

Biomedical Research Advisory Council

Bankhead-Coley Cancer Research Program

James and Esther King Biomedical Research Program

Annual Report 2013-2014

Rick Scott Governor

John H. Armstrong, MD, FACS Surgeon General and Secretary of Health

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Florida Biomedical Research Program Overview

Since 2001, the Florida legislature has recognized the need to support vital research conducted in both academic and private institutions throughout the state through the James and Esther King Biomedical Research Program (Section 381.922, Florida Statutes) and the Bankhead-Coley Cancer Research Program (Section 215.5602, Florida Statutes). In 2013-2014 this funding continued to improve the health of Florida's families, expanded the research infrastructure of the state, and advanced efforts to bring external research funding to the state. Research grants are issued based on a competitive peer-review process. Awards from the King and Bankhead-Coley Programs are based on scientific merit, as determined by independent peer review involving experts located outside Florida who are free from conflicts of interest. Researchers at any university or established research institute in the state are eligible to apply for state funding. In 2013-2014 the Legislature appropriated \$20 million, which funded a total of 42 grants.

Annually the Department submits a fiscal-year progress report, including the following information as required by statute:

- A list of recipients of program grants or fellowships.
- A list of publications in peer reviewed journals involving research supported by grants or fellowships awarded under the program.
- The state ranking and total amount of biomedical research funding currently flowing into the state from the National Institutes of Health.
- New grants for biomedical research which were funded based on research supported by grants or fellowships awarded under the program.
- Progress towards programmatic goals, particularly in the prevention, diagnosis, treatment, and cure of diseases related to tobacco use, including cancer, cardiovascular disease, stroke, and pulmonary disease.
- Recommendations to further the mission of the programs.

William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program

The Bankhead-Coley Cancer Research Program advances progress toward cures for cancer. Cancer is now the leading cause of death for Floridians, surpassing heart disease. Florida continues to have the second highest cancer burden in the nation. Funding through the Bankhead-Coley program significantly improves cancer research and treatment in the state by:

- Attracting new research talent and grant-producing researchers;
- Funding proposals that demonstrate the greatest ability to attract federal research grants;
- Encouraging the development of bioinformatics to allow researchers to exchange information;
- Facilitating technical collaboration, business development and support for intellectual property related to research; and
- Aiding multi-disciplinary research through greater participation in clinical trials networks and reducing the disparate impact of cancer on certain groups.

The James and Esther King Biomedical Research Program

The purpose of the James and Esther King Biomedical Research Program is to advance cures in tobacco-related diseases. The King program funds research initiatives that seek new insights and innovative solutions in the prevention, diagnosis, treatment, and cure of Floridians afflicted by tobacco-related diseases including cardiovascular disease, stroke, lung disease and tobacco-related cancers, leading causes of death in Florida and nationally.

Florida funds research that impacts the health of Floridians

As of 2012-2013, over 3300 Floridians were enrolled in ongoing research studies funded by these two biomedical research programs. People throughout the state volunteered their time to improve the lives of all Floridians, and received health benefits from participation in the research. Benefits to the current participants included screening and genetic counseling for breast cancer; screening for colon cancer; improved diagnosis of cancer of the throat and esophagus; and improved management of the side effects of bladder cancer treatment. A study involving healthy weight and breast cancer provided dietary counseling. A small number of patients were enrolled in the initial phase of a clinical study testing new drugs to cure cancer, including an innovative cancer vaccine study. More than 800 participants were enrolled in studies of heart disease. These participants received direct benefits such as smoking cessation counseling, which included counseling and education for pregnant women who smoke. In 2013-2014, the Biomedical Research Advisory Council developed a strategic research plan with specific milestones and results to focus grant funding on health impacts and issues that matter most to Florida's families.

Florida funds research infrastructure

Studies funded by these programs improved the research infrastructure of the state. Peerreviewed research expanded the Florida Cancer Registry Data System, the largest cancer registry in the nation, to begin to create a nationally representative cancer research database. State funding for the Florida Translational Research Program Collaborative Drug Discovery Initiative at the Sanford-Burnham Medical Research Institute supported researchers funded through the King and Bankhead-Coley programs working to discover new drugs to cure cancer and tobacco-related diseases.

Florida funds research projects that help the state attract external research funding.

Florida's biomedical research programs have the distinction of being recognized by the National Cancer Institute. When Florida's funding is awarded through the rigorous peer-review mechanisms in the biomedical research programs, researchers are able to cite those grants when applying for federal funding. The National Cancer Institute accepts Florida's grant programs as evidence when conducting peer review, which is particularly important for new researchers, who do not yet have a history of federal funding.

