeanette Shea is the owner and Chief Executive Officer for Jeanette Shea & Associates, L.L.C., a full service consultation and training firm. As the former Assistant Director for the Arizona Department of Health Services, Public Health Prevention Services, Commissioner Shea was responsible for providing leadership in public health prevention services, overseeing the bureaus of Women's and Children's Health, Nutrition and Physical Activity, Health Systems Development and Tobacco and Chronic Disease. Trained as a Social Worker, specializing in planning, administration, and community development, she has worked in healthcare for more than 30 years. Commissioner Shea has also served as a liaison with federal, state, and local health agencies.

Commissioner Shea's term expired on April 2, 2015. Her service was greatly appreciated.

### Brandy Wells, MS

Director of Public Affairs and Education
Translational Genomics Research Institute (TGen)

Commissioner Brandy Wells is the Director of Public Affairs and Education at the non-profit Translational Genomics Research Institute (TGen) in Phoenix, Arizona. In this role, she interacts with the science, business and lay communities to interpret the scientific research of the Institute, increase public knowledge of translational medicine and its relevance to healthcare delivery and economic competitiveness. She also directs TGen's science education initiatives including training programs and scientific conferences.

A native Floridian, Commissioner Wells moved to Phoenix from Washington, D.C. in 2009. She earned a BS in Biology and Secondary Education from American University in Washington, DC and MS in Biotechnology from Johns Hopkins University in Baltimore, MD. She previously taught secondary-level science at public schools in Washington, D.C. and Phoenix.

Commissioner Wells is a fellow of the Flinn-Brown Civic Leadership Academy in the Arizona Center for Civic Leadership, sits on the Board of Directors as Treasurer for the Women's Metropolitan Arts Council and volunteers with Hospice of the Valley at the St. Joseph's Hospital and Medical Center Palliative Care Unit.

ABRC welcomed Commissioner Wells on March 17, 2015.

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## Commissioner Bios—Medical Community

### Peter C. Kelly, M.D.

Infectious Diseases Consultant
Arizona Department of Health Services
Bureau of Public Health Emergency Preparedness

Commissioner Peter Kelly is an infectious disease physician. Dr. Kelly was educated at Providence College and Boston University School of Medicine. He completed an Internal Medicine residency and an Infectious Diseases fellowship at the State University of New York at Buffalo. He is a diplomat of the American Board of Internal Medicine and Infectious Diseases.

Commissioner Kelly maintains professional affiliations with the American College of Physicians, the American Society for Microbiology, the Infectious Diseases Society of America and the Arizona Medical Association. Commissioner Kelly is a past president of the Arizona Infectious Diseases Society.

Early in his career, Commissioner Kelly joined the medical staff at Maricopa Medical Center as Chief of Infectious Diseases in the Department of Internal Medicine and later served as President of the Medical Staff. He was active in the Internal Medicine Residency Program and was Program Director for a portion of his time there. He was also Chairman of the Infection Control Committee for many years. He has a career long interest in Coccidioidomycosis and has published in this field.

Currently, Commissioner Kelly is an infectious disease consultant to the Arizona Department of Health Services in the Bureau of Public Health Emergency Preparedness.

**Howard C. Pitluk, M.D., M.P.H.**
Vice President for Medical Affairs and Chief Medical Officer
Health Services Advisory Group (HSAG)

Commissioner Pitluk, HSAG's Vice President for Medical Affairs and Chief Medical Officer, works closely with healthcare providers and stakeholders to furnish information and guidance on the public reporting of clinical data, development of quality improvement plans, and incorporation of evidenced-based quality improvement clinical measures into all aspects of patient care. His special interest in health information technology is focused on the use of electronic health records (EHRs) to advance patient care, enhance quality measurement and outcomes, and facilitate transitions of care between clinical settings.

Commissioner Pitluk has more than 35 years of experience in healthcare. From 1979 through 1998, he practiced general and vascular surgery in Cleveland, Ohio and was an Associate Clinical Professor of Surgery at Case-Western Reserve University College of Medicine. He has held Board Certification from the American Board of Surgery and remains a Fellow of the American College of Surgeons. Upon completion of his Master's Degree in Public Health in 2001, he led the formation of the Institute for Consumer Empowerment, a consortium of healthcare professionals dedicated to the education and self-activation of patients and providers in a holistic approach to wellness and disease prevention.

Commissioner Pitluk joined Health Services Advisory Group in 2001 as a Physician Advisor and has been continuously engaged in the promotion of a multidisciplinary approach to patient centered care leading to his present position.

Commissioner Pitluk's term expired on April 2, 2015. His service on the commission was greatly appreciated.

**Mitchell Dennis Shub, M.D.**
Division of Gastroenterology, Co-Chair, IRB, Phoenix Children's Hospital
Professor and Vice-Chair, Department of Child Health
University of Arizona College of Medicine-Phoenix

Commissioner Mitchell Shub is a Pediatric Gastroenterologist and received his M.D. from the University of Vermont. He completed a residency in Pediatrics at Duke University Medical Center and a fellowship in Pediatric Gastroenterology at Massachusetts General Hospital and Harvard Medical School. After serving on the faculty at the University of North Carolina, Chapel Hill, he joined the full time faculty at Phoenix Children's Hospital (PCH). He previously served as Co-director of the Pediatric Residency Program and as Division Chief of Gastroenterology. Commissioner Shub was elected President of the Medical Staff and served a 2 year term and was appointed as the first Medical Director of Research at PCH.

Commissioner Shub is Vice-chair and Professor, Department of Child Health for the University of Arizona College of Medicine, Phoenix. He has been actively engaged in research throughout his career and recently was part of a team that identified the gene mutation for a rare digestive disorder, microvillous inclusion disease. On a national level, Commissioner Shub has been appointed to various leadership positions in the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition. He also served as the Chairman of the Medical Advisory Committee for the Southwest Chapter of the Crohn and Colitis Foundation of America and was honored with the Chapter's "Physician of the Year Award."

### Hugo Vargas, MD

Professor of Medicine, Chair, Director of Hepatology,
Vice-Chair, Division of Gastroenterology and Hepatology at Mayo Clinic Arizona

Commissioner Hugo E. Vargas is a Transplantation Hepatologist at the Mayo Clinic Arizona. He is a graduate of UC Davis and the Hahnemann Medical College (now Drexel University College of Medicine). He completed a residency in Internal Medicine at the University of Utah Medical Center and a fellowship in Gastroenterology and Hepatology at the University of Pittsburgh Medical Center. He served in the faculty at the University of Pittsburgh as the director of Hepatology and Medical Director of Liver Transplantation. In 2000 he joined the staff of the Mayo Clinic in Arizona as part of the multidisciplinary team in adult liver transplantation. He has served as chair of the Division of Hepatology and currently is the Vice Chair of the Division of Gastroenterology and Hepatology.

Commissioner Vargas' research interests include Hepatitis C viral infection, particularly in the setting of cirrhosis and liver transplantation. Currently he is the Director of the Office of Clinical Research in Mayo Clinic Arizona and the site representative for the Mayo Clinic CTSA. He has kept a leadership profile in national and international societies including the American Association for the Study of Liver Diseases, American Gastroenterological Association, American College of Gastroenterology, and the American College of Physicians.

## Commissioner Bios—Scientific Community

### Kasey L. Benson, Ph.D.

Commissioner Kasey Benson earned her Ph.D. in Biochemistry and Molecular Biology from Colorado State University (Fort Collins, CO), and a B.S. in Biology from Rocky Mountain College (Billings, MT). She is a Good Laboratory Practices (GLP)-trained biochemist with research experience for Covance, Amgen and the Mayo Clinic, among others.

As part of Commissioner Benson's most recent work with the Mayo Clinic, she focused on identifying ways to improve treatment of myeloproliferative neoplasms via the screening of drugs in leukemic cell lines and primary patient samples. Earlier, with Covance, Commissioner Benson was the scientific lead for the immunogenicity program, which included design and conduct of immuno- and bio-assays.

Commissioner Benson's term expired on April 2, 2015. Her service on the commission was greatly appreciated.

**Iman A. Hakim, M.B.B.Ch., Ph.D., M.P.H.**
Dean, Mel & Enid Zuckerman College of Public Health
University of Arizona

Commissioner Iman Hakim is the Dean of the University of Arizona Mel and Enid Zuckerman College of Public Health (MEZCOPH). She is the Mel and Enid Zuckerman Endowed Chair in Public Health and the founding director of the Global Health Institute at MEZCOPH. She is internationally known for her translational research and work on the role of phytochemicals such as green tea and limonene in modulation of oxidative damage and prevention of chronic diseases such as cancer and cardiovascular diseases. Her research focuses on health promotion, dietary interventions, and the role of gene-environment and gene-nutrition interactions in chronic disease prevention. She has been the principal investigator of several large-scale, behavioral change interventions and clinical trials focused on nutrition and cancer prevention; tea consumption and coronary heart disease; nutrition and tobacco; chemoprevention of lung carcinogenesis using green tea; dietary interventions to study the effects of tea consumption on smoking-related oxidative stress; and role of citrus-cancer association in Mediterranean diet.

Commissioner Hakim earned her medical degree from Cairo University in Egypt where she completed her Pediatric residency. She received her Ph.D. in childhood studies from Ain Shams University in Cairo and her MPH from the University of Arizona. Commissioner Hakim worked as a researcher and as an assistant and associate professor at the National Research Center in Egypt. She is a tenured Professor at the University of Arizona. Her current other academic appointments at the University of Arizona include the Arizona Cancer Center, the Sarver Heart Center, the College of Medicine and the Department of Nutritional Sciences at the College of Agriculture and Life Sciences.

Commissioner Hakim's term expired on April 2, 2015. Her service on the commission was greatly appreciated.

**Thomas Lon Owen, Ph.D.**
Professor Emeritus of Biological Sciences
Northern Arizona University

Commissioner T. Lon Owen received his B.A. in Zoology from the University of California, a Master's Degree in Biology from California State University at Sacramento, and his Ph.D. in Physiology from University of California-Davis. He was a National Institutes of Health Postdoctoral Fellow at Michigan State University and visiting associate professor in the Pharmacology Department of the University of Arizona College of Medicine.

Commissioner Owen has chaired the Research Committees of the American Heart Association at both the Arizona affiliate and Southwestern Regional levels. He has been published in the areas of cardiovascular, aging, and environmental physiology. He is Professor Emeritus at Northern Arizona University.

Commissioner Owen's term expired on April 30, 2015. His service on the commission was greatly appreciated.

## Clayton Dehn

Executive Director of Metabolic Diseases, Celerion

Commissioner Clayton Dehn is the Executive Director of Metabolic Diseases at Celerion. He completed a Master of Science degree in physiology at Texas Tech University / Texas Tech Health Sciences Center. His career initially focused on reproductive physiology and endocrinology. He holds a patent for a substance and process for disturbing the inheritance pattern of ion channelopathic disorders and served as the Director of Clinical Research and Development for a small biotech company that was tasked with bringing improved assisted reproductive technologies to market.

Commissioner Dehn then received glucose clamp training from a leading authority on diabetes who was, at the time, an associate professor of medicine at Harvard Medical School. It was then that he refocused his research interests on metabolic disturbances. His research program emphasizes special assessments that offer early predictive signals of safety or efficacy in the development of therapies related to diabetes, obesity, dyslipidemia, hypertension, cardiovascular outcomes, Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH). Commissioner Dehn also serves on the editorial boards of Clinical Research and Trials and the International Journal of Diabetes and Clinical Research.

ABRC welcomed Commissioner Dehn on June 15, 2015.

## Commission Meetings

A.R.S. §36-272(E) states that the Commission shall meet at least quarterly at the call of the chairperson. During 2014, the Commission met four (4) times to evaluate processes, identify a marketing and communications campaign strategy, and review proposed research projects.

