Linking Research and Researchers

Boston University Research
Interdisciplinary Biomedical Research Office
www.bu.edu/research/ibro

Evans Center
For Interdisciplinary
Biomedical Research
www.bumc.bu.edu/evanscenteribr

MISSION STATEMENT

Affinity Research Collaboratives (ARCs) consist of faculty and trainees from different disciplines across campuses, and are organized around foci of common research interests. The extraordinary strength in biomedical and physical sciences at Boston University, and the support and development of the ARCs create opportunities for new interdisciplinary approaches to both research and training in biomedical research. Basic science discovery promoted by ARCs are also available to the Clinical and Translational Science Institute and to other centers for collaborative translational applications.

SUPPORTED BY

The Evans Center for Interdisciplinary Biomedical Research, open to faculty across BU campuses, is supported by the Department of Medicine, its chair (Dr. David Coleman) and the vice chair for research, and by the Evans Medical Foundation (2009-present). The Boston University Interdisciplinary Biomedical Research Office (BU IBRO) (2015-present) within the office of BU Associate Provost for Research and BU Clinical and Translational Sciences Institute (CTSI) (2010-present) provide additional collaborations and support.

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- **Mobile and Electronic Health (ME-Health) ARC** | Directors: Drs. Belinda Borrelli, Lisa Quintiliani and Julie Keysor — Pg. 19
- **Systems Biology Approaches to Microbiome Research ARC** | Directors: Drs. Daniel Segrè and W. Evan Johnson — Pg. 19
- **Precision Medicine for Alzheimer Disease and Related Disorders ARC** | Directors: Drs. Rhoda Au, Alice Cronin-Golomb and Lindsay Farrer — Pg. 19

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The Evans Center for Interdisciplinary Biomedical Research (ECIBR) and BU Interdisciplinary Biomedical Research Office (BU IBRO)

Founding Director: Katya Ravid, Professor of Medicine and Biochemistry, Fulbright Research Scholar

BY THE NUMBERS

ARC Outcomes and Types of Metrics for Monitoring and Evaluating Success (2009-2017):

1. 12 multidisciplinary ARCs have received funding to investigate novel research topics that included 220 faculty (about 100 core participants), **97 predocs & 50 postdocs**. Minority researchers and trainees have similar percent representation as in the faculty body.
2. 4 multidisciplinary ARCs have engaged with 4 hubs in CTSA network; Adoption of the ARC Model by 2 hubs in the CTSA network.
3. 421 collaborative publications catalyzed by ARCs, 75% of co-authors had never published together prior to the ARC.
4. 123 external grants awarded to ARC affiliated projects out of 222 applied for with at least two ARC faculty in the co-PI or co-I roles.
5. ARCs catalyzed investigators from 19 departments & industry to form multidisciplinary research projects.
6. Average of 12 seminars, 3 workshops, 2 retreats and 4 symposia per year attracted an average of 60 investigators & 25 trainees per event; Annual 'Shining Light on Trainees' seminars and mini-symposia present the dynamic research contributed to the ARCs by **predocs and postdocs**.
7. ARC spin-off: new BU Program in Oral Cancer & BU Head & Neck Cancer SPORE submission for regional cancer network (in review); BU Thrombotic Microangiopathy Collaborative; two university-wide research cores in Arterial Biomechanics & Bioenergetics; 4 provisional IP filings to ARC affiliated projects; new BU Research Program in Nanomedicine.
8. Institutionalization of 2 new Team Science Members Directed Masters Programs launched, training in Nanomedicine and in Biomedical Research Technologies.
9. 4 publications about the influence of the ARC Model and best practices shared with the CTSA network.
10. Institutionalization of university-wide Interdisciplinary Biomedical Research Office to advance team science starting 2015.

KEYS FOR SUCCESS: THE FIVE Cs

1. **Capability**
   Creative research ideas
2. **Cooperation**
   Willingness to learn
3. **Communication**
   Effective scientific exchanges
4. **Coaching**
   Generous mentoring/insights by the Center's Director and ARC leadership
5. **Conditions**
   Supportive resources and academic culture

PUBLICATIONS

"Thrombotic Microangiopathy: A Multidisciplinary Team Approach."
Gordon CE, Chitalia VC, Sloan JM, Salant DJ, Coleman DL, Quillen K, Ravid K, Francis JM.
Am J Kidney Dis. 2017 Nov;70(5):715-721.
›› View at http://bit.ly/2k9qLG8

"Catalyzing Interdisciplinary Research and Training: Initial Outcomes and Evolution of the Affinity Research Collaboratives Model."
Ravid K, Seta F, Center D, Waters G, Coleman D.
Acad Med. 2017 Oct;92(10):1399-1405.
›› View at http://bit.ly/2kdXH0g

"Promoting interdisciplinary research in departments of medicine: results from two models at Boston University School of Medicine."
Coleman DL, Spira A, Ravid K.
Trans Am Clin Climatol Assoc. 2013;124:275-82.
›› View at http://bit.ly/2kdYgXW

"Building interdisciplinary biomedical research using novel collaboratives."
Ravid K, Faux R, Corkey B, Coleman D.
Acad Med. 2013 Feb;88(2):179-84.
›› View at http://bit.ly/2AKOJhU

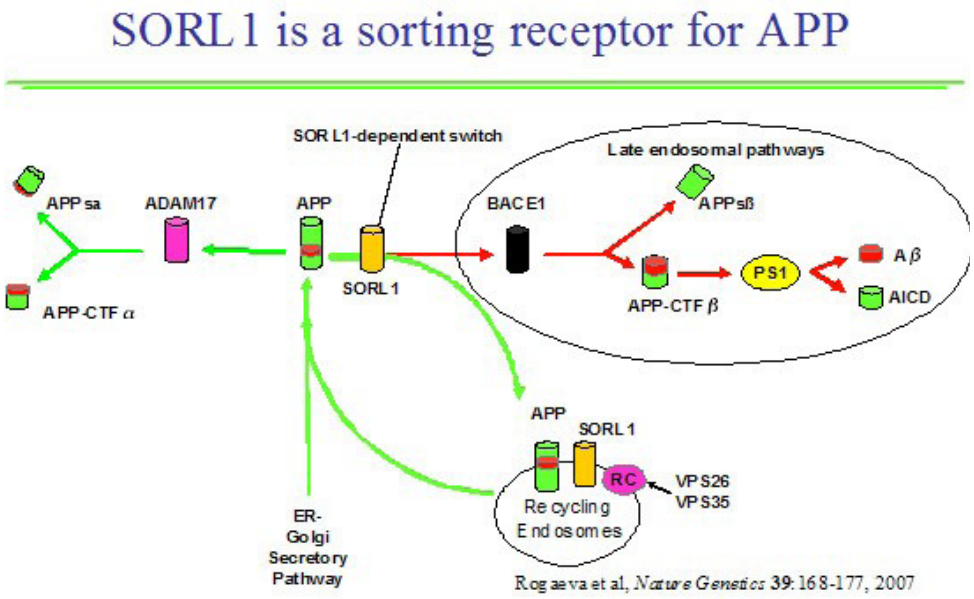
Protein Trafficking and Neurodegenerative Disease

Director: Dr. Lindsay Farrer

(ARC, 2009-2012; ARC Program, 2013-Present)

SYNOPSIS

Recycling of the amyloid precursor protein (APP) from the cell surface via the endocytic pathways plays a key role in the generation of amyloid ß-peptide (Aß), the accumulation of which is thought central to the pathogenesis of Alzheimer disease (AD).