Biomedical Research Advisory Council

The Biomedical Research Advisory Council (Section 215.5602, Florida Statutes) advises the State Surgeon General regarding the direction and scope of the biomedical research program. The responsibilities of the council include, but are not limited to:

- Providing advice on program priorities and emphases;
- Providing advice on the overall program budget;
- Participating in periodic program evaluation;
- Assisting in the development of guidelines to ensure fairness, neutrality, and adherence to the principles of merit and quality in the conduct of the program;
- Assisting in the development of appropriate linkages to nonacademic entities, such as voluntary organizations, health care delivery institutions, industry, government agencies, and public officials;
- Developing criteria and standards for the award of research grants;

- Developing guidelines relating to solicitation, review, and award of research grants and fellowships, to ensure an impartial, high-quality peer review system; and
- Reviewing reports of peer review panels and making recommendations for research grants and fellowships.

Biomedical Research Advisory Council Membership as of June 30, 2014

Daniel Armstrong, Ph.D., Chair, Professor and Executive Vice Chair, Pediatrics, Director, Mailman Center for Child Development, and Senior Associate Dean for Faculty Affairs(Interim) University of Miami Miller School of Medicine. Seat: American Cancer Society Representative.

Mark Brantly, M.D., Co-Chair, Chief, Division of Pulmonary and Critical Care Medicine University of Florida, College of Medicine. Seat: American Lung Association Representative.

Charles Wood, Ph.D., Professor and Chair, Department of Physiology and Functional Genomics, University of Florida College of Medicine. Seat: American Heart Association Representative.

Barbara Centeno, M.D., Director of Cytopathology and Anatomic Pathology Quality Assurance/Moffitt Cancer Center, Professor of Oncologic Sciences and Pathology and Cell Biology/University of South Florida. Seat: House of Representatives.

Randal H. Henderson, M.D., MBA, Associate Medical Director, Proton Therapy Institute Professor of Radiation Oncology, University of Florida, Jacksonville. Seat: House of Representatives.

Edith Perez, M.D., Deputy Director at Large, Mayo Clinic Cancer Center; Director, Breast Cancer Translational Genomics Program, Serene M. and Frances C. Durling Professor of Medicine, Mayo Clinic, Jacksonville. Seat: Senate.

Penny Ralston, Ph.D., Director, Dean Emeritus and Professor, Center on Better Health & Life for Underserved Populations, Institute of Science & Public Affairs, Florida State University. Seat: Senate.

Albert Latimer, B.B.A., Senior Vice President, External Affairs & Investor Relations Enterprise Florida, Inc. Seat: Governor.

David Decker, MD, Executive Director, Florida Hospital Cancer Institute. Seat: Governor.

Paul Jacobsen, Ph.D., Professor, Division of Population Science, H. Lee Moffitt Cancer Center and Research Institute.

Bankhead-Coley Cancer Research Program Fiscal Year 2013-2014			
Grant Recipients	Research Projects	Institution	Award Amount
Chang, Lung-Li	T cell engineering targeting small cell lung cancer	University of Florida	\$ 400,000
Chinnaiyan, Prakash	Metabolomic Underpinnings of Malignant Glioma Tumorigenesis	Moffitt Cancer Center	\$ 400,000
Copik, Alicja	Establishing Particle- Activated Natural Killer Cell Therapy for Treatment of AML in preclinical NSG Mouse Model	University of Central Florida	\$ 400,000
Franzmann, Elizabeth	Early Detection for Smoking- Associated HNSCC	University of Miami	\$ 400,000
Hromas, Robert	Targeting histone methylation for triple negative breast cancer	University of Florida	\$ 400,000
Ince, Tan	Analysis of Heat Shock Factors in Tumor Stem Cell Regulation	University of Miami	\$ 400,000
Komanduri, Krishma	Selective Inhibition of GVHD for Allogeneic Transplantation for Cancer	University of Miami	\$ 400,000
Komatsu, Masanobu	Micro-RNA regulation of vascular functions in colorectal cancer	Sanford-Burnham Medical Institute	\$ 400,000
Luesch, Hendrik	Chemistry and Biology of esch, Hendrik Apratoxins		\$ 400,000
Najmunnisa, Nasreen	Micro-RNA Based Novel Targeted Therapy for Malignant Pleural Mesothelioma	University of Florida	\$ 400,000
Pal, Tuya	Investigation of Genetic Risk Assessment for Inherited Breast Cancer (IGRAB)	Moffitt Cancer Center	\$ 400,000
Parker, Alexander	Exploration of serum and urine-based bio-markers of benign versus malignant renal masses	Mayo Clinic	\$ 400,000
Grant Recipients	Research Projects	Institution	Award Amount
Radisky, Derek	Wnt mediators as breast cancer biomarkers and	Mayo Clinic	\$ 400,000