For the upcoming year, the Commissioners will be focused on determining funding categories, streamlining the application process, and establishing a regular funding cycle.

| Meeting Date | Meeting Highlights |
|---|---|
| September 12, 2014 | Review Grant Applications |
| September 26, 2014 | Review Grant Applications |
| October 5, 2014 | Review Grant Applications |
| April 1, 2015 | ABRC Strategic Plan, Funding Categories, Funding Cycle |

*Agendas and meeting minutes can be viewed at www.azdhs.gov/biomedical/index.php#commission-meetings

# Financial Summary

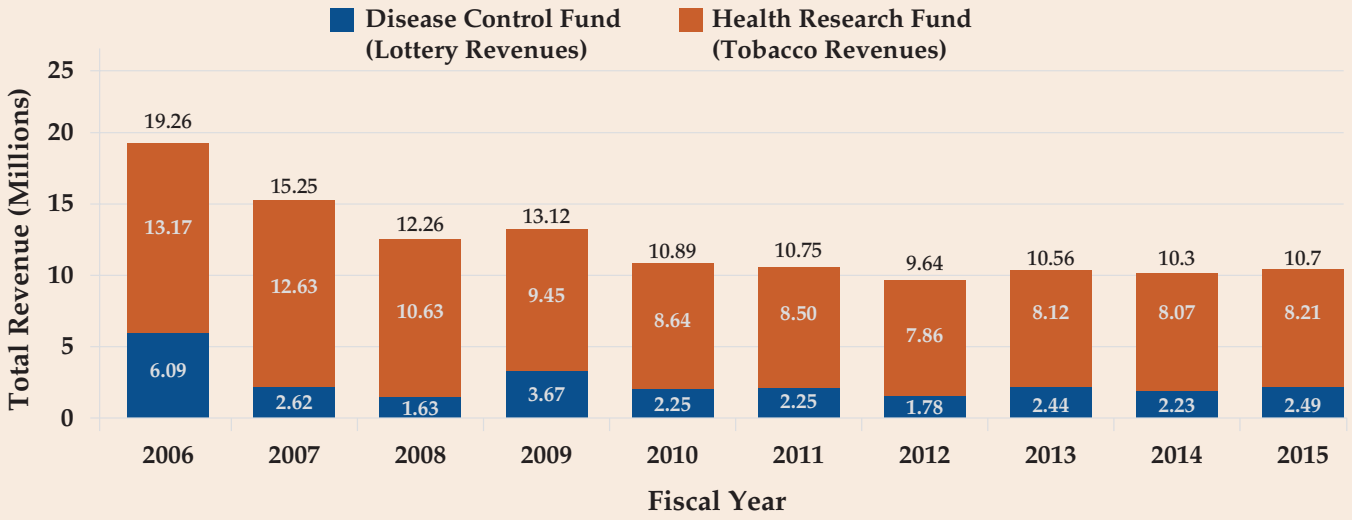
The purpose of the Commission, envisioned by its founders, was to provide competitively awarded funding for research in Arizona. The original funding source was tax penalties and interest from delinquent sales tax collections. Today, ABRC receives its funding from two sources: the Disease Control Research Fund (ARS §36-274) and the Health Research Fund (ARS §36-275).

The Disease Control Research Fund consists of monies received from the Arizona lottery which have been allocated under the Lottery's Health and Welfare programs. The Health Research Fund consists of monies received from the tobacco tax; ABRC receives 5 cents of each dollar deposited into the Tobacco Products Tax Fund and the Tobacco Tax and Health Care Fund. Both the Disease Control Research Fund and the Health Research Fund are non-lapsing, non-appropriated fund sources. In addition to the revenue received from the Arizona lottery and the state's tobacco tax, both funds earn interest on the balances invested with the State Treasurer.

## Revenue

For Fiscal Year 2015, ABRC's total combined revenue was $10.7 million. The distribution of all the revenue sources, seen in the below chart, breaks out as follows: the Disease Control Research Fund equated to $2.49 million or 23% of ABRC's total revenue and the Health Research Fund revenue makes up $8.21 million or 77%.

### Historic ABRC Revenue Distribution

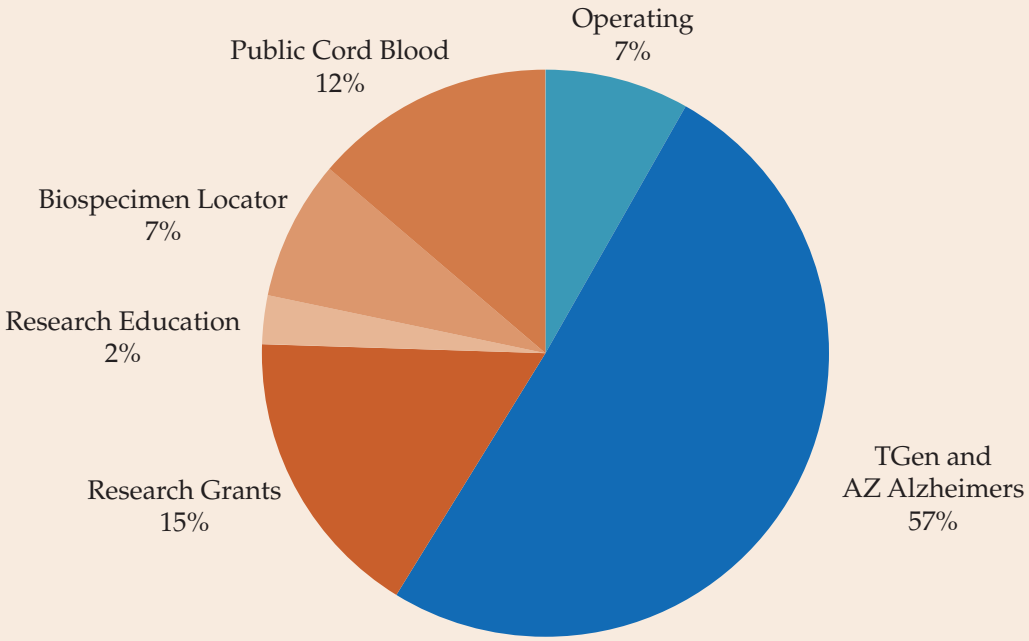


## Expenditures

In FY 2015, ABRC expended $6.7 million. This included $1.1 million in research grants, 17% of all expenditures. Of the research funding, $3.4 million went towards non-competitive research awards, which included the Translational Genomic Research Institute – Tgen ($2 million) and the Arizona Alzheimer's Consortium ($1 million).

To meet the needs of ABRC's three other core programs (Biospecimen Locator Program, Research Education Program, and the Arizona Public Cord Blood Program), a combined total of $1.63 million was expended; these three areas constituted 24% of ABRCs total expenditures. In FY 2015, $0.54 million, 7% of expenditures, was used to cover program operations. The pie chart provides a breakout of ABRC's FY 2015 expenditures.

### ABRC FY 2015 Expenditures



# Program Activities

# Program Activities

The Arizona Biomedical Research Commission is a bioscience leader in Arizona. ABRC's mission, to identify and support innovative biomedical research to improve the health of all Arizonans is accomplished through four distinct programs:

- Research Grants Program
- Research Education Program
- Biospecimen Locator Program
- Arizona Public Cord Blood Program

ABRC's support has resulted in several positive impacts on Arizona.

- Research Projects
  ABRC supported 29 research projects.
- Additional research dollars brought into Arizona
  ABRC funded research was used to apply for 9 new federal grants .
- Jobs
  ABRC provided support to 66 part-time and full-time Arizona researchers, with a total of 32.2 FTEs.
  ABRC issued new Request for Grant Applications (RFGAs) to award up to $4 million in new grants.
- Publications and presentations
  Thirteen (13) ABRC funded researchers submitted publications and presentations.

# Research Grants

# RESEARCH GRANTS

## Program Highlights

Continued support to 29 ongoing research projects

Issued new Request for Grant Applications (RFGAs) to award up to $4 million in new grants

## About the Program

Supporting and developing Arizona researchers to become more successful in securing additional or federal research funding, such as from the National Institutes of Health (NIH), is central to ABRC's mission. The Research Grants program supports early stage investigators and more seasoned investigators who need more data to submit a successful application for federal funding. Funding is provided through a competitive grant process to accelerate promising research toward clinical testing and breakthroughs designed to improve the health of all Arizonans. While our strong emphasis is on funding basic and translational research projects to generate preliminary data, we continue to seek innovative projects that leverage all of Arizona's resources and strengthen collaboration.

Research projects supported include those that may advance the prevention and treatment of tobacco related diseases and addiction, and research that is aimed at the causes, epidemiology, and diagnosis of diseases, the formulation of cures, the medically accepted treatment, or the prevention of diseases, including new drug discovery and development; and that may include behavioral studies and attitude assessments.

## Funding Source Used

Health Research Fund

Disease Control Research Fund

# Ongoing Research Projects

Awards were funded in FY2014 based on three distinct categories:

## Arizona Biomedical Early Stage Investigator Award (AZ ESI):

- The AZ ESI Award was established to help new investigators generate the preliminary data necessary to apply for a larger federal grant.
- Project Period: October 23, 2014 to October 22, 2017
- Up to $75,000 for three years

## Arizona Biomedical Catalyst Award (ABC):

- The ABC Award was established to support investigators whose projects were favorably reviewed by a federal granting agency (i.e. NIH, NSF, or DOD) but were just outside the respective funding score. The goal of this award was to provide funding for the investigator to generate additional data, with the intent to resubmit the application to the respective federal granting agency within twelve to eighteen months of receiving the ABC award.
- Project Period: October 23, 2014 to October 22, 2015
- Up to $125,000 for one year

## Arizona Biomedical Investigator Grant (AZ BIG):

- The AZ BIG is a competitive research grant requiring a rigorous scientific and collaborative approach. Collaborations among investigators could include within an institution, across institutions, or across disciplines.
- Project Period: October 23, 2014 to October 22, 2017
- Up to $250,000 for three years


## Bridget Marie Barker, Ph.D.

Northern Arizona University


### Annual Award Amount

$74,990

### Project End Date

October 22, 2017

### Understanding Early Innate Immune Responses to Infection with Coccidioides, Causal Agent of Valley Fever

In the first year of this grant, we have optimized media and culture conditions that support both the growth of host immune cells as well as development of the spherules (parasitic phase) of the Valley Fever fungus Coccidioides posadasii. This first step was crucial, because methods for studying the early cell-cell interactions did not exist for Coccidioides. We have some preliminary data using a BSL2 (lower biosafety level) strain of C. posadasii and we can now replicate these experiments quickly and efficiently with wild type Coccidioides strains that must be handled within strict biosafety containment (BSL3). Our early data suggests that host alveolar macrophages (an immune cell type that is found in lungs of healthy people) do indeed engulf the fungal conidia (spores that are inhaled from the environment), and that the conidia start to turn into the parasitic form inside macrophages. Because the strain we were working with at the lower safety level does not complete this part of the life cycle, we are now transferring all this work to the BSL3. We have also begun working on creating a gene deletion of the SREBP gene described in our Aim 3. This gene in other fungal pathogens is critical for pathogenicity. Based on our growth experiments, it appears that lower oxygen favors the development of the parasitic phase, and thus we expect that this gene deletion strain will be attenuated and be able to handled in a BSL2 setting. This gene deletion and other information regarding host-interactions during infection will be useful in our exploration for potential drug targets and vaccines for Valley Fever.

### Publications


Lee, M. J., H. Liu, B.M. Barker, B.D. Snarr, F.N. Gravelat, Q. Al Abdallah, T. Xiao, N.V. Solis, M. Lehoux, S.D. Baptista, R.P. Cerone, S.G.W. Kaminskyj, D.C. Vinh, M.-C. Guiot, J.-P. Latgé, T. Fontaine, R.A. Cramer, S.G. Filler, D.C. Sheppard. 2015. Galactosaminogalactan mediates virulence in Aspergillus species by enhancing resistance to NADPH-Oxidase dependent neutrophil killing. PLoS Pathogens. 11(10):e1005187. doi: 10.1371/journal.ppat.1005187. PMID 26492565.

Shubitz, L.F., H.T. Trinh, J.N. Galgiani, M.L. Lewis, A.W. Fothergill, N.P. Wiederhold, B.M. Barker, E.R.G. Lewis, A.L. Doyle, W.J. Hoekstra, R.J. Schotzinger, and E.P. Garvey. 2015. Evaluation of VT-1161 for treatment of coccidioidomycosis in murine infection models. Antimicrobial Agents and Chemotherapy. 2015 Sep 14. pii: AAC.00593-15. [Epub ahead of print] PMID 26369964.

Vogler, A.J., R. Nottingham, K.L. Parise, P. Keim, B.M. Barker. 2015. Effective Disinfectants for Coccidioides immitis and C. posadasii. Applied BioSafety Journal. 20(3): 154-158.

Lewis, E. R. G., V. R. David, A. L. Doyle, K. Rajabi, J. A. Kiefer, P. Pirrotte, and B. M. Barker. 2015. Differences in host innate response among isolates of Coccidioides in a murine model of pulmonary coccidioidomycosis. Eukaryotic Cell. 14(10):1043-53. doi: 10.1128/EC.00122-15. PMID 26275879.

## Bridget Marie Barker, Ph.D. (cont.)

Rosen S., B. Barker, B. Larsen, I. Poojary. 2015. Medical image of the week: fungus ball. Southwest Journal of Pulmonary Critical Care. 10(4):182-3. doi: http://dx.doi.org/10.13175/swjpcc025-15.

### Invited Papers, Panels, Presentations

H.L. Mead, E.R.G. Lewis, A.L. Doyle, M.M. Teixeira, P.S. Keim, B.M. Barker. Fighting Valley Fever: Developing Tools to Investigate a Deadly Human Pathogen. Oral presentation at the Helios Symposium, Phoenix, AZ, July 2015.

## Christian Bime, M.D.

University of Arizona

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Effects of Aerobic Exercise on Asthmatic Responses in Obese Adults

Over the past two decades, there has been a significant increase in the number of asthma patients whose disease is not well controlled. This increase disproportionately affects African Americans and Hispanics living in poverty. Some possible explanations for this observation include increased allergen exposure, poor hygiene, or obesity. Interestingly, it has been observed that the increase in rate of poorly controlled asthma in the United States parallels an increase in rate of obesity. Therefore, we believe that there is an association between obesity and rate of asthma, especially poorly controlled asthma.