This ARC explores the role of vesicular sorting proteins and other genes involved in protein trafficking in the etiology and pathophysiology of AD and other neurodegenerative disorders. The power of this ARC lies in its diverse, interdisciplinary expertise, and ability to validate any finding using independent approaches of genetic epidemiology, cell biology, model systems and pathology.

HIGHLIGHTS

Novel analytical methods were applied to identify gene loci for AD in large family- based datasets from the Framingham Heart Study (FHS) and National Institute on Aging Late Onset Alzheimer Disease Study (NIA-LOAD) using a genome-wide association study (GWAS) approach. This ARC also led to the successful funding of a large NIH grant beginning in 2014.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Jun G, Asai H, Zeldich E, Drapeau E, Chen C, Chung J, Park JH, Kim S, Haroutunian V, Foroud T, Kuwano R, Haines JL, Pericak-Vance MA, Schellenberg GD, Lunetta KL, Kim JW, Buxbaum JD, Mayeux R, Ikezu T, Abraham CR, Farrer LA. PLXNA4 is associated with Alzheimer disease and modulates tau phosphorylation. Ann Neurol. 2014 Sep; 76(3):379-92. doi: 10.1002/ana.24219. Epub 2014 Jul 29.

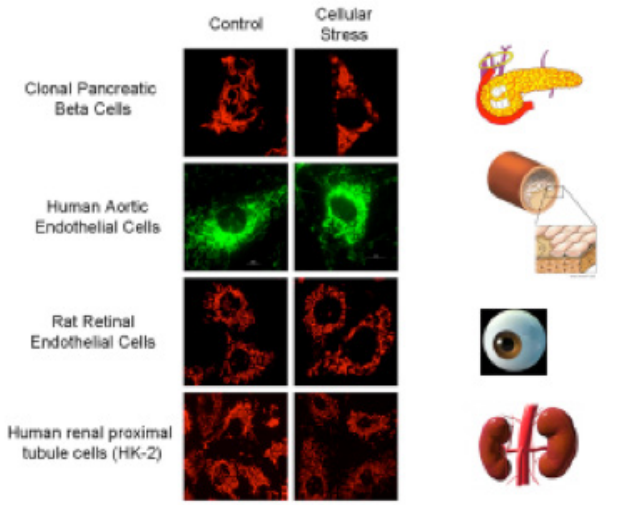
Mitochondrial Dynamics in Health and Disease (mtARC)

Directors: Drs. Orian Shirihai and Andrea Havasi

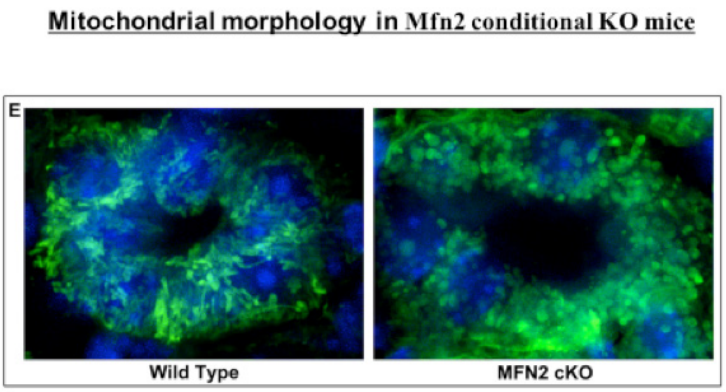
(ARC, 2009-2012; ARC Program, 2013-2016; The ARC gave rise to a Bioenergetics Core)

SYNOPSIS

The mtARC focused on the role of mitochondria in physiology and pathophysiology. Diverse membership encompassed 12 sections/departments with representation from both the Medical and Charles River Campuses. In addition, membership included labs from other universities and from industry. This ARC also provided training and tools for investigating mitochondrial bioenergetics, dynamics and reactive oxygen species (ROS) in various systems.



Data from the labs of Drs Shirihai, Vita, Roy & Borkan



HIGHLIGHTS

The mitochondrial ARC collaboratively discovered a role for mitofusin 2 (Mfn2) and mitochondrial dynamics in neurodegeneration and metabolic diseases in different organ systems, and was shown to have an important role in organ survival after ischemia. This ARC gave rise to an institutional Research Core focused on Bioenergetics.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Liesa M, Luptak I, Qin F, Hyde BB, Sahin E, Siwik DA, Zhu Z, Pimentel DR, Xu XJ, Ruderman NB, Huffman KD, Doctrow SR, Richey L, Colucci WS, Shirihai OS. Mitochondrial transporter ATP binding cassette mitochondrial erythroid is a novel gene required for cardiac recovery after ischemia/reperfusion. Circulation. 2011 Aug 16; 124(7):806-13. doi: 10.1161/CIRCULATIONAHA.110.003418. Epub 2011 Jul 25.

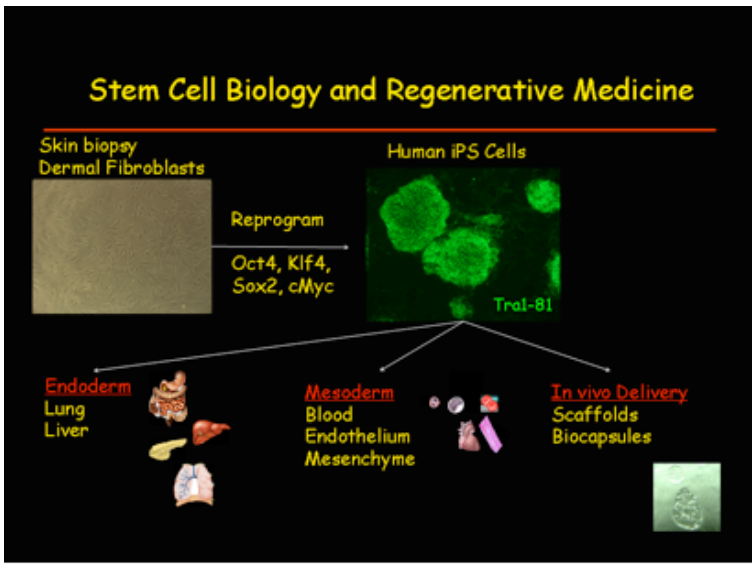
BU iPS Cell Bank

Directors: Drs. Darrell Kotton, Gustavo Mostoslavsky and George Murphy

(ARC, 2009-2012; ARC Program, 2013-2014; CReM (2014-Present)

SYNOPSIS

The discovery that mature somatic cells can be reprogrammed into induced pluripotent stem (iPS) cells provides unprecedented opportunities to better understand and treat a variety of human diseases.



