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2012

Florida Department of Health Biomedical Research Programs



Biomedical Research Advisory Council



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Appendix A: Letter to State Surgeon General, Dr. John Armstrong (page 22)

FLORIDA STATUTES 2012

<u>Title XIV</u>

TAXATION AND FINANCE

Chapter 215

FINANCIAL MATTERS: GENERAL PROVISIONS

215.5602 JAMES AND ESTHER KING BIOMEDICAL RESEARCH PROGRAM.*-

(10) The council shall submit a fiscal-year progress report on the programs under its purview to the Governor, the State Surgeon General, the President of the Senate, and the Speaker of the House of Representatives by December 15. The report must include:

(a) A list of research projects supported by grants or fellowships awarded under the program.

(b) A list of recipients of program grants or fellowships.

(c) A list of publications in peer reviewed journals involving research supported by grants or fellowships awarded under the program.

(d) The state ranking and total amount of biomedical research funding currently flowing into the state from the National Institutes of Health.

(e) New grants for biomedical research which were funded based on research supported by grants or fellowships awarded under the program.

(f) 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.

(g) Recommendations to further the mission of the programs.

*Report includes Bankhead Coley Florida Cancer Research annual data

FLORIDA BIOMEDICAL RESEARCH PROGRAM (FBRP)

The mission of the Biomedical Research Program is to provide increasingly significant levels of funding to Florida research institutions for the performance of high-quality and high-impact biomedical research and technology development to improve prevention, diagnosis, treatment, and cure of cancer and tobacco-related diseases including cardiovascular disease, stroke, and pulmonary disease.

The Florida Biomedical Research Programs:

- James and Esther King Biomedical Research Program (s. 215.5601, F.S.)
- Bankhead-Coley Cancer Research Program (s. 381.922, F.S.)
- Managed by the Florida Department of Health
- Key partners are American Heart Association, American Lung Association, and American Cancer Society
- Website = <u>www.floridabiomed.com</u>
- Email = <u>FBRP@doh.state.fl.us</u>
- The program has awarded 476 grants investing \$177.44 million in projects at 22 Florida Institutions

How our grants work:

We offer Florida Researchers merit-based grants, without regard for institutional affiliation, to address the prevention, diagnosis, treatment, and cure of cancer and tobacco-related diseases.

Grants Award Processes:

- Grants awarded using a competitive process through a "Request for Applications" (RFA)
- All research applications are scientifically peer reviewed (scientific experts) to attain the scientific merit of all research applications
- Funding recommendations, based primarily on scientific merit score, provided by the Biomedical Research Advisory Council (BRAC) to the State Surgeon General, who makes the final award decisions

Demonstration of Accountability:

- Grant Monitoring: Grantee progress reports are peer reviewed annually against research milestones and site visits are made to select grantees to evaluate scientific progress. Annual renewals of multiyear grants are dependent on satisfactory performance and availability of funds.
- Online Business Process: Secure web-based system provides user-friendly interface and streamlined processes for grant application, proposal review, grant management transactions, and database report generation.
- Program Evaluation and Performance Measurement: Documented policies and procedures set standards and guide consistent administration, and stakeholder feedback is collected to guide continuous improvement. Progress against metrics tied to program goals informs policy making and strategic planning.

BIOMEDICAL RESEARCH ADVISORY COUNCIL (BRAC)

Richard J. Bookman, Ph.D., Chair, Senior Advisor to the Dean, University of Miami Miller School of Medicine, Special Assistant to the Provost, University of Miami Seat: Advisory Council Chair and American Heart Association Representative

Daniel Armstrong, Ph.D., Professor and Associate Chair, Pediatrics, Director, Mailman Center for Child Development, University of Miami Miller School of Medicine **Seat:** American Cancer Society Representative

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

Randal H. Henderson, M.D., MBA, Associate Medical Director, Proton Therapy InstituteProfessor of Radiation Oncology, University of Florida, Jacksonville Seat: House – Cancer Program (ACoS)

Myra Hurt, Ph.D., Senior Dean, Research, Graduate, and Undergraduate Programs Florida State University College of Medicine **Seat:** Research University

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

Edith Perez, M.D., *Professor of Medicine, Hematology/Oncology, Mayo Clinic, Jacksonville* Seat: Senate – Cancer Program (ACoS)

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 - Behavioral/Social Research

Mary Lou Sole, R.N., Ph.D., CCNS, FAAN, *Professor, College of Nursing, University of Central Florida* Seat: House – Professional Medical Organization

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: Biomedical Research

Herbert Weissbach, Ph.D., Distinguished Research Professor and Director, Center for Molecular Biology and Biotechnology, Florida Atlantic University Seat: Advisory Council Vice-Chair