Our goal is to elucidate the mechanisms that underlie this association. To achieve this goal, we are pursuing an innovative pilot study to address the following specific aims: recruit and retain obese adults with asthma for a protocol that includes 12 weeks of moderate intensity aerobic exercise. In a randomized controlled manner, we will measure changes in obesity-related markers, markers of inflammation, and overall asthma control between those participants randomized to moderate intensity aerobic exercise versus those randomized to no exercise. This pilot study is important because to date, no human studies have determined the effects of aerobic exercise on pro-inflammatory markers on asthma.

This is a randomized controlled experiment and the intervention is a proven community-based exercise prescription guided by exercise coaches. Information about asthma control, exercise fitness level, lung function, blood samples for inflammatory markers is collected at baseline and at the end of 12 weeks for all patients enrolled for the study. Currently, 10 patients out of an anticipated total of 30 patients have been recruited for the study.

Information obtained from this pilot study will be the bases for submission of a large, multi-center and multi-investigator NIH grant through the American Lung Association Airways Clinical Research Centers (ALA-ACRC).

## Timothy Bolger, Ph.D.

University of Arizona

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Modulation of RNA Dynamics in Medulloblastoma by DDX3/Ded1

In Arizona, cancer afflicts tens of thousands of people of all ages, including children, each year. The most common brain cancer in children is called medulloblastoma, and even survivors suffer from developmental defects from current treatments. Therefore, more research into the causes of medulloblastoma is needed in order to design more targeted therapies. Recently, a particular gene (called *DDX3*) was found to be frequently mutated in medulloblastoma, although it had not previously been linked to this disease. Our study is examining how the mutations in the *DDX3* gene cause problems in cells that lead to medulloblastoma. Thus far, we have found that while the mutations cause significant effects on cells, they are not equivalent to simple non-functioning versions of the gene. Instead, the effects of the mutations are complex and somewhat variable, but currently we are examining possible shared aspects in order to determine which effects are most likely to be responsible for promoting cancer. In addition, we are also examining other cellular molecules that may interact with *DDX3* in cancer. This research has led to new discoveries in how *DDX3* (and its counterparts in other organisms) may be involved in mediating responses to changes in the extracellular environment. In the coming year, we anticipate making further progress in both of these research areas with the eventual goal of providing the biological framework for designing new treatments for medulloblastoma and other cancers.

### Invited Papers, Panels, Presentations

Bolger, TA. D-E-A-D and Alive: Controlling mRNA-Protein Dynamics in Normal and Cancer Cells. RISE Colloquium, San Francisco State University. November 2014.

Bolger, TA. D-E-A-D and Alive: Controlling mRNA-Protein Dynamics in Normal and Cancer Cells. Basic Medical Science seminar series, University of Arizona, College of Medicine, Phoenix, March 2015.

Aryanpur, PP. Working Under Stress: Insights into the Regulation of the DEAD-Box Protein Ded1. Joint Biology Research Retreat, Oracle, AZ. Oct 2015.


## Elena De Filippis, M.D., Ph.D.

Mayo Clinic


### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

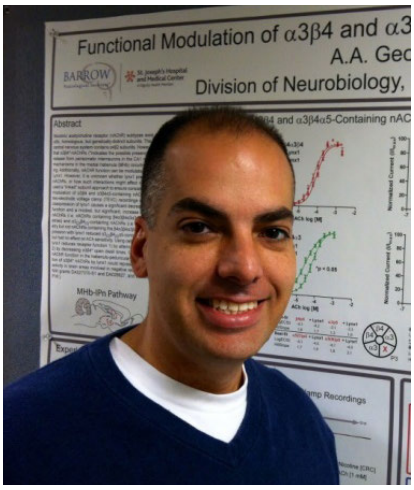
### Response Immunomodulatory Role of Eosinophils in Determining Inflammation and Insulin Sensitivity in Human Adipose Tissue

Obesity affects over 60% of the population in Arizona and is characterized by a state of low-grade, chronic **inflammation** of adipose tissue (AT), the scientific term for fat. In presence of obesity several metabolic dearrangements lead to development of mild to severe elevation of blood glucose (sugar) up to development of frank diabetes (uncontrolled blood sugar levels). Prior to the diagnosis of diabetes, obese people can be found to have mild elevation of fasting blood sugar levels together with elevation of insulin levels, a hormone normally produced by our pancreas in response to food intake. This state is called **insulin resistance**. In human fat, the relation between inflammation and insulin resistance is not clear. This project aims to gain more information on the role of a cell component of the inflammatory system, the eosinophils in modulation of the immune environment in human fat. In addition we wanted to evaluate whether the eosinophils may reduce inflammation and insulin resistance in human fat. We will test the hypothesis that eosinophils promote insulin sensitivity in human AT in two ways: *first* by releasing some mediators to sustain an anti-inflammatory enviroment by acting on promotion of other cell populations (alternatively activated M2 macrophages), and *second* by increasing generation of small anti-inflammatory molecules called protectins and resolvins.

In our first aim we proposed to evaluate whether differences in eosinophil content between different fat depots of lean and obese subjects and determine the correlation with insulin sensitivity assessed by euglycemic-hyperinsulinemic clamp. Currently, we have recruited half of the obese group, while we have not enrolled any of the lean subjects. Because of the nature of this aim, we cannot begin analysis of the collected samples unless we have a small number of "control" subjects. We are considering opening recruitment in local surgical clinic outside Mayo Clinic to increase our pool of potential volunteers.

In our aim 2, we sought to collect subcutaneous fat from obese, subjects before and after 3 months of fish oil supplementation to investigate whether supplementation of healthy fat improves adipose (fat) metabolism and inflammation via changes in eosinophil content, levels and/or generation of specific mediators. In the next few weeks we will complete the first 3 subjects (afetr 3 months of fish oil supplementation) and will begin analysis of data. Recruitment is still ongoing for this aim.

Altogether this study will define whether, like in mice, eosinophils play a crucial role in human fat metabolism and inflammation and potentially highlight new therapeutic targets.




## Andrew George, Ph.D.

St. Joseph's Hospital and Medical Center

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Amyloid Beta-induced Homeostatic Neuronal Instability in Basal Forebrain Cholinergic Neurons

Alzheimer's disease (AD), a progressive neurodegenerative disorder, is one of the most common causes of mental deterioration in the elderly. Brain regions associated with higher cognitive functions, particularly the neocortex, are affected by the characteristic pathology of AD. Several studies have correlated the cognitive severity associated with early-onset AD with a loss of basal forebrain cholinergic neurons. However, the precise mechanisms underlying cholinergic neurodegeneration and subsequent memory impairments remain unknown. During the first year of the proposal, my goal was to investigate the relationship between nicotinic receptor (nAChRs) function, elevated levels of amyloid-beta, and basal forebrain neuronal homeostatic stability. Using a combination of neuropharmacology and in vitro electrophysiology I have characterized the intrinsic functional properties of several populations of cholinergic neurons within the basal forebrain in the presence or absence of amyloid-beta. In addition, I have successfully implemented the use of transgenic mouse models to facilitate my investigation into the role of nAChRs in amyloid-beta induced alterations neuronal excitability. In anticipation of experiments to be carried-out in the second year of the proposal, I have successfully engineered and tested several concatenated versions of α7β2 nAChR subtypes that potentially underlie the escalating neuronal excitation, neurodegeneration and early cognitive impairment associated with AD. Concatenated versions of α7β2 nAChRs will be used to identify the precise receptor compositions that confer high sensitivity to amyloid-beta and, in turn, the corresponding homeostatic alterations in basal forebrain neuronal excitability.

## Karmella Haynes, Ph.D.

Arizona State University

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Synthetic Biology for Cancer Research

Disease states such as cancer arise from the disruption of chromatin, the central DNA-protein structures that package human genetic material. Cancer has led to over 10,000 deaths for Arizonans each year. The resistance of cancer to conventional treatment is a tenacious problem. Dr. Haynes has developed novel synthetic chromatin proteins that interfere with cancer-associated histone methylation signals. So far, Dr. Haynes' group has successfully transferred synthetic DNA into two different types of breast cancer cells (under lab conditions) and detected the production of the synthetic chromatin proteins. The next steps are to monitor the activity of genes that will reverse the process of cancer within these cells. The outcome will be a protein-based treatment for cancer that activates anti-cancer genes within breast cancer cells.

### Invited Papers, Panels, Presentations

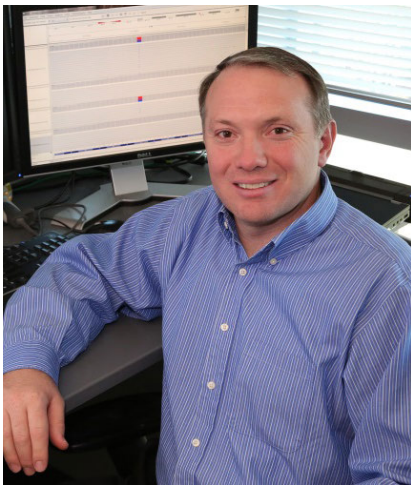
Haynes, K.A. "Engineering of Human Chromatin." Synthetic Biology Working Group, MIT, Boston, MA. Invited Talk, October 2014.

Haynes, K.A., Hom C., Damadzadeh B., Crawford M. "Foundations for the Engineering of Human Chromatin." Keck Annual Research Conference, Houston, TX. Invited Talk, November 2014.

Haynes, K.A., Hom C., Damadzadeh B., Crawford M. "Foundations for the Engineering of Human Chromatin." Cold Spring Harbor Asia. Suzhou, China. Invited Talk, December 2014.

Haynes, K.A., Hom C., Gardner, C. "Manipulating Human Chromatin with Synthetic Proteins." Institute for Biological Engineering Annual Conference, St. Louis, MO. Invited Talk, March 2015.

Haynes, KA. Epigenetic Engineering of Human Cells with Fusion Proteins. Gordon Research Conference. Waltham, MA. Aug 2015.




## Jesse Hunter, Ph.D.

Translational Genomics Research Institute


### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Identification and Functional Characterization of Novel Neuromuscular Disease-Causing Variants in Arizona Infants and Children

Neuromuscular disease (NMD) accounts for a significant proportion of infant and childhood mortality and devastating chronic disease in Arizona. Diagnosis of the underlying genetic cause of a child's NMD is challenging as there are many thousands of unique or rare genetic mutations that can result in overlapping NMD symptoms. Physicians face these challenges with limited resources, testing for mutations one at a time, rarely resulting in confirmation of the causal genetic aberration. Furthermore, there are no effective therapies for most NMDs. Without a genetic diagnosis, patients are left without answers, physicians cannot provide optimal treatment, and researchers cannot develop effective therapeutics. Whole exome sequencing (WES) is a contemporary and powerful technique that can overcome genetic diagnostic limitations by sequencing all genes simultaneously. The primary goals of this project are to use WES to identify disease causing mutations in Arizona infants and children with NMD and to study these new mutations to lead to development of effective therapeutic strategies. Currently we have completed enrolling 16 families in our study, with 2 more families currently being enrolled. These families include 70 individuals with 26 affected individuals (21 affected Arizona infants and children and 5 affected first degree relatives). We have completed WES for 12 families including 45 individuals; with 4 more families (including 17 individuals) currently being sequenced. We have identified probable pathogenic mutations in 7 genes in 9 of 12 families that have completed WES, for a genetic research diagnostic rate of 75%. Probable pathogenic mutations identified in research have been clinically confirmed for 6 of these 9 families. In addition to these genetic studies, we are replicating probable pathogenic mutations in cell culture to work toward better understanding of disease mechanisms and future effective treatments. We have identified several mutations in the *SCML2* gene as the probable cause of a novel X-linked infantile lethal neuromuscular disease. We are using a gene editing technology called *CRISPR/Cas* to replicate *SCML2* mutations in cell culture. With this technology we have begun editing the *SCML2* gene in neuron-like cells and myoblast cells (muscle cell progenitors). We generated ~1800 clones that may have the *SCML2* gene altered by *CRISPR/Cas*. We have screened a small number of these clones by sequencing the *SCML2* gene, and have found that it appears to be edited, but we will need to further sub-clone these cell lines to get pure, unmixed cell lines. Our research is at the leading edge of personalized medicine and provides answers, understanding, and hope for Arizona families with infants and children suffering from NMD. We extend our deep gratitude to the families that willingly participate in our research study, even though they are enduring the difficulties and devastation of NMD, and thank the Arizona Biomedical Research Commission for their generous support.