	effectors of lobular involution		
	Methylation Profiling in Free Circulating DNA as a Biomarker for Risk Stratification of Prostate		
Singal, Rakesh	Cancer	University of Miami	\$ 400,000
Vadaparampil, Susan	Developing Intervention Components to Support Physician Recommendations of HPV Vaccinations in Males	Moffitt Cancer Center	\$ 400,000
Weber, Jeffrey	Tumor Biomarkers for Outcome with Checkpoint Protein Inhibitors	Moffitt Cancer Center	\$ 400,000
Gwede, Clement	Latinos CARES (Colorectal cancer awareness, research, education and screening) Project	Moffitt Cancer Center	\$ 399,986
Jiandong, Chen	Investigation of novel MDM2 and MDMX intra-molecular interactions	Moffitt Cancer Center	\$ 399,532
Meckes, David	Proteomic Analysis of Cancer Exosomes for Diagnostic and Therapeutic Targets	Florida State University	\$ 396,328
Wu, Jie	Optimization and Characterization of Shp2 Inhibitors	Moffitt Cancer Center	\$ 200,000
Law, Brian	Novel Anti-Metastasis Agents Targeting CDCP	University of Florida	\$ 100,000
Liao, Daiqing	Development of Novel Chemical Inhibitor of p300 for treating triple negative breast cancer	University of Florida	\$ 100,000
Rosen, Barry	Development of High- throughput Assays to Identify Drugs to Prevent Arsenic Carcinogenesis	Florida International University	\$ 100,000

James and Esther King Biomedical Research Program Fiscal Year 2013-2014				
Grant Recipients	Research Projects	Institution	Award Amount	
Antonia, Scott	Expansion of enduring infrastructure to support lung cancer screening research	Moffitt Cancer Center	\$ 1,600,000	
Shenkman, Elizabeth	OneFlorida Cancer Control Network	University of Florida	\$ 1,600,000	
Citron, Bruce	Preventing oxidative neurodegeneration after traumatic brain injury	Bay Pines Foundation	\$ 400,000	
Cole, Alexander	Utilizing a smoking cessation program to understand how cigarette smoke exacerbates nasal carriage of Staphylocccus aureus	University of Central Florida	\$ 400,000	
Dong, Chunming	MicroRNA Regulation of Smoking Induced Endothelial Progenitor Senescence	University of Miami	\$ 400,000	
Hayward, Linda	Impact of nicotine exposure on prenatal infection and a lifelong predisposition for cardiovascular disease	University of Florida	\$ 400,000	
Kapiloff, Michael	Therapeutic Targeting of RSK3 in Heart Failure	University of Miami	\$ 400,000	
Lu, Jianrong	A novel ubiquitin ligase in epithelial maintenance against tobacco smoke and lung cancer progression	University of Florida	\$ 400,000	
Ma, Teng	Translation of Human Mesenchymal Stem Cell Therapy for Stroke Treatment: Bioreactor Expansion, Functional Activation, and Intranasal Delivery	Florida State University	\$ 400,000	
Palacio, Ana	Improving Adherence to Cholesterol Lowering Medications among Minority Populations in Florida: A Randomized Trial	University of Miami	\$ 400,000	
Salihu, Hamisu	Preventing fetal body and brain size reduction in low- income smoking mothers; a randomized clinical trial	University of South Florida	\$ 400,000	

Grant Recipients	Research Projects	Institution	Award Amount
Jiandong, Chen	Nucleolar silencing and maintenance of cellular senescence	Moffitt Cancer Center	\$ 399,920
Jose-Miguez, Maria	Menthol or NOT Menthol: How Smoking is related to bone mineral density in people with and without HIV	Florida International University	\$ 399,659
Brandon, Thomas	Translating Extinction Research to Improve Pharmacotherapy for Tobacco Dependence: Intervention Development and Feasibility Trial	Moffitt Cancer Center	\$ 397,834
Brandon, Thomas	Feasibility of recruiting low- income Hispanic women for postpartum smoking intervention	Moffitt Cancer Center	\$ 197,412
Willing, Allison	HLA Interactions with human cord blood cells in a humanized mouse model of stroke	University of South Florida	\$ 150,000
Smith, Layton	Optimization of Novel Apelin Receptor Antagonists for the treatment of AMD	Sanford-Burnham Medical Institute	\$ 100,000
Stone, Geoffrey	Novel Cancer Therapy Targeting Lung Tumors for Autophagy and Antitumor Immunity	University of Miami	\$ 100,000
Bolser, Donald	An external device for rehabilitation of airway protective behaviors	University of Florida	\$ 98,422

Federal Research Funding 2013

State	NIH Funding	Rank	Total (NIH, CDC, NSH, AHRQ)*	Rank
California	3,334,417,000	1	4,985,551,000	1
Massachusetts	2,384,194,000	2	2,991,956,000	2
New York	1,946,868,000	3	2,839,882,000	3
Maryland	1,590,089,000	4	2,050,901,000	4
Pennsylvania	1,387,998,000	5	1,863,196,000	5
North Carolina	1,037,787,000	6	1,386,026,000	7
Texas	956,595,000	7	1,690,571,000	6
Washington	835,212,000	8	1,126,004,000	9
Illinois	760,095,000	9	1,322,208,000	8
Ohio	685,297,000	10	971,411,000	10
Michigan	575,889,000	11	954,657,000	11
Minnesota	493,986,000	12	689,927,000	15
Tennessee	456,096,000	13	632,924,000	17
Georgia	450,949,000	14	798,615,000	13
Connecticut	444,605,000	15	578,344,000	19
Florida	435,070,000	16	904,179,000	12
Missouri	409,220,000	17	561,028,000	20
Wisconsin	371,985,000	18	590,213,000	18
Virginia	319,864,000	19	651,724,000	16
Colorado	316,251,000	20	776,950,000	14