ARC members developed in the past a novel reagent, the lentiviral 'stem cell cassette' vector (STEMCCA) that allows the most efficient generation of iPS cells.

This ARC utilized this vector to develop an extensive bank of human iPS cells from individuals with diseases commonly found in the Boston Medical Center patient population: Sickle Cell Anemia, Amyloidosis, Emphysema, Inflammatory Bowel Disease, Scleroderma, and Diabetes.

HIGHLIGHTS

The iPS Cell Bank, Regenerative Medicine ARC initiative, among the first ARCs to be awarded at Boston University, facilitated the launch of an Open-Source stem cell bank that has grown over the years into one of the most widely shared NIH-sponsored stem cell repositories in the US. Today, this repository continues to serve as the heart of an new ARC- facilitated born Center for Regenerative Medicine, and has become the largest bank of disease- specific induced pluripotent stem (iPS) cells for studying sickle cell disease, amyloidosis, and genetic lung diseases including alpha-1 antitrypsin deficiency, cystic fibrosis, and a wide variety of genetic neonatal lung disorders.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Somers A1, Jean JC, Sommer CA, Omari A, Ford CC, Mills JA, Ying L, Sommer AG ,Jean JM, Smith BW, Lafyatis R, Demierre MF, Weiss DJ, French DL, Gadue P, Murphy GJ, Mostoslavsky G, Kotton DN. Generation of transgene-free lung disease-specific human induced pluripotent stem cells using a single excisable lentiviral stem cell cassette. Stem Cells. 2010 Oct. 28 (10):1728-40. doi: 10.1002/stem.495.

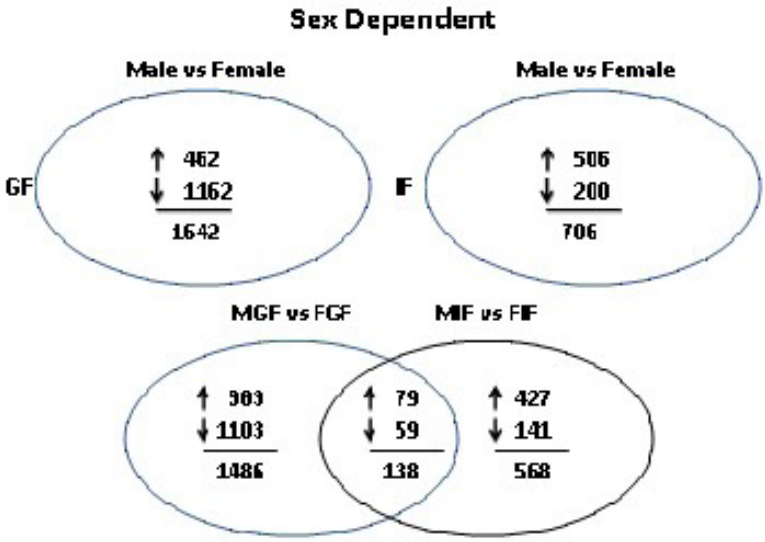
Sex Differences in Adipose Tissue Biology and Related Metabolic Disease

Directors: Drs. Susan K. Fried and Paul Pilch

(ARC, 2009-2012; ARC Program, 2013-2015; continued collaboration with BNORC)

SYNOPSIS

This ARC focused on the role of adipose tissue biology in the metabolic complications of obesity in men and women. Members have complementary expertise in biochemistry, cell biology, immunology and translational research in obesity, diabetes and cardiovascular disease. This ARC had a close relationship to an existing NIH-funded center, the Boston Nutrition and Obesity Research Center, and has initiated novel collaborations resulting in interdisciplinary grant proposals, including 'brite' adipocytes, adiporedoxin, a novel regulator adipocyte secretory function and adipocyte dysfunction in insulin resistance. The ARC also engaged in fruitful ARC-ARC collaborations with four other ARCs: Mitochondria, Arterial Stiffness, Cancer and Inflammation, and Metabolic Disease and Insulin Resistance: Studies in Patients Undergoing Bariatric Surgery.



HIGHLIGHTS

The ARC team found that glucocorticoids (GC) have profound effects on adipose tissue, adipogenesis and adipose tissue metabolic and endocrine function. With chronic excess GC, produced systemically or through local adipose tissue conversion, fat accumulates in central adipose depots and contributes to metabolic derangements.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Jedrychowski MP, Liu L, Laflamme CJ, Karastergiou K, Meshulam T, Ding SY, Wu Y, Lee MJ, Gygi SP, Fried SK, Pilch PF. Adiporedoxin, an upstream regulator of ER oxidative folding and protein secretion in adipocytes. Mol Metab. 2015 Sep 18;4(11):758-70. doi: 10.1016/j.molmet.2015.09.002. eCollection 2015 Nov. PMID: 26629401

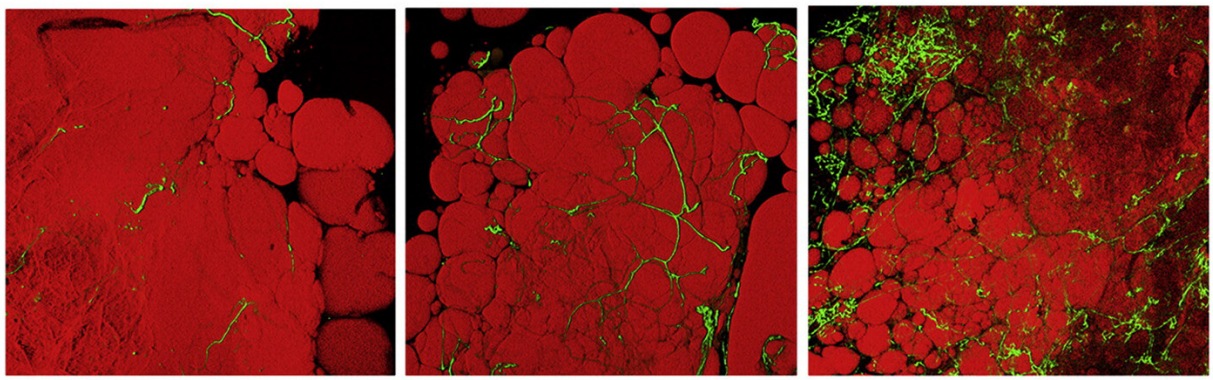
Cardiovascular Consequences of Metabolic Disease

Director: Dr. Kenneth Walsh

(ARC, 2009-2010; Successful completion with achievement of an NHLBI-funded PPG)

SYNOPSIS

Obesity promotes a chronic inflammatory state, which contributes to the development of insulin resistance and cardiovascular disease. This ARC intended to promote translational research by bringing basic and clinical research laboratories together to study the cardiovascular consequences of obesity and diabetes. Activities of basic science labs and clinical research labs were coordinated to assess the interrelationship between metabolic dysfunction and vascular disease.