## Jesse Hunter, Ph.D. (cont.)

### Invited Papers, Panels, Presentations

Jesse M. Hunter, Chris Balak, Mary E. Ahearn, Christophe Legendre, Winnie Liang, Ahmet Kurdoglu, Jason Corneveaux, Megan Russell, Matt Huentelman, David Craig, John Carpten, Saunder M. Bernes, Lisa Baumbach-Reardon. Identification of New Genes and Pathways for Rare Infantile Forms of Myopathies and Neuromuscular Disorders. ASHG (Baltimore, MD), 5-6pm, Oct. 7, 2015, Poster 2885W.

Jesse M. Hunter, Mary E. Ahearn, Jeff Kiefer, Brunhilde Wirth, Waibhav Tembe, Winnie Liang, Ahmet Kurdoglu, Jason Corneveaux, Megan Russell, Matt Huentelman, David Craig, John Carpten, Judith Hall, Saunder M. Bernes, Lisa Baumbach-Reardon. Novel Genetic Mutations that Result in Rare Congenital Neuromuscular Disorders and Myopathies. ACMG, Mar. 2015, Poster #560.

**Anita Koshy, M.D.**

University of Arizona

**Annual Award Amount**

$75,000

**Project End Date**

October 22, 2017

## Harnessing Evolution: Defining the Neuroprotective Effects of Chronic Toxoplasmosis

As we naturally age, our thinking abilities wane. We have very little understanding of the mechanisms that cause this decline, but, recently, age-associated increases in brain inflammation have been implicated in playing a role in this decline. The goal of this study is to try to understand how to limit age-associated brain inflammation in the hopes of developing new treatments to slow or reverse age-associated cognitive decline. Our approach is to study the brain-parasite interaction of a common brain parasite (Toxoplasma gondii) which naturally and silently infects the brain of up to a third of the world's population. Toxoplasma's ability to remain quietly in the brain suggests that the parasite decreases the brain's immune response, a capability with therapeutic potential and supported by recent laboratory studies showing that chronic toxoplasmosis can be neuro-protective in models of stroke and Alzheimer's disease. The goals of our study are to: 1) profile the distinct brain immune responses elicited by the genetically divergent type II and type III *Toxoplasma* strains, 2) identify the brain regions that different strains of *Toxoplasma* hone to, and 3) determine if brain functions served by parasite-enriched regions are protected against age-associated cognitive decline. To date, we have established that *Toxoplasma* type III parasites provoke a stronger T-cell and macrophage/ microglial pro-inflammatory response than type II parasites. Future work will confirm these findings and extend them into more chronic stages of disease. We are currently beta-testing our semi-automated system for detecting brain regions enriched for parasites interactions. Once fully operational, we will be able to map the enriched regions rapidly. In anticipation of this mapping, we have infected mice with either type II or type III parasites, and will perform cognitive testing on these mice in approximately 12 months. The completion of these studies will establish a global and comprehensive program in which to identify the cellular and molecular mechanisms that underlie *Toxoplasma's* neuroprotective effects. The identified mechanisms will offer new therapeutic targets for preserving our cognitive capacity even in the late-stages of life.


## Lalitha Madhavan, M.D., Ph.D.

University of Arizona


### Annual Award Amount

$74,943

### Project End Date

October 22, 2017

### Rejuvenating the Aging Brain by Improving Stem Cell Function

Aging is a phenomenon that carries an increased risk of a number of diseases, including neurodegenerative conditions such as Alzheimer's and Parkinson's disease. This creates an enormous socioeconomic impact since the aging population is rapidly growing worldwide. In fact in Arizona, 1 in 4 people will be above the age of 60 by year 2020. Our studies are motivated by this important concern, and develop a novel stem cell strategy to tackle detrimental age-related changes in the brain and to promote healthy aging.

Due to their regenerative ability, stem cells can promote the replacement and repair of dead or dysfunctional brain cells and are promising candidates to foster therapeutic approaches to promote healthy aging and treat neurodegenerative diseases. However, in order to exert such beneficial effects, stem cells need to survive and function efficiently in an aged brain environment. A significant challenge is that aging retards the regenerative capacity of brain stem cells, creating roadblocks towards developing effective stem cell therapies. In this context, our lab has identified the progressive reduction of a specific molecule called Nrf2, within the stem cells, as a mechanism contributing to their regenerative decline with advancing age. Given this, the current ABRC funded research project aims to increase Nrf2 within brain stem cells to investigate the potential utility of this approach to counteract the decline in stem cell regeneration during aging. The experimental plan involves aging animals which will (a) directly receive Nrf2 into existing brain stem cells via a gene transfer technology, or (b) alternatively be administered externally grown 'young' stem cells that have high Nrf2. So far, we have successfully created the reagents required for the gene transfer of Nrf2. Using these reagents we have delivered Nrf2 specifically into the brain stem cells of the aging animals. Presently, we are analyzing the long-term effects of increased Nrf2 in the brain stem cells by examining both the behavior and brain tissues of the treated animals.

These studies will provide important information on the potential of Nrf2 to improve stem cell function in the aging brain. They will also provide a foundation for future endeavors geared towards building clinically effective stem cell-based approaches to support healthy aging and treat age-related neurodegenerative disorders—which is our ultimate goal.

### Publications


Corenblum MJ, Ray S, Remley QW, Zhang DD, Min L, Harder B, Barnes CA, and Madhavan L. Reduced Nrf2 expression mediates the decline in neural stem cell function during a critical middle-ages period. Abstact submitted to Aging Cell.


### Invited Papers, Panels, Presentations

MJ Corenblum, S Ray, Remley QW, Long M, B Harder, DD Zhang, CA Barnes, and Madhavan. Abstract Title: A role for Nrf2 in neural stem cell function during aging. Society for Neuroscience annual meeting, Chicago, IL, October 17-21, 2015.


## Diego Mastroeni, Ph.D.

Banner Health (October 23, 2014–June 30, 2015)

Arizona State University (July 1, 2015–present)


### Annual Award Amount

$74,782

### Project End Date

October 22, 2017

### A Novel Compound to Protect Mitochondria against Oligomeric Abeta Toxicity: Implications for the Synapse

Synaptic dysfunction, or the loss of connections between neighboring nerve cells is one the earliest known problems in Alzheimer's disease (AD). Recent studies have suggested that oligomeric amyloid beta, a protein that is found in the Alzheimer's brain is responsible for the synaptic dysfunction. How exactly this occurs and what exactly are the main targets are yet to be fully understood. This proposal aims to look at the underlying targets which oligomeric abeta can affect the synapse, and offer a therapeutic approach to treating this problem.

There are huge numbers of variables that are affected by Abeta oligomers in AD, and in this proposal we focus on selected aspects of four: energy, epigenetics, chromatin structure and expression of synaptic genes. Aim 1) treat nerve cells with Abeta oligomers, and determine the effects of selected aspects of mitochondrial, epigenetic, chromatin structure and expression of synaptic genes; 2) obtain the same data as in (Aim 1) from identified neurons by laser capture from AD and non-diseased brains; 3) obtain the same data as in (Aim 1) and (Aim 2) from identified neurons by laser capture from the Osaka mouse model of AD; 4) compare data from (Aim1) (Aim 2) and (Aim 3); and 4) quantify same dependent variables in Abeta treated SY5Y cells that have had a)prior treatment with a novel coenzyme Q10 analog or b) treatment with a novel coenzyme Q10 analog following exposure to oligomeric Abeta at doses and times selected on the basis of Specific Aim 1.

Thus far the project has yielded little as far as challenges, but some important accomplishments have been made: 1) starting a neuronal cell line 2) synthesizing the oligomeric amyloid beta 3) synthesizing co-enzyme Q10 analogue 4) differentiating the sy5y's 5) treating and testing the cell model with select mitochondrial assays 5) isolating RNA, DNA and Protein from treated cells 6) prepared samples for RNA sequencing, chromatin analysis and western blotting 7) determined protein, RNA and DNA quality 8) selecting cases for Aim 2, and 9) secured brain tissue from the Mori mice (Aim 3) 10) Started cutting the Mori mice (Aim 2) 11) all the tissue from the brain bank has been secured (Aim 3), and most recently the samples from (Aim 1) have been sent to the translational genomics institute for RNA sequencing and analysis.

### Publications


Diego Mastroeni †‡, Omar M. Khdour §, Pablo M. Arce §, Sidney M. Hecht *§, and Paul D. Coleman *† *Novel Antioxidants Protect Mitochondria from the Effects of Oligomeric Amyloid Beta and Contribute to the Maintenance of Epigenome Function. ACS Chem. Neurosci.*, 2015, 6 (4), pp 588–598.

Diego Mastroeni, Elaine Delvaux, Jennifer Nolz, Yuyan Tan Andrew Grover, Salvatore Oddo, and Paul D. Coleman. Aberrant Intracellular Localization of H3k4me3 Demonstrates an Early Epigenetic Phenomenon in Alzheimer's Disease. Received: June 23, 2015; Received in revised form: July 27, 2015; Accepted: August 14, 2015; Published Online: September 09, 2015.

## Diego Mastroeni, Ph.D. (cont.)

### Invited Papers, Panels, Presentations

Presentation ASU School of Life Sciences seminar series. "Epigenic Dysregulation and the Pathophysiology of Alzheimer's Disease." Arizona State University, Phoenx, AZ, October 12, 2015.

Presentation at Arizona Alzheimer's Consortium Retreat. Overview of research project. Winslow, AZ, March 6, 2015.

## Chinh Nguyen, M.D.

Biomedical Research and Education Foundation of Southern Arizona

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Use of Whole Blood Immune Assay to Determine the Prognosis of Non-menigeal Coccidioidomycosis

Coccidioidomycosis, commonly known as Valleyfever, remains a major fungal infection in Arizona. Management of Valley fever can be challenging. Many cases resolve without intervention but others result in severe disease and hospitalization. The clinical and laboratory tools to clearly distinguish which patients may have a poor outcomes are currently lacking. Our laboratory has been developing a blood test that measures the protective immune response to Valley fever. It works by incubating blood from subjects with a killed portion of the Valley fever fungus and then measuring up to30 chemicals, called cytokines, released by the incubated immune cells. This test is analoguous to the recently approved skin test but, because the blood test measures multiple cytokines, it provides a wealth of information about the immune response of each patient studied with Valley fever infection. To date, we have collected and incubated the blood of 13 subjects with newly diagnosed Valley fever. Their samples are now stored. In addition, we have tested our assay system by incubating the blood of two donors with previously diagnosed Valley fever and assayed these for cytokines. We have found that the assay gives predictable and appropriate results, including in positive and negative control samples.

Our plan is to continue to collect samples from subjects with newly diagnosed Valley fever, store these and then, when samples from 25 subjects have been obtained, test these. The clinical outcome of these subjects after 6 months will be compared to the pattern of released cytokines seen from the blood test results at the time of diagnosis. After this, we will continue testing subjects to further refine the results. From this, we hope to be able to ascertain patterns of blood cytokine responses that predict the outcome of Valley fever. This should allow us to more specifically and appropriately provide care to this group of patients.

## Benjamin Renquist, Ph.D.

University of Arizona

### Annual Award Amount

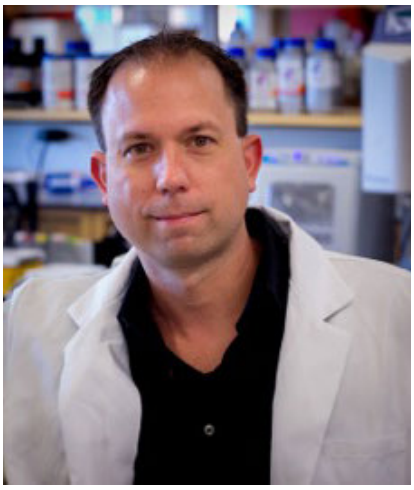
$74,867

### Project End Date

October 22, 2017

### Targeting the Hepatocyte/Vagal Nerve Communication to Develop Therapeutics for Type 2 Diabetes

The incidence of Type 2 diabetes in Arizona has more than doubled since 1990. Liver fat accumulation, a hallmark of insulin resistance, is a co-morbidity common in 60-80% of Type 2 diabetics. In fact, the severity of liver fat accumulation is directly related to the severity of insulin resistance. We propose that liver fat accumulation induces hyperinsulinemia and insulin resistance by communicating nutritional status to the peripheral nervous system. Preliminary data from our lab shows that pharmacologically mimicking the effects of lipid accumulation in hepatocytes inhibits activity of the hepatic afferent nerve and increases serum insulin. Studies proposed in this grant aim to understand the mechanism by which hepatocytes communicate to the vagal afferent nerve. The Renquist laboratory is uniquely suited to perform these studies, as we have developed an electrophysiology technique that allows for simultaneous measurement of liver cell membrane potential and hepatic vagal afferent nerve activity, while using a virus to specifically manipulate liver cell neurotransmitter release. Studies proposed in this grant will justify development of pharmacological agents that aim to treat type 2 diabetes by governing hepatocyte communication to the peripheral nervous system.