* www.report.nih.gov

*www.researchamerica.org

Total Follow-on Funding Awards Reported by Grantees: \$9,390,513

- Stefanovic, B, Bankhead-Coley (2014) Advanced Preclinical Evaluation of Novel-Antibrotic Drug Discovered at FSU; Validation of Efficacy in Chronic Models of Hepatic Fibrosis. FSU GAP grant \$28,500.00
- Velazquez, Omaida C., King (2013) Role of the Notch Signaling in atherosclerosis & Stem Cell-Mediated Arterial Repair. NIH, \$521,269.00
- 3. Fang, Jia, King (2013) MPP8-Mediated Epigenetic Network and Its Roles in Tumor Progression. NIH/NCI, \$1,748,187.00
- 4. Reisman, David, Bankhead-Coley, (2012) Establishing that BRM polymorphisms are predictive of lung cancer risk. NCI, \$141,00.00
- 5. Reisman, David, Bankhead-Coley, (2012) Determining if BRM polymorphisms are predictive of Cancer Risk in African Americans, NCI, \$200,000.00
- 6. George TJ, Bankhead-Coley (2012) Mucosal Inflammation and Digestive Cancer Correlation Science Biorepository, NIH/NCATS, \$20,000.00
- 7. Luesch, Hendrik, BC, (2012) Novel Targeted Anticancer Agents from Marine Cyanobacteria, National Institute of Health, \$2,872,557.00
- Borlongan, Cesar V., King (2011) Battlefield-Related Injury Translational Research, Post_traumatic Disease and Disability - Veterans Re-Intergration Strategy, DOD, \$1,800,000.00
- 9. Borlongan, Cesar V., (2011) Blood Brain Barrier Repair Cell Therapy for Stroke, National Institute of Health, \$2,200,000.00
- 10. Palacio, Ana, King, (2013) Improving Adherence to Cholesterol Lowering Medication among Minority Populations in Florida. James and Esther King, \$400,00.00

Publications in peer reviewed journals

Researchers reported 74 new publications in peer-reviewed journals between July 1, 2013 and June 30, 2014 based on Florida's research funding from the King and Bankhead Coley research programs.

- Cragun D, Camperlengo L, Robinson E, Caldwell M, Kim J, Phelan C, Monteiro, Vadaparampil S, Sellers TA, Pal T. Differences in BRCA Counseling and Testing Practices Based on Ordering Provider Type. Genet Med. 2014 Jun 12. [Epub ahead of print] PubMed PMID: 24922460.
- Salihu HM1, Salinas-Miranda A2, de la Cruz C3, Alio AP4. The role of folic acid in fetal programming of birth phenotypes and early human development: a biopsychosocial perspective. J Dev Orig Health Dis. 2013 Dec; 4(6):442-57. doi:10.1017/S2040174413000317.
- 3. Sart S1, Ma T2, Li Y2. Preconditioning stem cells for in vivo delivery. Biores Open Access. 2014 Aug 1;3(4):137-49. doi: 10.1089/biores.2014.0012.
- 4. Yang L, Mailloux A, Rollison DE et al. Naïve T-cells in myelodysplastic syndrome display intrinsic human telomerase reverse transcriptase (hTERT) deficiency. Leukemia. 27: 897-906, 2013.
- Vukmirovic M1, Manojlovic Z, Stefanovic B. Serine-threonine kinase receptor-associated protein (STRAP) regulates translation of type I collagen mRNAs. Mol Cell Biol. 2013 Oct; 33(19):3893-906. doi: 10.1128/MCB.00195-13. Epub 2013 Aug 5.
- Stefanovic B. RNA protein interactions governing expression of the most abundant protein in human body, type I collagen. Wiley Interdiscip Rev RNA. 2013 Sep-Oct; 4(5):535-45. doi: 10.1002/wrna.1177.
- 7. Blackstock CD1, Higashi Y, Sukhanov S, Shai SY, Stefanovic B, Tabony AM, Yoshida T, Delafontaine P. Insulin-like growth factor-1 increases synthesis of collagen type I via induction of the mRNA-binding protein LARP6 expression and binding to the 5' stem-loop of COL1a1

and COL1a2 mRNA. J Biol Chem. 2014 Mar 14; 289(11):7264-74. doi: 10.1074/jbc.M113.518951. Epub 2014 Jan 27.