Angiogenesis in adipose tissue (Walsh and Aprahamian et al.)

HIGHLIGHTS

The ARC identified and studied the role of angioenesis in adipose tissue biology, with focus on fat cell expansion.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

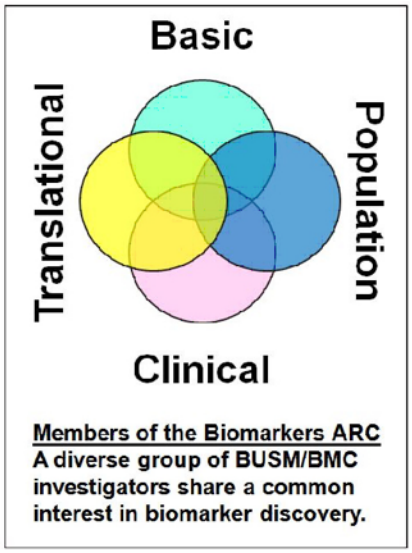
Bretón-Romero R1, Feng B1, Holbrook M1, Farb MG1, Fetterman JL1, Linder EA1, Berk BD1, Masaki N1, Weisbrod RM1, Inagaki E1, Gokce N1, Fuster JJ1, Walsh K1, Hamburg NM2. Endothelial Dysfunction in Human Diabetes Is Mediated by Wnt5a-JNK Signaling. Arterioscler Thromb Vasc Biol. 2016 Mar;36(3):561-9. doi: 10.1161/ATVBAHA.115.306578. Epub 2016 Jan 21.

Biomarkers of Disease

Directors: Drs. Mark McComb, Richard A. Cohen and Catherine Costello

(ARC, 2009-2012; ARC Directors re-directed efforts into a newly funded NIH grant to support a National Proteomic Center at BU)

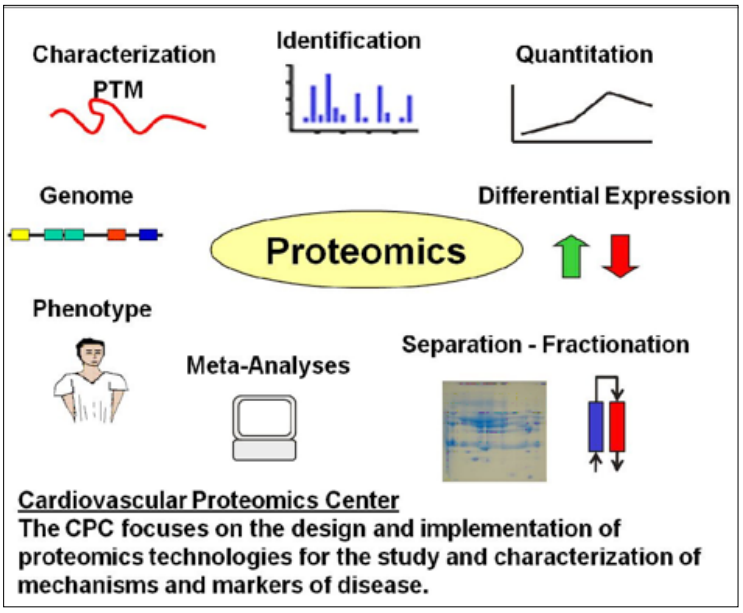
SYNOPSIS



Projects designed by this ARC were to build on existing expertise and to take advantage of preliminary research studies performed at BUMC in transgenic mice and animal models of metabolic disease. A discovery-based proteomics approach was designed to identify candidate biomarkers related to metabolic disease. The studied hypothesis was that metabolic changes in diseased tissues may be detected by changes in plasma protein abundances that betray leakage of tissue-specific proteins, and by post-translational modifications (PTMs) that reflect abnormal tissue metabolism.

HIGHLIGHTS

This ARC team discovered changes in metabolic function that may be maladaptive, leading to a situation in which substrate supplied to the heart for energy generation is adequate in amount but cannot be fully utilized. They provided a model to offer specific molecular insights regarding the cellular and physiological mechanisms that lead to metabolic heart disease.



EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

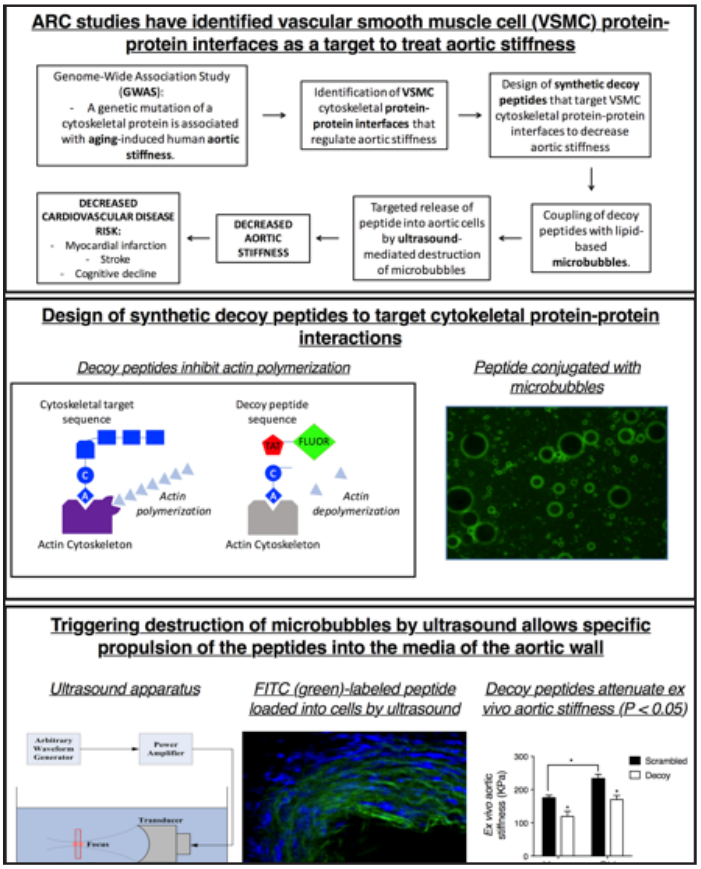
Behring JB, Kumar V, Whelan SA, Chauhan P, Siwik DA, Costello CE, Colucci WS, Cohen RA, McComb ME, Bachschmid MM. Does reversible cysteine oxidation link the Western diet to findings that demonstrate that noncanonical Wnt5a signaling and JNK activity contribute to vascular insulin resistance and endothelial dysfunction and may represent a novel therapeutic opportunity to protect the vasculature in patients with diabetes mellitus. FASEB J. 2014 May; 28(5):1975-87.