## Dominik Schenten, Ph.D.

University of Arizona

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Innate Control Mechanisms of Adaptive Immunity to Live Infections

The detection of microbes such as bacteria, viruses, and fungi by the immune system induces many molecular signals that collectively control the activation and outcome of immune responses. However, the signals necessary to induce protective immunity against future infections are currently poorly understood. Our preliminary work indicates that the immune response to immunizations with dead microbes depends on specific signals that are dispensable for immune responses to live infections. This observation suggests a fundamental difference between the regulation of immune responses to immunizations and to infections. We are currently analyzing the immune response in mice infected with the model pathogen Listeria monocytogenes in order to compare this response to immunizations with heat-killed Listeria. Specifically, we are investigating the role of two signaling molecules, namely IL-1 and IL-6, in the regulation of the immune response to live and dead Listeria. This work will help us to determine which immune signals distinguish the immune responses to live and dead microbes. The identification of such signals will be critical for understanding of the parameters that define protective immune responses and is essential for the development of new vaccine strategies.

### Invited Papers, Panels, Presentations

Seminar "The Role of TLR-induced IL-1 and IL-6 in the Control of Adaptive Immunity." Department of Basic Medical Sciences, College of Medicine - Phoenix, University of Arizona. December 11, 2014.

**Brittany Dugger, Ph.D.** (until November 2015)
**Geidy Serrano, Ph.D.** (as of November 2015)
Banner Health

### Annual Award Amount

$74,800

### Project End Date

October 22, 2017

### The Effects of APOE Genotype on APP/Aβ Levels in Human Liver and Brain

It has been established for nearly 30 years that Apolipoprotein E (APOE) genotype alters the risk of developing Alzheimer's disease (AD). Although great advances have been made in understanding these alterations in the brain, little is known of how this genotype may alter peripheral tissues in AD. This is especially critical since genotypes are present in all cells and understanding if a genotype known to alter the brain can also alter peripheral organs. This study utilizes an innovative approach by examining the liver, which is known to synthesize ApoE and is the major clearing point for one of the main protein aggregates in AD, amyloid-β (Aβ). Our goal is to investigate whether Aβ levels are dependent on APOE genotype in normal controls (NC) and AD and how these proteins in the liver relate to brain. Over the last year we analyzed post-mortem human liver and brain tissue from the Brain and Body Donation Program (BBDP) located at the Banner Sun Health Research Institute in Sun City, Arizona. The BBDP is an autopsy-based, research-devoted brain bank, where consented elderly volunteers living in Maricopa county and metropolitan Phoenix, Arizona can leave a legacy through donating their time during life through clinical evaluations and then their tissues after death. If successful, this we could provide an initial foundation for the discovery of peripheral biomarkers that could help in the understanding, early detection, and diagnosis of AD utilizing the legacy left by Arizonians who donated their tissues to the BBDP.

## Sarah Stabenfeldt, Ph.D.

Arizona State University

### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Redecorating the Neural Injury Landscape to Promote Regeneration

Traumatic brain injury (TBI) is the leading cause of injury related death in America. However, current clinical treatment modalities for TBI focus on minimizing the secondary symptoms and complications associated with TBI; however, no clinical treatments currently exist to address the underlying neuropathology for any level of TBI severity ranging from mild to severe. The long-term goal of the proposed research is to develop novel intervention strategies that directly tackle neurodegenerative cues and promote regeneration. This proposal is the first step in achieving our long-term goal whereby our primary objective is to mask and "redecorate" the neurodegenerative cues in injured neural tissue. The proposed work will employ a molecular biology screening technique to identify molecules that bind to markers that are more abundant in injured neural tissue versus healthy neural tissue. These targeting molecules will then be investigated to mask and "redecorate" the injured tissue with regenerative cues. Ultimately, this approach will contribute significant advances to improved understanding of how the extracellular microenvironment impacts neural regeneration after brain injury. Our group has successfully completed the first phase of the biopanning assays to identify unique targeting domains to neural pathologies. We look forward to continued success with this project.

### Invited Papers, Panels, Presentations

Song, S, Marsh, W, Stabenfeldt, SE*. "Exploiting astrocytic phenotypic alterations to augment the neural injury microenvironment". Gordon Research Conference – 2015 Biomaterials & Tissue Engineering, Girona, Spain, July 2015. *Award for Outstanding Junior Faculty Poster Presentation.

Arens, D, Witten, A, Song, S, Marsh, W and Stabenfeldt, SE. "Targeting the neural injury microenvironment after traumatic brain injury." Submitted to the World Congress of Biomaterials (May 2016).


## Theresa Thomas, Ph.D.

Arizona State University


### Annual Award Amount

$75,000

### Project End Date

October 22, 2017

### Experimental TBI-Induced Endocrine Dysfunction: Timing, Mechanisms and Treatment

As many as 20-55% of patients with a history of traumatic brain injury (TBI) experience chronic endocrine dysfunction, leading to impaired quality of life, impeded rehabilitation efforts, and lowered life expectancy. Endocrine dysfunction after TBI is thought to result from acceleration-deceleration forces to the brain within the skull, creating enduring hypothalamic and pituitary neuropathology, and subsequent hypothalamic-pituitary endocrine (HPE) dysfunction. The first set of experiments were designed to test the hypothesis that a single diffuse TBI results in chronic dysfunction of testosterone, and corticosterone (CORT), a glucocorticoid released in response to stress, with evidence of structural damage to the HPE axis. We used a rodent model of diffuse TBI induced by midline fluid percussion (mFP). At 2 months post-injury, circulating levels of CORT were evaluated at rest, under restraint stress and in response to dexamethasone, a synthetic glucocorticoid commonly used to test HPE axis regulation. Further, we assessed changes in injury-induced neuron morphology (Golgi stain) and neuropathology (silver stain) in the paraventricular nucleus (PVN) of the hypothalamus. Resting plasma CORT levels were decreased at 2 months post-injury and there was a blunted CORT increase in response to restraint induced stress. These changes in CORT were observed concomitantly with altered complexity of neuron processes in the PVN over time. Results provide evidence that a single moderate diffuse TBI leads to hormonal and structural changes, as it pertains to the HPE axis, which can contribute to the persistence of endocrine dysfunction. Future experiments aim to evaluate additional HP-related hormones and anatomical pathology following diffuse TBI.

### Publications


R.K. Rowe, B.M. Rumney, H.G. May, P.D. Adelson, S.M. Harman, P. Permana, L. Lifshitz, T.C. Thomas. Diffuse traumatic brain injury affects chronic endocrine function and alters dendritic morphology in the paraventricular nucleus. Manuscript–Submitted 7-15-2015.


### Invited Papers, Panels, Presentations

T.C. Thomas, R.K. Rowe, B.M. Rumney, H.G. May, C.D. Conrad, P.D. Adelson, S.M. Harman, P. Permana, L. Lifshitz. Experimental diffuse brain injury leads to chronic corticosterone dysfunction with evidence of comprised neuron morphology in the hypothalamus. Third Annual Phoenix Children's Hospital Research Day, The 33rd Annual National Neurotrauma Symposium. Santa Fe, MM. June 29-July 1, 2015.

T.C. Thomas, R.K. Rowe, B.M. Rumney, H.G. May, C.D. Conrad, P.D. Adelson, S.M. Harman, P. Permana, L. Lifshitz. Diffuse traumatic brain injury affects chronic corticosterone levels and alters neuron morphology in the paraventricular nucleus. 45th Annual Meeting for the Society for Neuroscience. Chicago, IL. 2015


## Mingwu Wang, M.D., Ph.D.

University of Arizona


### Annual Award Amount

$74,999

### Project End Date

October 22, 2017

### NHE8 and the Ocular Surface Homeostasis

Much of Arizona has a typical desert climate and overall the lowest annual average relative humidity in the US. Thus, dry eye disease is endemic in our state. Dry eye disease is mainly caused by insufficient tear secretion and/or increased tear evaporation. The conjunctiva modulates the tear film by maintaining an optimal balance of water and electrolytes in order to protect the ocular surface. In our study, we have verified that lack of a sodium/hydrogen exchanger, NHE8, can lead to dry eye in mice. To corroborate with animal study, we have collected ocular surface tissues from subjects with and without dry eye. The preliminary results showed that with the level of NHE8 being low in the conjunctival tissue, the level of Muc5ac expression, one major ocular surface secreted mucin, also decreases. Such a correlation is consistent to what is seen in mice. Next, we will investigate the mechanism of such correlation and hope that our discoveries may help unravel potential new therapies for dry eye disease.

### Publications


H. Xu, Y. Zhao, J. Li, M. Wang, F. Lian, M. Gao, F. Ghishan: Loss of NHE8 Expression Impairs Ocular Surface Function in Mice. American Journal of Physiology – Cell Physiology. 2015;308(1):79-87.

## Christopher Buneo, Ph.D.

Arizona State University

### Annual Award Amount

$100,000

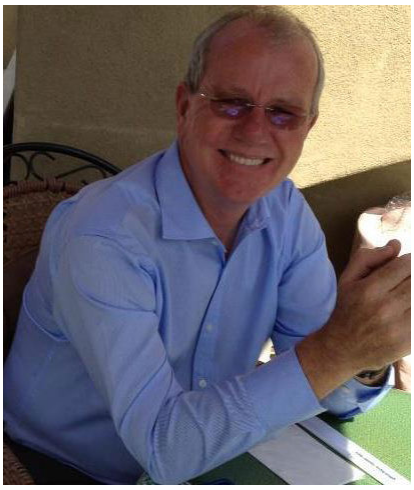
### Project End Date

April 22, 2016

### Neural Correlates of Cooperative Manipulative Actions

Cooperative or 'joint' actions involve two or more individuals coordinating their behavior in space and time to perform a particular task. Examples can be found in sport, as with the passing of a ball between two soccer teammates, art, as during ballroom dancing or the performance of a musical duet, and even rehabilitation, as when a therapist of rehabilitation robot assists a patient during therapeutic exercise. However, surprisingly little is known about how joint actions are represented in the activity of cells in the brain, information which is necessary to create the next generation of neural prosthetic and rehabilitative systems. Such systems are expected to be in widespread usage in the next few decades, and will be critical for improving the quality of life of Arizonans with disabilities resulting from stroke, Parkinson's disease and other conditions.

The work performed here was focused on characterizing brain activity during one of the most fundamental and commonly performed joint actions, object handovers (e.g., the passing of book between two individuals). In this project, animals are trained to perform partial or full handover tasks as activity is recorded in brain areas thought to be important for successful performance of these tasks. In a 'virtual' version of these tasks, animals move their arms in a custom-made virtual reality environment to a designated handover position and receive juice rewards if the movements are performed correctly. In a second 'physical' task, animals receive food rewards that are presented to them through a custom-made Plexiglas barrier. Thus far, activity has been successfully recorded and characterized in one animal during the virtual task; a second animal is currently being trained to perform both the virtual and physical tasks. We are also currently preparing to record and analyze the full arm motion of one animal, as well as a human subject, during the performance of the physical task. This will enable programming of a robot to perform similar motions while interacting with the animals.



## David Galbraith, Ph.D.

University of Arizona

### Annual Award Amount

$100,000

### Project End Date

October 22, 2016

### Identification of Changes in Gene Expression at the Earliest Stages of Prostate Oncogenesis

When normal organs become diseased, for example in cancer, this involves an alteration in state of a very few cells which then grow and multiply. It is hard to detect early indicators of few cells in disease states within the overwhelming background of normal cells. The current screening tests to detect early prostate cancer are not very accurate or sensitive, and cannot assure men that there is no risk of cancer. The objective of our work is to apply a novel approach that we have devised to identify potential biochemical markers for early cancer detection in single cells. Our ultimate aim is to use these for the discovery of new drugs to stop prostate cancer.

The approach uses genetically-engineered mice that have tumor-suppressor genes which, when switched off, cause prostate cancer. We have developed a Genetically-Engineered Mouse Model to specifically analyze the initial stages of cancer development within single cells following this switch-off. The model produces green fluorescence within the nuclei of cells that are initiating the cancer process, and this allows us to directly isolate these individual nuclei using fluorescence-activated sorting. We have devised molecular methods to characterize the genes that are active in the individual sorted nuclei. These nuclei are in the process of making messenger RNA which contains the coding information for all the proteins in the cancer-initiated prostate cells. Through sequencing the messenger RNA from each single sorted nucleus, we identify which prostate genes have become active in the cancer-initiated cells but not in the normal cells. This approach should allow us to identify those gene changes that occur in the human prostate long before tumors develop.

### Publications

Samadder P, Weng N, Doetschman T, Heimark RL, Galbraith DW (2015). A floxed GFP reporter line for analysis of Cre-based activation of global transcription. In preparation.

### Invited Paper, Panels, Presentations

Doetschman (Platform Presenter), Galbraith, Heimark: Cancer Biology Research Conference "Single Cancer Cell Transcriptions Analysis," March 9, 2015.

Samadder (poster presenter), Galbraith, Heimark, Doetschman: Arizona Cancer Center Retreat "Analyzing Oncogenesis at the Level of Single Cells," April 10, 2015.