- 8. Stefanovic B1, Stefanovic L2. Screening for antifibrotic compounds using high throughput system based on fluorescence polarization. Biology (Basel). 2014 Apr 10;3(2):281-94. doi: 10.3390/biology3020281.
- 9. Pitter, D.R.G.; Wigenius, J.; Brown, A.S.; Baker, J.D.; Westerlund, F.; Wilson, J.N. "Turn-On, Fluorescent Nuclear Stains with Live Cell Compatibility", Org Lett, 2013, 15, 1330.
- 10. Wilson, J.N.; Wigenius, J.; Pitter, D.R.G.; Qiu, Y.; Abrahamsson, M.; Westerlund, F. Base Pair Sensitivity and Enhanced ON/OFF Ratios of DNA-Binding: Donor-Acceptor-Donor Fluorophores, J. Phys. Chem. B, 2013, 117, 12000.
- 11. Wilson, J.N., Ladefoged, L.K., Babinchak, W.M., SchiØtt, B. Binding-Induced Fluorescence of SERT Lingands: A Spectroscopic and Structural Study of APP+ analogs, ACS Chem. Neurosci., 2014, 5, 296.
- Huang W., Liang, J., Kazmierczak, K., Muthu, P., Duggal, D., Farman, G.P., Sorenson, L., Pozios, I., Abraham, T., Moore, J.R., Borejdo, J., Szczesna-Cordary, D. (2014) Hypertrophic Cardiomyopathy Associated Lys104Glu Mutation in the Myosin Regulatory Light Chain Causes Diastolic Disturbance in Mice. J Mol Cell Cardiol. 74:318-329.
- Muthu, P., Liang, J., Schmidt, W., Moore, J.R., and Szczesna-Cordary, D. (2014) In Vitro Rescue Study of a Malignant Familial ypertrophic Cardiomyopathy Phenotype by Pseudo-Phosphorylation of Myosin Regulatory Light Chain. Archives of Biochemistry and Biophysics 2014 Jun 15;552-553:29-39 PMID:24374283 <u>http://www.dx.doi.org/10.1016/j.abb.2013.12.011</u>.
- 14. Three-dimensional Aggregates of Mesenchymal Stem Cells: Cellular Mechansims, Biological Properties, and Applications. Dr. Sebastien Sart, Ang-Chen Tsai, Dr. Yan Li, and Dr. Teng Ma. Tissue Engeneering Part B: Reviews. Doi:10.1089/ten.TEB.2013.0537, 2013.
- 15. Acellullar Biomaterials in Mesenchymal Stem Cell-mediated Endogenous Tissue Regeneration. Teng Ma, Journal of Materials Chemistry B, 2, 31-35, 2014.
- Zheng H, Chen L, Pledger WJ, Fang J, Chen J. p53 promotes repair of heterochromatin DNA by regulating JMJD2b and SUV39H1 expression. Oncogene. 2014 Feb 6; 33(6):734-44. doi: 10.1038/onc.2013.6. Epub 2013 Feb 4.
- Unwalla HJ1, Ivonnet P, Dennis JS, Conner GE, Salathe M. TGF-beta 1 and Cigarette Smoke Inhibit the Ability of β2-agonists to Enhance Epithelial Permeability. Am J Respir Cell Mol Biol. 2014 Jun 30. [Epub ahead of print] PMID: 24978189.
- Dickson, Kevin M., Christopher B. Gustafson, Juan I. Young, Stephan Züchner, and Gaofeng Wang. "Ascorbate-induced generation of 5-hydroxymethylcytosine is unaffected by varying levels of iron and 2-oxoglutarate." Biochemical and biophysical research communications 439, no. 4 (2013): 522-527.
- 19. Wang, Gaofeng. "Chromosome 10q26 locus and age-related macular degeneration: a progress update." Experimental eye research 119 (2014): 1-7.
- Moraes, Carlos T., Sandra R. Bacman, and Sion L. Williams. "Manipulating mitochondrial genomes in the clinic: playing by different rules." Trends in cell biology 24, no. 4 (2014): 209-211.
- Somatic Variation in the Mitochondrial Genome of Aged Human Putamen Sion L. Williams*, Deborah Mash, Stephan Zuchner and Carlos T. Moraes, PLoS Genet. 2013 Dec; 9(12):e1003990.

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22. Pohjoismäki, Jaakko LO, Siôn L. Williams, Thomas Boettger, Steffi Goffart, Johnny Kim, Anu Suomalainen, Carlos T. Moraes, and Thomas Braun. "Overexpression of Twinkle-helicase protects cardiomyocytes from genotoxic stress caused by reactive oxygen species." Proceedings of the National Academy of Sciences 110, no. 48 (2013): 19408-19413.