Molecular, Biomechanical and Genetic Mechanisms of Arterial Stiffness

Directors: Drs. Richard Cohen, Kathleen Morgan and Francesca Seta

(ARC, 2010-2013; ARC Program, 2014-Present; Arterial Function Core)





SYNOPSIS

Arterial stiffness, a vascular condition characterized by loss of elastic compliance of large arteries, is an independent predictor of, and probable cause of, subsequent adverse cardiovascular events. Targeting arterial stiffness could represent a novel approach to decrease the risk of developing cardiovascular diseases, which remain the major cause of mortality and morbidity in US. The Arterial Stiffness ARC was conceived as an interdisciplinary collaborative group of basic scientists, epidemiologists and bioengineers, from BUSM/BMC, The Framingham Heart Study and CRC, to tackle the complex question of what causes arterial stiffness with the common goal of identifying therapeutic targets.

HIGHLIGHTS

This ARC team initiated efforts to identify therapeutic target molecules to prevent or reverse aortic stiffness, discovered that activation of the lysine deacetylate sirtuin-1 has potent anti-inflammatory and anti-oxidant effects on the vascular wall decreasing arterial stiffness in a model of diet-induced obesity, and successfully applied GWAS data to identify candidate molecules to develop cell permeant, microbubble targeted decoy peptides that are effective in decreasing aortic stiffness in an aged rodent model.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

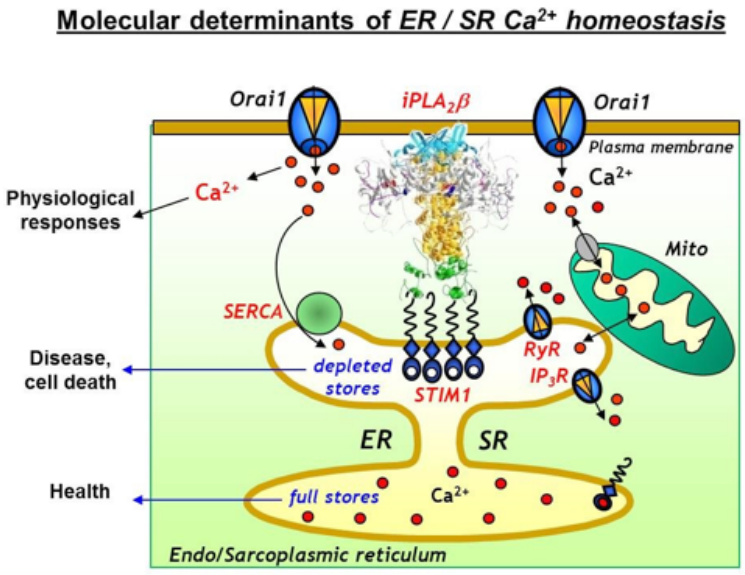
Fry JL, Al Sayah L, Weisbrod RM, Van Roy I, Weng X, Cohen RA, Bachschmid MM, Seta F. Vascular Smooth Muscle Sirtuin-1 Protects Against Diet-Induced Aortic Stiffness. Hypertension. 2016 Sep;68(3):775-84. doi: 10.1161/HYPERTENSION.116.07622. Epub 2016 Jul 18. PMID:27432859

Calcium Homeostasis in Health and Disease

Directors: Drs. Victoria Bolotina and Michael Kirber

(ARC, 2010-2013; ARC Program, 2014-2015)

SYNOPSIS



Comprised of experts in complementary fields from 18 laboratories in 15 Sections/ Departments from BUSM and Charles River BU campuses, this ARC looked at the mechanisms of cellular function from many different perspectives, which enabled the group to identify common molecular determinants and mechanisms of Ca2+ signaling in diverse cell types, and allowed their translation to human disease to address the mechanisms of impairment in Ca2+ homeostasis in cardiovascular, neurological, pancreatic and other systems.

HIGHLIGHTS

Calcium ARC supported a ground-breaking discovery of a novel Ca2+ signaling mechanism of Parkinson's disease, and has provided school-wide expertise in the study of calcium homeostasis.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

ZhouQ, Yen A, Rymarczyk G, Asai H, Trengrove C, Aziz N, Kirber MT, Mostoslavsky G, Ikezu T, Wolozin B, Bolotina VM. Impairment of PARK14-dependent Ca(2+) signalling is a novel determinant of Parkinson's disease. Nat Commun.2016 Jan 12;7:10332. doi: 10.1038/ncomms10332.

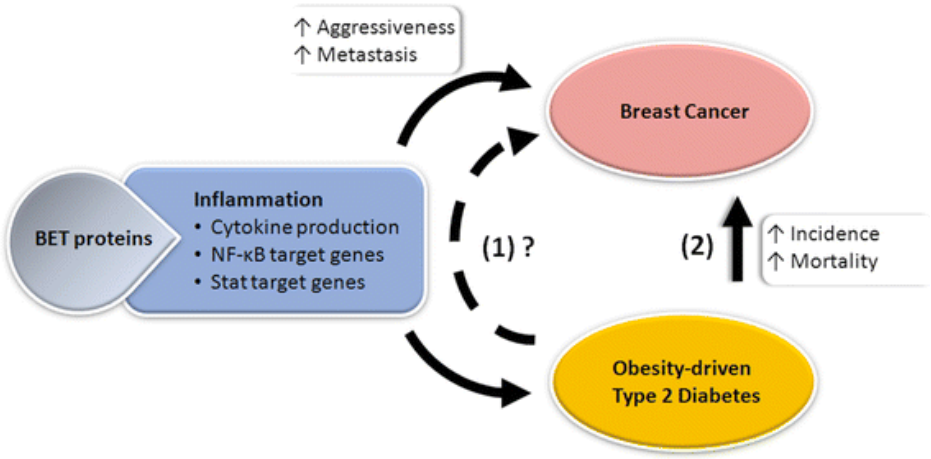
Obesity, Inflammation and Cancer

Directors: Drs. Gerald V. Denis and Barbara Nikolajczyk

(ARC, 2010-2013)

SYNOPSIS

Population studies identify cohorts of high body mass index (BMI) subjects with unexpectedly reduced risk for breast and colon cancer, and normal BMI subjects with unexpectedly elevated risk for breast cancer, provoking hard thinking about cellular and molecular mechanisms that most strongly couple obesity to cancer occurrence or progression. Emerging work suggests that abnormal metabolism and its associated chronic inflammation make the difference.



Nichols et al, *Cell Molecular Life Science* **74(2)**: 231-233, 2017

HIGHLIGHTS

Discoveries made by this ARC support a new hypothesis: metabolic disease in obesity promotes breast cancer incidence and metastasis.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Nicholas DA1,2, Andrieu G1, Strissel KJ1, Nikolajczyk BS2, Denis GV3,4. BET bromodomain proteins and epigenetic regulation of inflammation: implications for type 2 diabetes and breast cancer. Cell Mol Life Sci. 2017 Jan;74(2):231-243. doi: 10.1007/s00018-016.