## Kaushal Rege, Ph.D.

Arizona State University

### Annual Award Amount

$100,000

### Project End Date

October 22, 2016

### Nanoassemblies for Gene Silencing

Cancer is the second leading cause of death in the United States. The estimated number of new cancer cases within the US for 2015 is 1,658,370 with 589,430 deaths projected during the same year. Urinary bladder cancer is the fourth most common type of cancer in men with 74,000 new cases and 16,000 deaths expected for both men and women in 2015. The current work focusses on knockdown of genes that enable survival of bladder cancer cells. Of particular importance are Heat Shock Proteins (HSPs); these are present at low levels under normal conditions. However, these proteins are overexpressed in cancer cells, and are responsible for resistance against chemotherapy and radiation treatment. Hence, HSPs are potential diagnostic, prognostic, as well as therapeutic targets for cancer therapy. Thus, inhibiting HSPs using small molecules and / or knocking down their expression in cells using short interfering RNA (siRNA) - either alone or in combination with chemo / radiation therapy - are attractive potential treatment strategies for cancer diseases. In our present research, HSP90 knockdown was achieved by delivering small interfering RNA (siRNA) to UMUC3 bladder cancer cells using novel lipopolymer nanoparticles. Briefly, cells were plated in 6-well plates (100,000 cells/well) overnight and treated with Hsp90 or the scrambled non-targeting siRNA (25 nM) the following day. Cells were then harvested 96 h following treatment and HSP90 protein levels were analyzed using Western blots. Actin, a cytoskeletal protein, was used as the loading control. Lipopolymers that resulted in the highest levels of HSP90 knockdown in cancer cells were identified; HSP90 knockdown levels as high as 64% were obtained. These results suggest that lipopolymer nanoparticles can be successfully used for knocking down Hsp90 levels and possibly other HSPs. This can help sensitize cancer cells to other treatments including anticancer drugs and nanoparticle-induced heat treatment. Further validation of these studies is currently in progress, and other combination strategies (e.g. including nanoparticle mediated heat treatment), will be explored together with Hsp silencing for effective destruction of bladder cancer.


## Donato Romagnolo, Ph.D.

University of Arizona


### Annual Award Amount

$99,740

### Project End Date

October 22, 2015

### Early-life Exposure and Risk of Breast Cancer

Sporadic breast cancers, which represent the vast majority (~90%) of breast tumor cases, do not have mutations in the BRCA-1 gene, but have absent or markedly reduced levels of BRCA-1 protein. The main objective of this project is to explore the mechanisms that contribute to silencing of BRCA-1. Aims: This project deals with mechanisms that go under the definition of epigenetics, i.e. changes in gene expression that do not involve modifications of the DNA sequence. Because epigenetic changes are reversible, they represent a potential target in breast cancer prevention and treatment.

Information from animal models and population studies indicate that mammary tumor promotion in adult life may be influenced by prior exposure to epigenetic modifiers. The central hypothesis of this project is that *early-life exposure to agents that bind a nuclear receptor termed aromatic hydrocarbon receptor (AhR) silences the BRCA-1 gene, and that this event predisposes to the epigenetic development of triple-negative breast cancers in adult life*. The rationale for this project stems from evidence women are exposed to many agents that activate the AhR and are known carcinogens. These include dietary compounds, metabolites of dietary fatty acids, environmental contaminants, and photoproducts generated in the skin from ultraviolet radiation, (i.e. sun exposure). Therefore, this project integrates etiological and lifestyle factors with broad implications for breast cancer therapy.

### Publications


Romagnolo DF, Selmin OI. Development of Endocrine Tumors in Women and Dietary Prevention. Preventive Nutrition: The Comprehensive Guide for Health Professionals, Fifth Edition. Adrianne Bendich, Ph.D., FASN, FACN and Richard J. Deckelbaum, M.D., FRCP(C) (In Press, 2015).

Donato F. Romagnolo, Andreas J. Papoutsis and Ornella I. Selmin. Increased BRCA-1 promoter hypermethylation as biomarker of mammary tumorigenesis associated with increased expression and activation of AhR. BMC Cancer.

Selmin OI, Papoutsis JA, and Romagnolo DF. BRCA-1 promoter CpG hypermethylation as biomarker of mammary tumorigenesis associated with increased expression and activation of AhR. BMC Cancer, 2015 (submitted August 12, 2105, under review).

Romagnolo DF, Selmin OI. Repression of BRCA-1 expression in AhR-activated breast cancer cells and reversal with dietary antagonists of the AhR. In preparation (Breast Cancer Research).

## Nafees Ahmad, Ph.D.

University of Arizona

### Annual Award Amount

$250,000

### Project End Date

October 22, 2017

### Viral, Immunological and Clinical Factors in HIV-1 Aging Patients

HIV infection may influence the aging process of the immune system in HIV-infected individuals and those infected individuals who have aged with HIV infection while being treated with anti-HIV drugs. Furthermore, the elderly population also experiences an accelerated aging of the immune system. These age-related changes may result in altered functions of the immune system and reduced response against other infections. We have been investigating the role of HIV in older HIV-infected individuals, especially the specific properties of HIV that may alter the functions of the immune system in HIV aging patients and compare with aging uninfected individuals. We have created a cohort of HIV-infected who are receiving medical care at the University of Arizona and uninfected individuals (all aged >50 years). These patients are clinically evaluated and blood samples are collected every 4 months followed by isolation peripheral blood mononuclear cells (PBMC). HIV envelope gene was amplified by polymerase chain reaction (PCR) from patients PBMC DNA followed by cloning and characterization of correct size recombinants. These recombinants are being sequenced to determine the specific features of HIV that persist in these older infected individuals. In addition, we have optimized two panels consisting of 12 antibodies for markers of CD4 and CD8 T cells that are associated with the aging of the T cells. These two panels are being used to determine the function of T cells in HIV-infected older individuals and uninfected older individuals. Results from this study may provide new information to develop strategies for prevention and treatment of HIV infection in older infected patients, including improving the aging of the immune system in older population.

**Yin Chen, Ph.D.**
**Yitshak Zohar, Ph.D.**

University of Arizona

### Annual Award Amount

$250,000

### Project End Date

October 22, 2017

### A Microfuidic Ex Vivo Lung Model (MEVL) for Studying Pulmonary Diseases

The main goal of the present project is to develop a novel system that can mimic the physiological condition of the human lung and can respond to environmental stimuli similarly to the human lung. In this proposal, we plan to construct a miniature lung on a microchip-like device (microfluidic ex vivo lung, or MEVL), which is able to "breathe" and to respond to the external stimuli similarly to the actual lung. In this first grant period, we have successfully established the 1st-generation MEVL, in which primary human airway epithelial cells have achieved full mucociliary differentiation for the first time in the miniature device that we have invented. The differentiated culture has mucous production and cilia formation similar to airway epithelium under physiological condition. This is in direct contrast to all other lung-on-chip models currently on the market containing only cancer cell lines that bear little resemblance to the in vivo epithelium. In addition, we are re-inventing various molecular methods (e.g. PCR, immunofluorescence, transfection, etc.), previously developed for the macroscale operations, for the application on this miniature device. In the next step, we plan to further optimize the MEVL by introducing other interacting cell types such as endothelial cells and macrophages, and by testing its response to different environmental insults such as pollutants (e.g. nanoparticles) and pathogens (e.g. bacteria). Once succeed, this system ("MEVL") will be extremely useful for a number of high-throughput applications such as drug testing, toxicant screening, anti-terrorism etc.

## Robert Handa, Ph.D.

University of Arizona

### Annual Award Amount

$250,000

### Project End Date

October 22, 2017

### Fetal Risk Factors for Obesity and Comorbid Depression

These studies represent a collaboration between scientists at the University of Arizona College of Medicine- Phoenix and at Brigham and Women's Hospital, Harvard Medical School. Our studies investigate potential common developmental origins of adult diseases such as major depressive disorder (MDD) and cardiometabolic disease using both a human cohort and animal models. Of importance, these studies will identify sex-specific developmental changes in gene expression that might underlie the sex-selectivity of adult risk for these diseases. The Boston team has been examining a cohort of patients that participated in the National Collaborative Perinatal Project (NCPP) which followed individuals in utero (born from 1959-1966) through adulthood (ages 49-57 yrs of age). Current analyses are underway that evaluate relationships between gene biomarkers associated with prenatal stress and the risk for MDD and cardiometabolic diseases in adulthood. The Phoenix team is using preclinical approaches to identify new risk biomarkers in animal models of prenatal stress and glucocorticoid exposure. Recent studies have identified several cytokines/chemokines that may correspond to alterations in adult function and changes in gene expression during development that may give rise to physiological changes in adulthood.

### Invited Paper, Panels, Presentations

Hale TM, Carbone DE, Madhavpeddi L, Thomson MK, Handa RJ. Sex Differences in Cardiovascular Responses to Stress in Adult Rats Prenatally Exposed to Dexamethasone. Abstract, American Physiological Society Conference on Cardiovascular, Renal and Metabolic Diseases: Physiology and Gender. Annapolis, MD, November 17-20, 2005.

**Karl Kern, M.D.**

University of Arizona

**Annual Award Amount**

$249,383

**Project End Date**

October 22, 2017

## A Pilot Randomized Clinical Trial of Early Coronary Angiography Verson No Early Coronary Angiography for Post-Cardiac Arrest Patients without ECT ST Segment Elevation

This is a randomized clinical trial (RCT) to evaluate the value of early coronary angiography after cardiac arrest in patients without ST segment elevation on their ECG. This clinical trial will evaluate this question. The potential impact is large since approximately three-fourths of all resuscitated cardiac arrest patients DO NOT have ST segment elevation on their post arrest ECG. If such a strategy benefits this subgroup of patients as it does those patients with ST segment elevation, many additional lives will be benefited and long-term outcomes improved. Due to the emergent nature of cardiac arrest and the importance of rapid and timely treatment of this condition, this research must be performed under the strict Federal regulations for "Exception for Informed Consent."

The first year of the grant was dedicated to successfully obtaining IRB approval to proceed with this project under the strict Federal regulations for "Exception for Informed Consent" (EFIC). We have made progress, and our major accomplishment during this period has been the completion of the Southern Arizona community consultation survey in regards to performing this research in our area. We surveyed a total 822 individuals living in Southern Arizona, including 603 at the PIMA County Fair and 219 through social media (Facebook).

A comparison with Federal census data shows a reasonable correlation between the published proportion of Hispanics in the Tucson community and the proportion of Hispanic responses to our community consultation survey.

| | Federal Census | PEARL Community Survey |
|---|---|---|
| Hispanic | 35.7% | 28.2% |

The sample acquired from social media (Facebook) had less Hispanic representation, but the PIMA County Fair sample was very representative of the proportion of Hispanics in our community according the most recent Census data.

| | Federal Census | PIMA County Fair Sample |
|---|---|---|
| Hispanic | 35.7% | 32.01% |

Results of our community survey:

| Q2: Is it acceptable to you for this research to be conducted in your community? | | | Q5: If you were brought to the hospital unconscious after a suffering a cardiac arrest and the emergency physician or cardiologist thought you were eligible for this study, would you accept being enrolled in this study even though you could not provide consent? | | |
|---|---|---|---|---|---|
| All: (n=822) | Yes | 765 (93%) | All: (n=822) | Yes | 604 (74%) |
| | No | 13 (2%) | | No | 68 (8%) |
| | Prefer not to answer | 44 (5%) | | Uncertain | 130 (16%) |
| | | | | Didn't answer | 20 (2%) |

A previous Southern Arizona community survey for a trauma study (PROPPR) had similar results.

## Karl Kern, M.D. (cont.)

| Q: "Is it acceptable to you for this research to be conducted in your community?" | | | Q: "If you were brought to the hospital unconscious after a suffering a cardiac arrest and the emergency physician or cardiologist thought you were eligible for this study, would you accept being enrolled in this study even though you could not provide consent?" | | |
|---|---|---|---|---|---|
| | PEARL | PROPPR | | PEARL | PROPPR |
| YES | 93% | 87% | YES | 74% | 71% |
| NO | 2% | 8% | NO | 8% | 19% |
| UNCERTAIN | 5% | 5% | UNCERTAIN | 18% | 10% |

### Publications

Hollenbeck RD, McPherson JA, Mooney MR, Unger BT, Patel NC, McMullan P, Hsu C-H, Seder DB, Kern KB. Early Cardiac Catheterization is Associated with Improved Survival in Victims of Cardiac Arrest Without STEMI. Resuscitation 2014;85:88-95.

Rab T, Kern KB, Tamis-Holland JE, Henry TD, McDaniel M, Dickert NW, Cigarroa JE, Keadey M, Ramee S. Cardiac Arrest: A treatment algorithm for emergent invasive cardiac procedures in the resuscitated comaose patient. J Am Coll Cardiol 2015;66:62-73.

Kern KB, Lotun K, Patel N, Mooney MR, Hollenbeck RD, McPherson JA, McMullan PW, Unger B, Hsu C-H, Seder DB. Outcomes of Comatose Cardiac Arrest Survivors With and Without ST Elevation: The Importance of Coronary Angiographic Findings. J Am Coll Cardiol Intv 2015;8:1031-1040.