- Bacman, Sandra R., Siôn L. Williams, Milena Pinto, Susana Peralta, and Carlos T. Moraes. "Specific reduction of mutant mitochondrial genome load in patient-derived cells by mitoTALENs." Nature medicine 19, no. 9 (2013): 1111-1113.
- 24. Bacman, Sandra R., Sion L. Williams, Dongsheng Duan, and Carlos T. Moraes. "Manipulation of mtDNA heteroplasmy in all striated muscles of newborn mice by AAV9-mediated delivery of a mitochondria-targeted restriction endonuclease." Gene therapy 19, no. 11 (2011): 1101-1106.
- 25. Freiser, Monika E., Paolo Serafini, and Donald T. Weed. "The immune system and head and neck squamous cell carcinoma: from carcinogenesis to new therapeutic opportunities." Immunologic research 57.1-3 (2013): 52-69.
- 26. Serafini, Paolo. "Myeloid derived suppressor cells in physiological and pathological conditions: the good, the bad, and the ugly." Immunologic research 57.1-3 (2013): 172-184.
- 27. Darst RP, Nabilsi NH, Pardo CE, RIva A and Kladde MP. (2014) DNA methyltransferase accessibility protocol for individual templates by deep sequencing. Methods Enzymol. 513: 185-204. PMID 22929770.
- 28. Pardo CE, Darst RP and Kladde MP. (2013) Intergrated DNA methylation and chromatis structural analysis at single-molecule resolution. Methods Mol. Bio., in press.
- 29. Nabilsi NH, Deleyrolle LP, Darst RP, Riva A, Reynolds BA and Kladde MP. (2014) Multiplex mapping of chromatin accessibility and DNA methylation within targeted single molecules identifies epigentic heterogeneity in neural stem cells and glioblastoma. Genome Res. 24(2): 329-339. PMID: 24105770.
- 30. Lin S, Shen H, Li JL, Tang S, Gu Y, Chen Z, Hu C, Rice JC, Lu J*Wu L.* (2013). Proteomic and functional analyses reveal teh chromatin reader SFMBT1's role in regulating epigenetic silencing and teh myogenic gene program. J Biol Chem 288: 6238-6247.
- 31. Tang M, Shen H, Jin Y, Lin T, Cai Q, Pinard MA, Tran Q, Li Q, Lin S, Gu Y, Law BK, Zhou L, Mckenna R, Wu L, *Lu J.* (2013). The MBT domain protein SFMBT1 is an integral histone reader subunit of the LSD1 demethylase complex for chromatin association and epithellal-to-mesenchymal transition. J Biol Chem, 288: 27680-27691.
- 32. Khin ZP, Ribeiro ML, Jacobson T, Hazlehurst L, Perez L, Bas R, Silva AS. A preclinical assay for chemosensitivity in multiple myeloma. Cancer Res. 2014, 74(1): 56-67.
- Gebhard AW, Jain P, Nair RR, Emmons MF, Argilagos RF, Koomen JM, McLaughlin ML, Hazlehurst LA. MTI-101 (cyclized HYD1) binds a CD44 containing complex and induces necrotic cell death in multiple myeloma. Mol Cancer Ther. 2013 Nov; 12(11): 244658. DOL: 10.1158/1535-7163. MCT-13-0310. Epub 2013 Sep 18. PubMed PMID 24048737; PubMed Central PMCID: PMC3859963.
- 34. Joel G. Turner, Jana Dawson, Michael F. Emmons, Christopher L. Cubitt, Michael Kaufmann, Sharon Shacham, Lori A> Hazlehurst, Daniel M. Sullivan. CRM1 Inhibition Sensitizes Drug Resistant Human Myeloma Cells to Topoisomerase II and Proteasome Inhibitors both In Vitro and Ex Vivo. J. Cancer 2013; 4(8): 614-625. doi: 10.7150/jca.7080.
- Wang, L., Rundek, T., Beecham, A., Hudson, B., Blanton, S.H., Zhao, H., Sacco, R.L. Dong, C. (corresponding author), Genome-wide interaction study indentifies RCBTB1 as a modifier for smoking effect on carotid intima-media thinkness. Arterioscter THromb Vasc Biol. 2014 Jan; 34:219-25 PubMed PMID: 24202307.
- Della-Morte, D., Wang, L., Beechman, A., Blanton, S.H., Zhao, H., Sacco, R.L., Rundek, T., Dong, C. (corresponding author), Novel Genetic Cariant Modify the Effect of Smoking on Carotid Plaque Burden in Hispanics. J Neuroi Sci. 2014 Sep; 344:27-31. PubMed PMID: 24954085.
- Fernandez, Jamie Winderbaum, et al. "Postpartum depression in rats: Differences in swim test immobility, sucrose preference and nurturing behaviors." Behavioural brain research 272 (2014): 75-82.