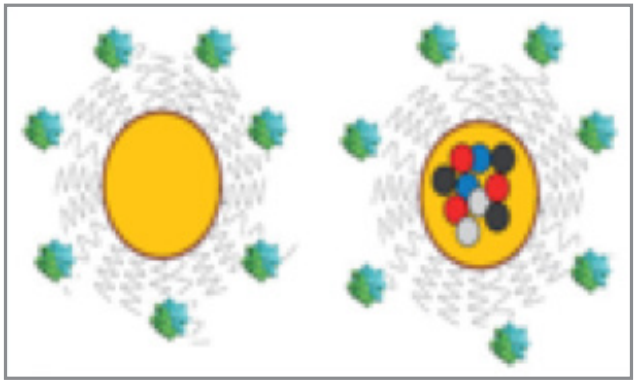
Nanotheranostics

Directors: Drs. Victoria Herrera, Mark Grinstaff, Joyce Wong and Karl Karlson

(ARC, 2012-2015; ARC Program, 2015-2017 giving rise to Master of Science and research programs in Nanomedicine)

SYNOPSIS

Nanotheranostics is defined as the integrated combination of target-specific diagnostics and delivery of therapeutics based on nanotechnology platforms. The ARC-program has provided the opportunity to utilize prototype nanotechnology platforms and proof of concept imaging formats. Operationalization of the experiments to test the diagnostics, therapeutic and intraoperative survival visualization and resection required the inter-disciplinary expertise and capabilities of several departments: Chemistry, Biomedical Engineering, Molecular Medicine, Pathology, and Surgery.



HIGHLIGHTS

The ARC discovered and proved that low pH-responsive expansile nanoparticles (eNPs) home to and selectively localize intracellularly in pancreatic cancer cells in xenograft model of pancreatic peritoneal carcinomatosis, while sparing peri-tumoral normal cells – endothelium, mesothelium, adipocytes, pancreatic tissue, and all normal intra-abdominal organs including the liver and spleen where all other nanoparticles typically end-up by default.

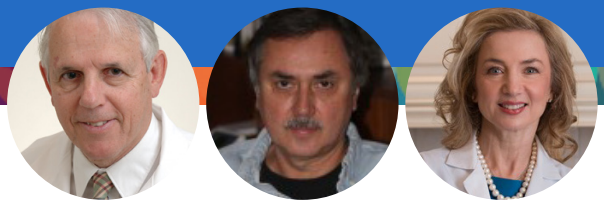
EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Herrera VL, Colby AH, Tan GA, Moran AM, O'Brien MJ, Colson YL, Ruiz-Opazo N, Grinstaff MW. Evaluation of expansile nanoparticle tumor localization and efficacy in a cancer stem cell- derived model of pancreatic peritoneal carcinomatosis. Nanomedicine (Lond). 2016 May;11(9):1001-15. doi: 10.2217/nnm-2015-0023. Epub 2016 Apr 14. PMID: 27078118

Metabolic Diseases and Insulin Resistance: Studies in Patients Undergoing Bariatric Surgery

Directors: Drs. Neil Ruderman, Konstantin Kandror and Caroline Apovian

(ARC, 2012-2014; 2015-on, members joined other metabolic-related ARCs)

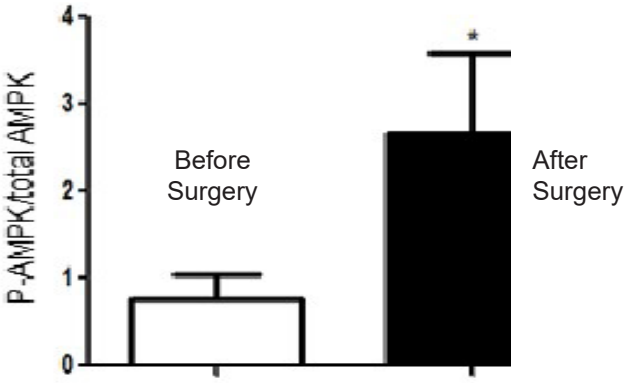


SYNOPSIS

Morbidly obese individuals are predisposed to a wide range of diseases including type 2 diabetes, atherosclerotic cardiovascular disease (ASCVD), fatty liver disease, and certain cancers, all of which can be improved or prevented by bariatric surgery. This ARC team, along with a few other groups, have observed that approximately 25% of morbidly obese individuals are insulin sensitive (IS) and the remainder, are insulin resistant (IR). Intriguingly, compared to the IR group, the IS patients are less likely to develop ASCVD, and presumably other obesity- associated comorbidities.

HIGHLIGHTS

The ARC found that the activity of fuel sensing enzyme AMP-activated protein kinase (P-AMPK) in adipose tissue is markedly diminished (70%) in the insulin resistant patients at the time of surgery. Likewise, 3-months post-operatively decreased AMPK activity was eliminated.



Comparison of AMPK phosphorylation in the subcutaneous fat of 11 matched pre- and post-bariatric surgery patients (*p<0.05).

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Xu XJ, Apovian C, Hess D, Carmine B, Saha A, Ruderman N. Improved Insulin Sensitivity 3 Months After RYGB Surgery Is Associated With Increased Subcutaneous Adipose Tissue AMPK Activity and Decreased Oxidative Stress. Diabetes. 2015 Sep;64(9):3155-9.

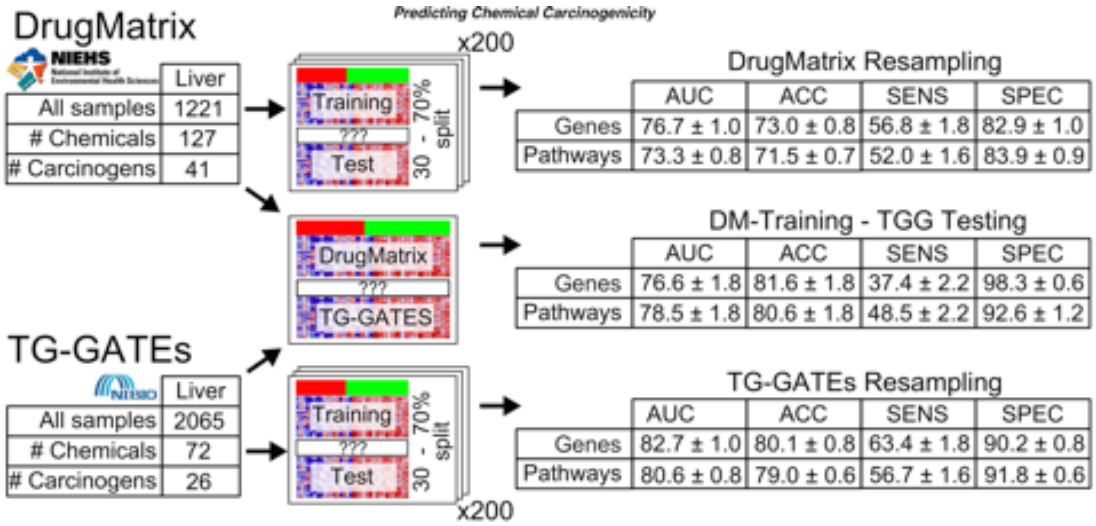
Computational Genomics Models of Environmental Chemical Carcinogenicity

Directors: Drs. Stefano Monti and David Sherr

(ARC, 2013-2016; ongoing discussions related to a new Environmental Toxicity Program)

SYNOPSIS

This project was centered around the over-arching goal of developing genomic models of carcinogenicity for cancer prevention and tailored treatment, the goal being to develop accurate and cost-effective methods for the identification of threats to our health from exposure to chemical and environmental carcinogens. An essential component of this ARC is the research into development and application of novel computational approaches to the analysis and integration of multi-dimensional, multi-omics data.