Callaway CW, Donnino MW, Fink EL, Geocadin RG, Golan E, Kern KB, Leary M, Meurer WJ, Peberdy MA, Thompson TM, Zimmerman JL. Part 8: post–cardiac arrest care: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132(suppl 2):S465–S482.

### Invited Paper, Panels, Presentations

"The Role of the Cardiac Cath Lab in Treating Post Cardiac Arrest Patients" University of Alabama-Birmingham School of Medicine, Cardiology Grand Rounds. Birmingham, AL, October 29, 2014.

"Post Resuscitation Care is the Next Frontier for Improving Outcomes After Cardiac Arrest" University of Alabama-Birmingham School of Medicine, Emergency Medicine/Critical Care Grand Rounds, Birmingham, AL, October 30, 2014.

"Hypothermia: To Cool or Not to Cool - That is the Question" Cardiovascular Symposium: PCI, Cooling and Out-of-Hospital Cardiac Arrest: Current Controversies-2014, AHA Scientific Sessions, Chicago, IL, November 16, 2014.

"The Role of Early Post Arrest Coronary Angiography" Special Session: Management of the Resuscitated Cardiac Arrest Patient: Growing Insights to the Bundle of Care Approach-2014, AHA Scientific Sessions, Chicago, IL, November 17, 2014.

"Cooling anf Cathing" Post Resuscitation for Myocardial Infarction: Evolving Guidelines and Standards. 15th Annual Multispeciality Conference on Medical Negligence & Risk Management, Kona, Hawaii, January 7, 2015.

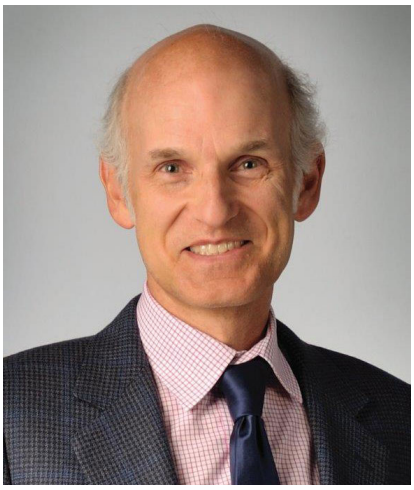
"Physiology of Cardiac Arrest-How to be Awesome." Scottish Cardiac Arrest Symposium 2015, Edinburgh, Scotland, March 27, 2015.

## Karl Kern, M.D. (cont.)

"Post Resuscitation Outcomes in Patients with and without ST Elevation: The Importance of Coronary Angiographic Findings." The XIII Institute of Critical Care Medicine, Wolf Creek Conference, Shanghai, China, April 17, 2015.

"The Role of Early Postarrest Coronary Angiography and PCI" 79th Annual Scientific Meeting of the Japanese Circulation Society, Osaka, Japan, April 26, 2015.

"Angiographic Findings Post Resuscitation in the Cath Lab" Complex Cardiovascular Catheter Therapeutics Conference (C3), Orlando, FL, June 17, 2015.



## Diego Martin, M.D., Ph.D.

University of Arizona

### Annual Award Amount

$249,963

### Project End Date

October 22, 2017

### MRI of Non-Alcoholic Steatohepatitis (NADH) Biomarkers

The goal of the research project that is supported by the ABRC is to improve diagnosis, therapy and outcomes related to Non-Alcoholic Fatty Liver Disease (NAFLD) and Steatohepatitis (NASH). The main objective of the project is to developing new magnetic resonance imaging (MRI) biomarkers that can be used to diagnose and follow progression of these liver conditions. NAFLD/NASH is associated with diabetes and obesity and affects ~2 million Arizonans; Native and Mexican-Americans have higher risk. A subset of NAFLD patients will develop NASH with hepatic fibrosis and a risk to develop liver cancer. Currently, we rely on biopsies to diagnose NAFLD/NASH which is an invasive procedure and limited to a handful of subjects. As a consequence many patients will not be diagnosed early on and present symptoms associated with advanced liver disease including cirrhosis liver cancer. The proposed non-invasive imaging biomarkers will allow diagnosing NAFL/NASH at earlier stages and facilitate development of therapy. The first step of the project is to use liver samples obtained at autopsy to develop a diagnostic system based on MRI to characterize NAFLD and NASH. The next step is to test the diagnostic system in a set of patients with biopsy-proven fatty liver disease. During the first year of the grant we have worked in developing the MRI-based diagnostic system and started initial testing in humans.

### Publications

Brand JF, Furenlid LR, Altbach MI, Galons JP, Bhattacharyya T, Bhattacharyya A, Bilgin A, Li Z, Martin DR, Autocorrelation Analysis of Hepatic Fibrosis on MRI, Proceedings of the International Society for Magnetic Resonance in Medicine, 23, 4136, 2015.

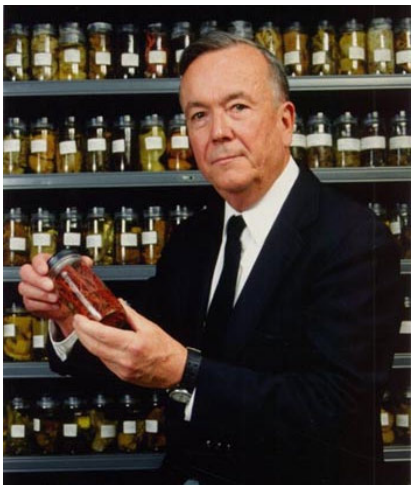
### Invited Paper, Panels, Presentations

Brand JF, Furenlid LR, Altbach MI, Galons JP, Bhattacharyya T, Bhattacharyya A, Bilgin A, Li Z, Martin DR, Autocorrelation Analysis of Hepatic Fibrosis on MRI, Proceedings of the International Society for Magnetic Resonance in Medicine, 22, 4136, 2015, Toronto, Canada, June 2015.

Brand JF, Furenlid LR, Altbach MI, Bhattacharyya A. Sharma P, Martin DR, Localized Hotelling observer analysis of liver fibrosis in MRI, to be presented at the SPIE Medical Imaging Conference, San Diego, CA, February 2016 (oral presentation).

Pandey A, Sharma P, Martin DR, Altbach MI, Bilgin A, Saranathan M, Multiresolution imaging using golden angle stack-of-stars and compressed sensing, submitted to the Annual Meeting of the ISMRM, Singapore, 2016.

Li Z, Berman BP, Galons JP, Bilgin A, Altbach MI, Martin DR, Rapid High-resolution T1 mapping using highly accelerated radial steady-state free-precession acquisition, submitted to the Annual Meeting of the ISMRM, Singapore, 2016.




## George Pettit, Ph.D.

Arizona State University


### Annual Award Amount

$250,000

### Project End Date

October 22, 2017

### Discovery of Powerful Anticancer Drugs for Monoclonal Anticancer Drugs (ADC) Development Capable of Improving Cancer Treatments

The urgent objective of our ABRC research is the discovery and development of promising new anti-cancer drugs with highly effective anti-cancer properties that offer the potential for ultimate clinical activity against human cancer. Fortunately an exceptional recent advance in human cancer treatment has been achieved (from past ABRC financial support) with an anti-cancer drug discovery necessary to development of the first successful antibody drug conjugate (ADCETRIS) for cancer treatment. The drug component of the antibody drug conjugate (ADC) is desmethyl auristatin E of our discovery of auristatin E and is now approved in 50 countries over the world. The sharply focused objective of our ABRC research will continue to be the accelerated discovery and pre-clinical development of new and structurally unique anti-cancer drugs. Special emphasis will continue to be placed on discovery of such new drugs powerful enough to be the ADC drug candidates for linkage to a broad variety of monoclonal antibodies representing a spectrum of human cancer types. Over the past year the ABRC financial assistance has been profoundly crucial and has led to outstanding advances in our research productivity (6 peer reviewed research publications, and 2 submitted). Illustrative was our discovery of the very potent (ADC candidate) cancer cell growth inhibitor series designated the Silstatins from a South Pacific Ocean micro-organism lead. Presently we are advancing our most recent discovery of a new series of quite powerful (ADC lead) anti-cancer drugs. Such a very important series of new anti-cancer drugs for clinical development would not have been possible without the present and future ABRC financial support!

### Publications


Pettit, George R., Rui Tan, Pettit, Robin K., Doubek, Dennis L., Chapuis, Jean-Charles, Weber, Christine A. "Antineoplastic agents 596. Isolation and Structure of Chromomycin A5 from a Beaufort Sea Microorganism." RSC Advances; 2015, 5, 9116-9122.

Pettit, George R., Smith, Thomas, Arce, Pablo, Flahive, Erik, Anderson, Collin, Chapuis, Jean-Charles, Xu, Jun-Ping, Groy, Thomas, Belcher, Paul, Macdonald, Christian. "Antineoplastic Agents. 599 Total Synthesis of Dolastatin 16." Journal of Natural Products, 2015, 78(3), 476-485, 2015 and appeared in the March 2015 JNP special issue.

Pettit, George R., Smith, Arce, Pablo, Chapuis, Jean-Charles, Macdonald, Christian. "Antineoplastic Agents. 600 From the South Pacific Ocean to the Silstatins." Journal of Natural Products, 2015, 78(3), 510-523 and appeared in the March 2015 JNP special issue.

Noemi Kedei, Matthew B. Kraft, Gary E. Keck, Cherry L. Herald, Noeleen Melody, George R. Pettit, Peter M. Blumberg. "Neristatin 1 Provides Critical Insight into Bryostatin 1 Structure - Functional Relationships." Journal of Natural Products, 2015, 78(4), 896-900.

## George Pettit, Ph.D. (cont.)

George R. Pettit, Bryan R. Moser, Delbert L. Herald, John C. Knight, Jean-Charles Chapuis, Xing Zheng. "The Cephalostatins 23. Conversion of Hecogenin to a Steroidal 1, 6-Dioxaspirol [5.5] nonane Analogue for Cephalostatin 1." Journal of Natural Products, 2015, 78(5), 1067-1072.

George R. Pettit, Jun-Ping Xu, Jean-Charles chapuis, Noeleen Melody. "The Cephalostatins 24. Isolation, Structure and Cancer Cell Growth Inhibition of Cephalostatin 20." Journal of Natural Products, 2015, 78(6), 1446-1450.

George R. Pettit, Qinghua Ye, John C. Knight, Fiona Hogan, Noeleen Melody, Venugopal J.R.V. Mukku, Dennis L. Doubek, and Jean-Charles Chapuis. "Isolation and Structure of Cancer Cell Growth Inhibitory Tetracyclic Triterpenes from the Zimbabwean Monadenium lugardae (Euphorbiaceae)1a." Journal of Natural Products; submitted.

George R. Pettit, Justin Searcy, Rui Tan, Gordon M. Cragg, John C. Knight, Noeleen Melody and Jean-Charles Chapuis; "Antineoplastic Agents 585. Isolation of Bridelia ferruginea Anticancer Podctphyllotoxins and Synthesis of 4-Aza-Podophyllotoxin Structural Modifications"; Journal of Natural Products; submitted.


## Kaushal Rege, Ph.D.

Arizona State University


### Annual Award Amount

$250,000

### Project End Date

October 22, 2016

### Targeted Therapeutics for Triple Negative Breast Cancer Disease

The estimated number of new cases of breast cancer in the United States is over 200,000, which leads to death of approximately 40,000 women. In the state of Arizona, two deaths occur due to breast cancer and more than 4,600 cases are diagnosed every year (American Cancer Society). Triple-negative breast cancer (TNBC) is diagnosed in 15-30% of all breast cancer cases, and represents an aggressive form of the disease. The lack of estrogen, progesterone, and HER2 receptors in this disease type makes discovery of effective targeted therapies further challenging. We have shown that mitoxantrone, a DNA damaging drug, can sensitize triple-negative breast cancer cells to TRAIL, which is a protein that can selectively kill cancer cells. In this one-year period, we formulated nanoparticles (liposomes; 110-160 nm in diameter) for encapsulation and delivery of mitoxantrone to cancer cells. Five different liposomes, consisting of lipid-containing polymers (lipopolymers) synthesized in our laboratory, were formulated and characterized for their size, surface charge, and stability. The efficacy of mitoxantrone-encaspulated liposomes for ablation of TNBC (and other) cancer cells was evaluated both as a single-agent treatment and in combination with TRAIL. Treatment with liposomal mitoxantrone and TRAIL resulted in synergistic death of cancer cells, indicating the promise of this approach. Cell-based studies with liposomal mitoxantrone together with other chemotherapeutic drugs indicated high efficacy albeit in an additive manner. We have also generated lipopolymers conjugated with folic acid in order to facilitate the targeting of TNBC cells which overexpress the folate receptor. We are currently formulating these folic acid conjugated lipids into liposomes to enable targeted drug delivery. Finally, we are initiating studies for evaluating the pre-clinical efficacy of these approaches using mouse models of TNBC disease.