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- Anais Chavaroche, Mare Cudic, Marc Guilianotti, Richard A. Houghten, Gregg B. Fields, and Dmitriy Minond* Glycosylation of a Disintegrin and Metalloprotease 17 (ADAM17) Affects it Activity and Inhibition. Anal Biochem. 2013 Dec 19; 449C:68-75. PMID: 24361716.
 *indicates senior authorship.
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- 41. Kuruppu, Sanjaya, Niwanthi W. Rajapakse, Dmitriy Minond, and A. Ian Smith. "Production of soluble Neprilysin by endothelial cells." Biochemical and biophysical research communications 446, no. 2 (2014): 423-427.
- 42. Jianliang Zhang, Rony Francois, Renuka Iyer, Mukund Seshadri, Maria Zajac-Kay and Steven Hochwald. Current understanding of the molecular biology of pancreatic neuroendocrine tumors. J Natl Cancer Institute v105, 1005-1017, 2013.
- 43. Smith, Tasha R., Wen Liu-Mares, Beth O. Van Emburgh, Edward A. Levine, Glenn O. Allen, Jeff W. Hill, Isildinha M. Reis et al. "Genetic polymorphisms of multiple DNA repair pathways impact age at diagnosis and TP53 mutations in breast cancer." Carcinogenesis 32, no. 9 (2011): 1354-1360. PubMed PMID: 21700777.
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Appendix I



Biomedical Research Advisory Council

Strategic Goals and Tactics 2014

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http://www.floridahealth.gov/provider-and-partnerresources/research/FINAL-BRAC-Strategic-Goals-and-Tactics.pdf



Biomedical Research Advisory Council

Strategic Research Goals and Tactics 2014

Background

Since 2001, the Florida legislature has recognized the need to support vital research conducted in both academic and private institutions throughout the state through the James and Esther King Biomedical Research Program (Section 381.922, Florida Statutes) and the Bankhead-Coley Cancer Research Program (Section 215.5602, Florida Statutes). This funding has improved the health of Florida's families, expanded the research infrastructure of the state, and bolstered efforts to bring external research funding to the state.

The purpose of the James and Esther King Biomedical Research Program is to seek cures in tobacco-related diseases. Heart disease is the second leading cause of death in Florida. Diseases related to tobacco, such as emphysema, chronic obstructive pulmonary disease, and other chronic lower respiratory diseases, were the third leading cause of death in 2012. The King program funds research initiatives that seek new insights and innovative solutions in the prevention, diagnosis, treatment, and cure of Floridians afflicted by cardiovascular disease, stroke, lung disease and tobacco-related cancers.

The William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program advances progress toward cures for cancer. Cancer is now the leading cause of death for Floridians, surpassing heart disease. Florida has the second highest cancer burden in the nation. In the three year period from 2009-2011 (the latest time period that national data are available), the total number of cancer deaths was 122,921. On average, 100,000 new cancers are diagnosed in Florida every year. Funding through the Bankhead-Coley program significantly improves cancer research and treatment in the state.

The Biomedical Research Advisory Council (BRAC) (Section 215.5602, Florida Statutes) advises the State Surgeon General as to the direction and scope of the biomedical research program.

BRAC Membership:

Daniel Armstrong, Ph.D., Chair, Professor and Executive Vice Chair, Pediatrics, Director, Mailman Center for Child Development, University of Miami Miller School of Medicine. Seat: American Cancer Society Representative. Mark Brantly, M.D., Co-Chair, Chief, Division of Pulmonary and Critical Care Medicine University of Florida, College of Medicine. Seat: American Lung Association Representative.

Charles Wood, Ph.D., Professor and Chair, Department of Physiology and Functional Genomics, University of Florida College of Medicine. Seat: American Heart Association Representative.

Barbara Centeno, M.D., Director of Cytopathology and Anatomic Pathology Quality Assurance/Moffitt Cancer Center, Professor of Oncologic Sciences and Pathology and Cell Biology/University of South Florida. Seat: House of Representaives.

Randal H. Henderson, M.D., MBA, Associate Medical Director, Proton Therapy Institute Professor of Radiation Oncology, University of Florida, Jacksonville. Seat: House of Representatives.

Albert Latimer, B.B.A., Senior Vice President, External Affairs & Investor Relations Enterprise Florida, Inc. Seat: Governor.

Edith Perez, M.D., Deputy Director at Large, Mayo Clinic Cancer Center; Director, Breast Cancer Translational Genomics Program, Serene M. and Frances C. Durling Professor of Medicine, Mayo Clinic, Jacksonville. Seat: Senate.

Penny Ralston, Ph.D., Director, Dean Emeritus and Professor, Center on Better Health & Life for Underserved Populations, Institute of Science & Public Affairs, Florida State University. Seat: Senate.

Claes Wahlestedt, M.D., Ph.D., Professor and Vice Chair (Research), Dep. of Psychiatry and Behavioral Sciences, Associate Dean for Therapeutic Innovation, Director, Center for Therapeutic Innovation, Hussman Institute for Human Genomics, University of Miami Miller School of Medicine. Seat: Governor.

Introduction

The purpose of this strategic plan for Florida's biomedical research funding is to specify defined objectives to be accomplished in specific time frames. This will allow the people of Florida to evaluate the health impacts of the research funded through the James and Esther King Program and the Bankhead-Coley Cancer Research Program.