HIGHLIGHTS

The ARC team confirmed the hypothesis that the genomic profile of human cells generated in response to short term exposure with environmental chemicals in vitro can predict, with up to 83% accuracy, a long term biologic consequence, in vivo cancer development. This discovery paves the way for predicting which of the 85,000 chemicals in consumer and industrial use are human carcinogens. To date, only ~2.5% of those chemicals have been tested for carcinogenicity.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Gusenleitner D, Auerbach SS, Melia T, Gomez HF, Sherr DH, Monti S. Genomic models of short-term exposure accurately predict long-term chemical carcinogenicity and identify putative mechanisms of action. PLoS One. 2014;9(7):e102579. Epub 2014/07/25. doi: 0.1371/journal.pone. 0102579PONE-D-14-11756 [pii]. PMID: 25058030

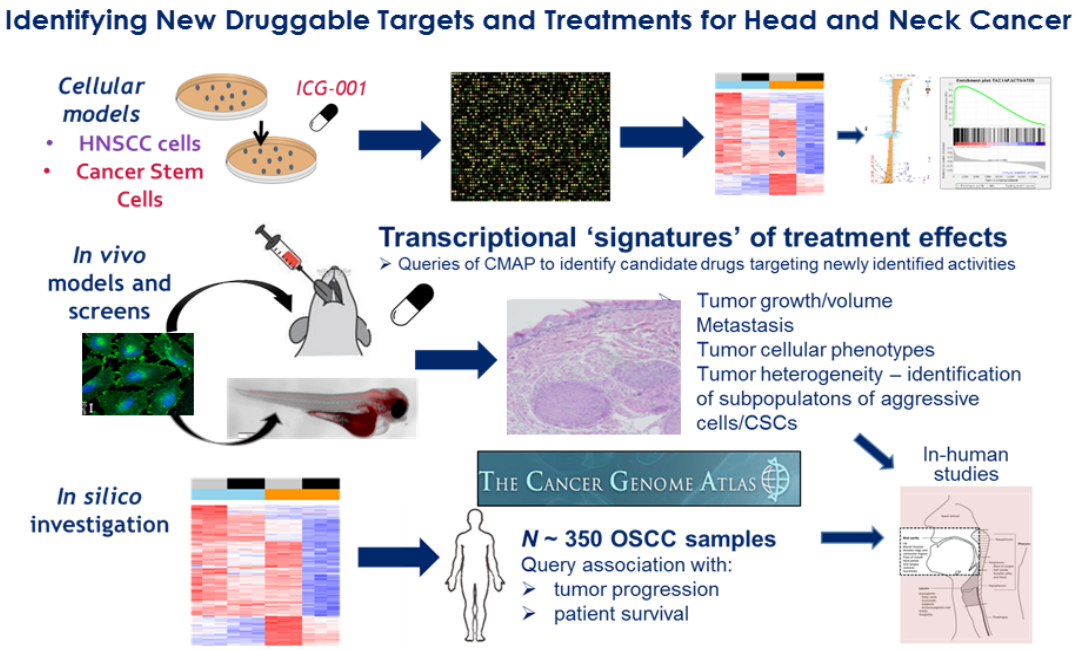
Etiology & Pathogenesis of Oral Cancer

Directors: Drs. Maria Kukuruzinska, Maria Trojanowska and Avrum Spira

(ARC, 2014-2017; 2017-Present ARC Program)

SYNOPSIS

Studies conducted by the Etiology & Pathogenesis of Oral Cancer (EPOC) ARC have been conducted by an array of faculty from different schools, aiming at developing new pathways and understanding of this pathology.



HIGHLIGHTS

EPOC activities have led to significant new findings related to: 1) the mechanisms of oral squamous cell carcinoma (OSCC) development and progression with a focus on the early pathways involving the N-glycosylation/ß-catenin/TAZ-YAP signaling axis, as well as the role of aryl hydrocarbon receptor in tumor initiation in collaboration with the oral microbiome; 2) the remodeling and activation of OSCC tumor stroma and its role in cancer progression; and 3) personalized early detection and treatment of oral cancer, with emphasis on early detection and amelioration of radiation treatment-induced fibrosis.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Stanford EA, Ramirez-Cardenas A, Wang Z, Novikov O, Alamoud K, Koutrakis P, Mizgerd JP, Genco CA, Kukuruzinska M, Monti S, Bais MV, Sherr DH. Role forthe Aryl Hydrocarbon Receptor and Diverse Ligands in Oral Squamous Cell Carcinoma Migration and Tumorigenesis. Mol Cancer Res. 2016 Aug;14(8):696-706. doi: 10.1158/1541- 7786.MCR-16-0069. Epub 2016 Apr 29.

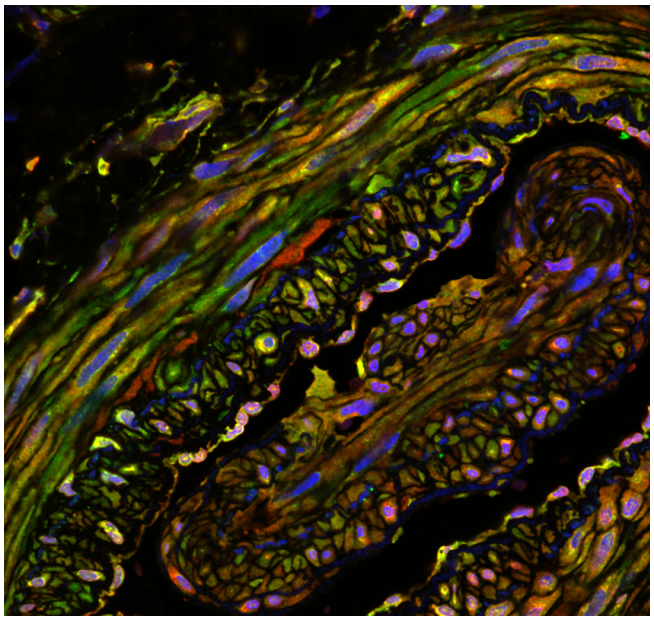
Thrombosis and Hemostasis in Health and Disease

Directors: Drs. Vipul Chitalia, Katya Ravid and Jean Francis

(ARC, 2015-Present)



SYNOPSIS



Vasa vasorum: tissue factor (red) and its cognate ubiquitin ligase, STUB1 (green); On the Cover of *Science Translational Medicine*

Highly controlled process of thrombus formation is orchestrated by the dynamic interaction of vessel wall factors and blood consisting of soluble coagulation factors and different cellular components.