## Marwan Sabbagh, M.D.

St. Joseph's Hospital and Medical Center (October 23, 2015–present)

Banner Health (October 23, 2014–October 22, 2015)

### Annual Award Amount

$248,629

### Project End Date

October 22, 2017

### Longitudinal Assessment of Florbetapir PET, FDG PET, and MRI in Down Syndrome Individuals with and without Alzheimer's Dementia

Changes in the brain can happen long before Alzheimer's disease is noticed by a patient or by a patient's family. People with Down syndrome are much more likely to develop Alzheimer's disease. This makes people with Down syndrome a good population for the investigators to work with during this study. This study aims to track the development of Alzheimer's disease by using multiple methods to examine changes in the brain before and after a patient develops Alzheimer's disease. Methods include (a) cognitive status tests (which determine mental ability) and (b) brain scans (which show brain images). The imaging scans include Magnetic Resonance Imaging (MRIs), FDG-PET, Florbetapir PET, and we are now adding tau-PET scans, all of which provide different kinds of pictures of the brain. Tests and brain scans will be performed at different times over several years, which will allow the investigators to begin a long-term analysis of the study participants. To date, the study has recruited 9 patients. Of the 9 patients:

- 6 received all baseline assessments (MRI, PET FDG, PET FBP), excluding tau.
- 1 received all baselines including tau.
- 2 patients were screened out due to medical issues unrelated to this study.

Efforts are currently underway to transfer the study from Banner Health to Barrow Neurological Institute. Once all the proper approvals are in place, the study will resume enrollment and continue collection of additional tests and brain scans over time for those patients already enrolled. Preliminary analysis of the images collected has led two published papers. Additionally, Dr. Sabbagh, is working to involve the patients in this study in two additional research grants. The first, in collaboration with Dr. Matt Huentelman of the Translation Genomics Research Institute (TGen), has been awarded an Alzheimer's Association Investigator Initiated Research Grant to collect a small amount of blood monthly from the patients participating in this study in the hopes of developing a risk assessment tool which will eventually assist in identifying those patients that may benefit from Alzheimer's prevention approaches. For the second grant, Dr. Sabbagh will be leading the Barrow Neurological Institute as a site on the Biomarkers of Alzheimer's Disease in Down Syndrome initiative. It is hoped this study, combined with data gained on the same population through the additional grants, will provide the foundation to guide future Alzheimer's disease treatment and prevention trials.

## Marwan Sabbagh, M.D. (cont.)

### Publications

Hartley D, Blumenthal T, Carrillo M, DiPaolo G, Esralew L, Gardiner K, Granholm AC, Iqbal K, Krams M, Lemere C, Lott I, Mobley W, Ness S, Nixon R, Potter H, Reeves R, Sabbagh M, Silverman W, Tycko B, Whitten M, Wisniewski T. Down syndrome and Alzheimer's disease: Common pathways, common goals. Alzheimers Dement. 2014 Dec 12. pii: S1552-5260(14)02860-X. doi: 10.1016/j.jalz.2014.10.007.

Danna Jennings, John Seibyl, Marwan Sabbagh, Florence Lai, William Hopkins, Santi Bullich, Corneila Reininger, Barbara Putz, Andrew Stephens, Ana Catafau, and Ken Marek. Age dependence of brain β-amyloid deposition in Down syndrome: a [18F]florbetaben PET study. Neurology. 2015 Jan 7. pii: 10.1212/WNL.0000000000001212. [Epub ahead of print]

Sabbagh MN, Edgin JO, Clinical Assessment of Cognitive Decline in Adults with Down Syndrome, Current Alzheimer's Research 2015

Marwan N. Sabbagh, MD1,2,, Kewei Chen, PhD2,3,4,, Joseph Rogers, PhD5, Adam S. Fleisher, MD2,3,6,, Carolyn Liebsack, RN1,2,, Dan Bandy, MS2,3,, Christine Belden, PsyD1,2,, Pradeep Thiyyagura,MS,2,3,, Xiaofen Liu, MS 2,3,, Auttawut Roontiva, MS 2,3,, Sandra Jacobson, MD1,2,, Michael Malek-Ahmadi, MSPH1,2, , Stephanie Parks, BS2,3,, Jessica Powell PsyD1,2,, Eric M. Reiman, MD2,3,7, Florbetapir PET, FDG PET, and MRI in Down Syndrome Individuals with and without Alzheimer's Dementia. Alzheimers Dement. 2015 Apr 4. pii: S1552-5260(15)00084-9. doi: 10.1016/j.jalz.2015.01.006. [Epub ahead of print] PUBLISHED

# Biospecimen Locator

# BIOSPECIMEN LOCATOR

## Program Highlights

Over 4400 specimens were collected

Over 675 specimens were distributed for research

Over 14 studies are supported by ABRC funded Arizona Biospecimen Locator (ABL) hospitals

Phoenix Children's hospital received College of American Pathologists (CAP) Accreditation

Strong ABL presence at the 2015 International Society for Biological and Environmental Repositories (ISBER) conference

Initiated the development of a strategic plan for program sustainability

Research on new website and tracking specimen

## About the Program

Acquiring quality biospecimens is one of the largest obstacles researchers face as they strive to advance medical science and improve patient care. The Arizona Biospecimen Locator (ABL) was designed to provide researchers with specimens needed to advance their research studies. The ABL is a web-based biospecimen database of both diseased and normal solid tissues, cells, fluids and molecular samples stored at participating Arizona hospitals and tissue banks. Researchers will use the ABL to search and request biospecimens which are organized by disease, type of specimen, preservation type, anatomic source and demographics of participants to use in their qualified research studies. Using ABL encourages research collaboration that may lead to more effective treatments and potential cures.

The Arizona hospitals that participate in the program and currently link to the ABL include Dignity Health St. Joseph's Hospital and Medical Center, Maricopa Integrated Health System, and Phoenix Children's Hospital.

## Funding Source Used

Disease Control Research Fund

# Research Education

At-A-Glance

# RESEARCH EDUCATION

## Program Highlights

Partnered with the University of Arizona, Tucson to plan the following for FY 2016:

General Research Funding and Management Workshops – Two sessions to cover grant writing, grant management, publishing, and successful collaboration within the industry.

Clinical Trial Management and Compliance Workshop – Two sessions to cover budgeting and contracting for clinical trials, successfully navigating IRB, HIPPAA, and other areas of regulatory compliance, quality assurance, and communicating about clinical trials with the public.

Partnered with the University of Arizona, College of Medicine, Phoenix to plan the following for FY 2016

Research Conference – provide an opportunity for ABRC award recipients to showcase their research and collaborate with Flinn Foundation awardees.

Cord Blood Conference – provide an opportunity to create awareness of the Arizona Public Cord Blood Program amongst various levels of the community, including business, researchers, and hospitals.

Three workshops – topics TBD based on input from surveys and feedback from local researchers.

IRB workshop – provide two workshops on IRB topics to assist Arizona researchers with IRB guidelines and practices, policies and procedures, certification and training, and regulatory issues.

Partnered with the Northern Arizona University to plan the following for FY 2016

Sources of Funding for Health Research – Search Engines Workshop - provide an overview of funding for health research and finding the sources, developing a concept, exploring rules, processes, and technical issues, and matching goals objectives and funding opportunities

Developing a Research Concept and a Research Team Workshop – discuss initial goals and objectives, review of existing knowledge, finding the cutting edge, establishing the appropriate personnel, and budgeting

Designing Community-Based Participatory Research Projects Workshop – cover research design, existing knowledge, community engagement, matching resources with design, and methodology, statistics, and tests.

IRB Issues for Health Disparities Research in Northern Arizona Workshop – series of three workshops on health equities research design and IRB actions focused on population health research with underserved populations in Northern Arizona

# Research Education

## About the Program

In working with Arizona researchers and through its commitment to the Arizona Biosciences Roadmap, ABRC identified a need to make high quality educational resources available. The Research Education Program seeks to create a shared sense of community by bringing national and local experts together to engage Arizona researchers and clinical professionals in emerging topics at little or no cost to the research community. ABRC is partnering with local universities to provide educational opportunities on topics such as Institutional Review Boards (IRBs), networking opportunities, and opportunities to share current research and cultivate new collaborations among Arizona researchers.

## Funding Source Used

Disease Control Research Fund

# Public Cord Blood

At-A-Glance

# PUBLIC CORD BLOOD

## Program Highlights

From the program's inception to July 31, 2015, 20 cord blood units were sent for transplantation

1542 cord blood units were collected in FY 2015

Over 5000 cord blood units have been collected to date

111 cord blood units were banked in FY 2015

101 cord blood units were distributed for research in FY 2015

Tucson Medical Center joined the Arizona Public Cord Blood Program and collected 1,000 cords in its first year!

Six cord blood units collected at St. Joseph's Hospital and Medical Center were sent for transplantation

The very first cord blood unit collected by the Arizona Cord Blood Program was collected at Abrazo Central Campus (formerly Phoenix Baptist Hospital), and they recently partnered with a nursing school to teach students about the program.

Maricopa Integrated Health Services is integrating cord blood donation education in pre-natal classes

## About the Program

Currently, seven out of ten people will not have a suitable matched donor in their family and will depend on the National Marrow Donor Program (NMDP) registry to find a bone marrow or cord blood match to treat or cure life-threatening diseases like cancer. Adding diverse units to the registry increases the likelihood that all patients will find a match.

Umbilical cord blood is blood that remains in the blood vessels of the placenta and the umbilical cord after the baby is born, and the cord has been clamped and cut. It contains hematopoietic stem cells (cells that can form other blood cells). These blood-forming cells are also found in bone marrow.

In the past, the placenta and umbilical cord were thrown away. Today, the blood can be collected, stored, and made available for transplant to children and adults that have certain genetic or life-threating diseases such as leukemia or lymphoma.

## About the Program (cont.)

The Arizona Public Cord Blood Program was created to advance the collection of and increase the number of cord blood units donated and made available for transplantation. Cord blood units that are unsuitable for transplantation are made available (with the mother's consent) to researchers developing cures or treatments for genetic or life-threatening diseases.

Participating hospitals include Abrazo Central Campus, Dignity Health St. Joseph's Hospital and Medical Center, and Maricopa Integrated Health Center in Phoenix, and Tucson Medical Center. The Save the Cord Foundation is an educational partner for the Arizona Public Cord Blood Program.

The Arizona Public Cord Blood Program officially began collecting donated cord blood in late 2011.

## Funding Source Used

Disease Control Research Fund

# Arizona Alzheimer's Consortium

# Arizona Alzheimer's Consortium

The Arizona Alzheimer's Consortium is the nation's leading state-wide collaboration in Alzheimer's disease research, and its core mission is to find a way to end Alzheimer's disease as quickly as possible. Established in 1998, the Consortium is comprised of about 150 researchers and colleagues from seven principal institutions: Arizona State University, Banner Alzheimer's Institute, Barrow Neurological Institute, Mayo Clinic Arizona, Banner Sun Health Research Institute, Translational Genomics Research Institute (TGen), and University of Arizona. It also seeks to educate Arizona's residents about the disease, research progress in the state and the resources needed to help patients, families and professionals manage the disease.

Under an Appropriation, the Consortium receives $2,000,000 for Alzheimer Disease research. Of that amount, the Consortium is required to match $1,000,000.

A complete guide to all of the Consortium's research summaries, key personnel, project progress reports, publications, manuscripts, poster abstracts and grants can be found at http://azalz.org/about-us/2015-aac-annual-report/

## 2015 Highlights

Since inception:

- Generated more than 4000 publications
- 1000 grants and contracts
- $1 billion in new investments

# Translational Research Facility

# Translational Research Facility

In 2002, Arizona identified the need for "a nonprofit medical research foundation in Arizona that specializes in biotechnology and that collaborates with universities, hospitals, biotechnology and health science research centers and other public and private biotechnology businesses in Arizona." Seeking to fulfill this need, ABRC contracted with the Translational Genomics Research Institute (TGen).

In FY 2015, $2,000,000 of the Health Research Fund (tobacco tax) was appropriated by the Arizona legislature to support the basic operational infrastructure of a translational genomics research facility. Funds are used for genomic based research and clinical work aimed at discovering the underlying causes of disease progression and fostering collaboration-based projects.


## 2015 Highlights

Promised Economic Benefits: Positive Economic Benefits of TGen on the State of Arizona, 2014 - TGen released an economic impact study in April 2015.

## Summary of FY 2015 TGen Activities:

- TGen filed 55 patent applications in FY15 based on discoveries stemming from TGen-led research, and 18 patents were issued.
- 41 publications and presentations resulting from projects supported by ABRC
- 31 projects were supported by ABRC
- Released economic impact study, "Promised Economic Benfits: Positive Economic Benefits of TGen on the State of Arizona 2014"
- Released Consolidated Financial Statements for calendar years 2013 and 2014
- ABRC partially supports 4 TGen staff as well as many support personnel.

Arizona Department of Health Services

# Arizona Biomedical Research Commission

Grants • Biospecimen Locator • Education • Public Cord Blood

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