This strategic plan defines the Biomedical Research Advisory Council's substantive areas of focus, and specifies timeframes for evaluating success at one year, three years, five years, and

ten years to guide funding opportunities issued by the Department of Health. The strategic plan focuses on the health impact of research and making Florida a destination for cancer care and research. Although this research agenda articulates substantive areas of focus, decisions about fund awards are always made through a competitive, peer-reviewed process. Because cancer and tobacco-related diseases have disparate impacts on Floridians, health equity and opportunity are addressed throughout, including efforts to foster collaborations among institutions, researchers, and community practitioners. This strategic plan demonstrates our commitment to transparency in communicating program priorities. One priority is to increase collaboration by enhancing the ability of Florida researchers to participate in existing alliances and groups, and prevent duplication of studies.

Some substantive goals will take years to realize because the answers we seek require fundamental discoveries in basic science, translation to clinical studies, and then implementation in clinical practice. The time from basic science to implementation in clinical practice can take ten years or more. To achieve the longer-term goals we have identified intermediate goals that can be used to evaluate progress.

During the first year, we recommend issuing a funding opportunity for incidence/prevalence measurement targets so we can improve our ability to measure the health impact of the Strategic Plan. Within three years we recommend issuing a funding opportunity for descriptive studies of barriers, intervention targets, and treatment/intervention trials. Within five years we recommend funding to conduct interim measurement of strategic outcomes, including:

- 20% of Florida-funded investigator studies (between 2008-2016) leading to follow-on extramural (NCI Comprehensive qualifying grants excluding State of Florida funded grants)
- Improvements in health outcomes based on funded projects
- Progress on collaborative research efforts
- Florida's progress on becoming a destination site for cancer care and cancer research

Strategic Goals

- Conduct research with a focus on prevention and improved treatment or care delivery that contributes to decreased deaths in lung cancer by 15%, breast cancer by 15%, prostate cancer by 20%, colon cancer by 25%, and melanoma by 15% within 10 years.
- Develop research that contributes to reductions in deaths due to lung cancer by 30%, breast cancer by 30%, prostate cancer by 30%, colon cancer by 30%, and melanoma by 30% resulting from health disparities due to race, ethnicity, or income within 10 years.
- Improve screening accuracy, detection of high risk subgroups, and/or improved implementation of cancer screening program that result in a 20% increase in early detection of cancer or preventable cancer within 10 years.
- Establish at least five Investigational New Drug(IND)/Investigational Device Exemption (IDE)s based on Florida investigator drug discovery, biologic, or other therapeutics that result in at least two multi-center collaborative clinical trials within 10 years.

- Develop innovative basic and clinical research studies focused on lower incidence of high mortality/high morbidity cancers (e.g., sarcomas, pancreatic tumors, CNS tumors, myeloma, leukemia/myelodysplastic syndrome) that result in significant improvement in survival/quality of survival in adults and children in at least two of these cancers.
- Design research protocols that lead to academic-industry development of five new biotechnology products/companies that subsequently obtain incremental commercial funding (beyond Florida funding) within 10 years.
- Reduce tobacco use in children and adolescents to less than 4% and adults to less than 15% within 10 years.
- Enhanced understanding of the relationship between obesity, healthy weight, and cancer.
- Expand upon research that improves scientific understanding of causes and subsequent impact of cancer/cancer-treatment related morbidities in other systems (e.g., cardiovascular, pulmonary, endocrine, lymphatic, CNS, reproductive, developmental).

Tactics

- Fund peer-reviewed grants for shared research infrastructure
 - Existing: genetics/genomics, imaging & and imaging bank, radiation oncology, organize existing tissue banks, drug development, pathology cores
 - New: develop statewide genomics bank (full sequencing of cancer patients) with linkages to trial treatment and outcomes- pharmacogenomics and epigenomics (part of clinical trials infrastructure)- also applies to health disparities
 - New: Statewide bioinformatics for cancer
 - Utilize and expand existing clinical trials infrastructure for: Phase I/Phase II, Phase III/IV trials in the state
 - New: develop and expand investigator/community research network infrastructure to support health disparities research with high-risk populations that have multiple barriers to engagement.
 - o Integrated planning grants for strategic goals and outcome reporting
 - Common quality indicator data system
 - Improve regulatory process (e.g., State institutional review board or multi-center)
- Fund recruitments in areas that are not existent or inadequate for those goals (shared resource for the state)
 - Program recruitments that target strategic objectives
 - Recruitment/training of research support staff, research for core shared resources: augment currently existing programs, outcome goal for entire program
- Fund investigator initiated projects prioritized by potential impact:
 - Discovery science
 - New drug development
 - Prevention and Cancer Control
 - Screening and Detection
 - Health Services Outcomes and Access To Care
 - o Clinical Trials
 - Comparative Effectiveness Research
 - o Population Science

- o Health Disparities
- o Obesity
- Funds for different research model
 - New Investigators
 - Bridge funding
 - o Investigator-initiated
 - Team Science
 - Technology Transfer
 - o Comparative Effectiveness Research
 - Targeted Request for Applications
- Fund research that optimizes public-private partnerships in discovery science and health services research
 - o Tech transfer
 - o Health system, insurer
- Funding for conferences, cancer strategic plan summit
- Transdisciplinary interactions