Leveraging newly discovered thrombotic mediators including, Lysyl oxidase (LOX) and metabolites of tryptophan in thrombosis axis (tryptophan metabolite-Aryl Hydrocarbon Receptor signaling – tissue factor) in preclinical models, the Thrombosis and Hemostasis ARC probed close to 800 well-curated human samples with varying degree of renal dysfunction from two major clinical trials with discrete thrombotic-related primary outcomes to validate the prothrombotic nature of LOX and uremic thrombosis axis and develop a highly predictive model based on machine learning algorithms.

HIGHLIGHTS

The Thrombosis and Hemostasis in Health and Disease ARC had evaluated several facets of thrombosis spanning from novel mediators to the generation of the animal model up to validating the hypotheses in human cohorts. This ARC has investigated thrombosis using emerging techniques such as machine-learning techniques in the context of organ pathologies (e.g., renal failure), infectious disease (e.g., Shigella-Toxin mediated) and Thrombotic Microangiopathy Collaborative (TMA), a highly complex disease mediated primarily by the aberrant hyperactivation of complement system. The ARC established the first Boston University TMA initiative with BU CTSI.

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Shashar M, Belghasem ME, Matsuura S, Walker J, Richards S, Alousi F, Rijal K, Kolachalama VB, Balcells M, Odagi M, Nagasawa K, Henderson JM, Gautam A, Rushmore R, Francis J, Kirchhofer D, Kolandaivelu K, Sherr DH, Edelman ER, Ravid K, Chitalia VC. Targeting STUB1-tissue factor axis normalizes hyperthrombotic uremic phenotype without increasing bleeding risk. Sci Transl Med. 2017 Nov 22;9(417).

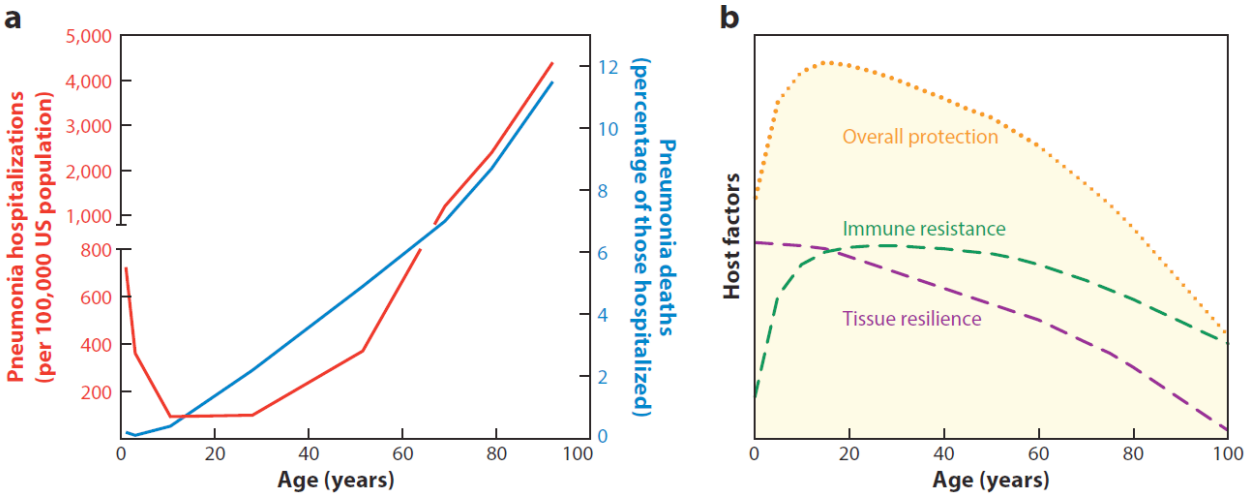
PneumoniARC

Director: Dr. Joseph 'Jay' Mizgerd

(ARC, 2016-Present)

SYNOPSIS

A multidisciplinary team was gathered, integrating critical distinct perspectives into this complex disease process, including the basic biology disciplines of Lung Biology, Immunology, and Microbiology, combined with clinical research realms from those caring for children (Pediatrics) or older adults (Pulmonary & Critical Care Medicine), to form the PneumoniARC. In order to attack the problem of high-susceptibility to pneumonia, this ARC is coordinating the knowledge bases, research tools, and investigational activities of 9 principal investigators from 4 academic units across 6 different buildings, all of whom have studies that are complementary with others in the group and relevant to pneumonia.



From Annual Rev Physiol, 2015

HIGHLIGHTS

The ARC indentified the B cell repertoire as a window into the nature and impact of the lung "Virome."

EXAMPLE OF A COLLABORATIVE DISCOVERY AMONG SEVERAL

Kristie L. Hilliard, Eri Allen, Katrina E. Traber, Kazuko Yamamoto, Nicole M. Stauffer, Gregory A. Wasserman, Matthew R. Jones, Joseph P. Mizgerd, Lee J. Quinton. The Lung-Liver Axis: A Requirement for Maximal Innate Immunity and Hepatoprotection during Pneumonia Am J Respir Cell Mol Biol. 2015 Sep; 53(3): 378–390. doi: 10.1165/rcmb.2014-0195OC PMCID: PMC4566062

Upcoming Projects

Mobile and Electronic Health (ME-Health) ARC



Director: Dr. Belinda Borrelli
Co-Directors: Drs. Lisa Quintiliani and Julie Keysor
(ARC, 2017-Present)

SYNOPSIS

The mission of the Mobile and Electronic Health (ME-ARC) ARC is to conduct state-of-the art research and training in mobile and electronic health to improve health and well-being, with a focus on underserved populations, across the lifespan. The ARC is transdisciplinary, consisting of a steering committee, external advisory board, trainees, and over 90 member affiliates across numerous departments and schools at Boston University. The ARC's steering committee members have expertise in: implementation science, behavioral science, medicine and informatics/bioinformatics.

Systems Biology Approaches to Microbiome Research ARC


Directors: Drs. Daniel Segrè and W. Evan Johnson
(ARC, 2017-Present)

SYNOPSIS

The goal of this ARC is to develop a new, multi-level mechanistic understanding of how microbe-microbe, microbe- environment, and microbe- host interactions determine microbial community dynamics, diversity and stability, and use this knowledge to understand how to engineer microbial communities for defined purposes.

Precision Medicine for Alzheimer Disease and Related Disorders ARC



Directors: Drs. Rhoda Au, Alice Cronin-Golomb and Lindsay Farrer
(ARC, 2017-Present)

SYNOPSIS

The primary aims of this ARC are to identify subtypes of AD within the Framingham Heart Study (FHS) dataset, validate these subtypes using other available data from the national AD Centers database and other public databases, investigate the biological underpinnings of these subtypes, and identify new therapeutic targets specific for these subtypes.

Boston University Research
Interdisciplinary Biomedical Research Office

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