LIST OF RECIPIENTS AND PROJECTS

Grantee Project Title Institution				
			Amount	
	Bankhead Coley Florida Cancer Research Grants			
Sarah McLaughlin	Enhancing the Ability to Predict Lymphedema Development Following Axillary Surgery for Breast Cancer and its Effects on Patient Survivorship			
Joseph Pidala	Regulatory T Cells for Prevention of Acute Graft-Versus-Host Disease	Moffitt Cancer Center & Research Institute	\$ 343,280	
Radka Stoyanova	Metabolic Tumor Volumes in Radiation Treatment of Brain Tumors	University of Miami	\$ 400,000	
Yijun Sun (Transferred to Aysegul Gunduz)	Derivation of Molecular Signatures for Accurate Breast Cancer University of Florida Prognosis		\$ 200,862	
Kristen Wells	Developing and Piloting a Patient Navigation Program for Breast Cancer Survivors	University of South Florida	\$ 360,000	
Kevin Brown	Epigenetic Basis of Neoplastic Progression in Human Cancers	University of Florida	\$1,500,000	
Olveen Carrasquillo	South Florida Center for the Elimination of Colorectal Cancer Health Disparities (SUCCESS-CRC)	University of Miami	\$1,500,000	
Lori Hazlehurst	Targeting the Tumor Microenvironment in Multiple Myeloma	Moffitt Cancer Center & Research Institute	\$1,500,000	
Jin Cheng	MicroRNA-155 in Breast Cancer	Moffitt Cancer Center & Research Institute	\$ 180,000	
Christopher Cogle	A Phase I/II Clinical Study of OXi4503 in AML and MDS	University of Florida	\$ 180,000	
Michael Crary	Sensory Alterations and Swallow Functions in RT Treated Head/Neck Cancer Patients	University of Florida	\$ 155,250	
David Gilbert	Replication Profiling as a Diagnostic Tool in B-cell Acute Lymphoblastic Leukemia	Florida State University	\$ 129,171	
Emina Huang	The Role of IL8 in Colitis-Associated Tumor Initiation	University of Florida	\$ 180,000	
Huabei Jiang	Combined Photoacoustic and Diffuse Optical Tomography	University of Florida	\$ 155,250	
Michael Kladde	Interplay of Epigenetic Mechanisms in Gene Silencing	University of Florida	\$ 180,000	
Javier Pinilla-Ibarz	Epigenetic Modifiers to Augment the Immunogenicity of Chronic Lymphocytic Leukemia	Moffitt Cancer Center & Research Institute	\$ 180,000	
E. Aubrey Thompson	MicroRNAs in Lobular Involution and Breast Cancer	Mayo Clinic	\$ 129,375	
Michael Wallace	Confocal Endomicroscopy for Colorectal Neoplasia	Mayo Clinic	\$ 179,848	
Lizi Wu	Regulation of Notch Pathway Transcription Factor CSL in Normal and Malignant Cells	University of Florida	\$ 180,000	
Xiangxi Xu	Ovarian Cancer: Nuclear Envelope Defects	University of Miami	\$ 180,000	
Charles Rosser	Development of a Panel of Monoclonal Antibodies to a Validated Bladder Cancer Diagnoistic Signature	M.D. Anderson Cancer Center	\$ 100,000	
Yanxia Liu	Development of scale-up synthetic method for Largazole, a novel drug for the treatment of colorectal cancer	University of Florida	\$ 100,000	

Lori Hazlehurst	lehurst Targeting CD44 with HM-27 in AML		\$ 100,000	
David Reisman	Validate BRM polymorphism as a Biomarker for lung cancer risk	Institute University of Florida	\$ 100,000	
Lei Zhou	A Novel in vivo Assay system for screening epigenetic University of Florida modulators that de-repress tumor suppressor genes		\$ 100,000	
Johnathan Lancaster	From BAD to Good: Developing an Assay to Predict Ovarian- Cancer-Chemo-Resistance and Survival	Good: Developing an Assay to Predict Ovarian- Moffitt Cancer Center		
Peter Sayeski	Improving the Metabolic Stability of the Jak2 inhibitor, G6	University of Florida	\$ 100,000	
Wei Li	Global Profiling of Colorectal Cancer Biomarkers	University of Miami	\$ 100,000	
John Barrett	hn Barrett Economical device using phosphorescence to measure cellular respiration		\$ 99,987	
	James & Esther King Biomedical Research Program Grants			
Paolo Serafini	A nanobased immunediagnostic approach for monitoring the immune response in HNSCC	University of Miami	\$ 100,000	
Chuanhui Dong	Gene-Smoking Interactions and Atherosclerosis	University of Miami	\$ 360,000	
Jamie Fernandez	Neuroendocrine Disruption and Nicotine Preference in a Rat Model of Postpartum Depression	University of South Florida	\$ 360,000	
Monica Hooper	Serotonergic Function and Impulsive Responding in Treatment- Seeking Smokers	University of Miami	\$ 359,998	
Jinliang Li	CIP4 Scaffold Protein Regulation of Cardiac Myocyte Hypertrophy and Survival	University of Miami	\$ 360,000	
Dmitriy Minond	Inhibitors of ADAM Proteases for Lung Cancer Therapy and Research	Torrey Pines Institute for Molecular Studies	\$ 360,000	
J Mocco (Transferred to Brian Hoh)	Hematopoietic Stem Cell Function Following Acute Stroke Therapy	University of Florida	\$ 359,262	
Charles Saunders	Improving Surveillance Measures of Tobacco Use in Florida's Adolescent Population	Florida State University	\$ 360,000	
Gary Wang	Molecular Identification of Subgingival Bacteria Associated with Progression of Periodontitis in Smokers	University of Florida	\$ 360,000	
Dileep Yavagal	Intra-arterial Mesenchymal Stem Cell Delivery in a Canine Model of Acute Ischemic Stroke	University of Miami	\$ 360,000	
Gregory Conner	Regulation of Airway Lactoperoxidase Host Defense	University of Miami	\$ 180,000	
Zhongwei Li	RNA Quality Control Against Oxidative Damage	Florida Atlantic University	\$ 103,500	
Roberto Vazquez- Padron	Leukadherins as Novel Compounds for Treating Restenosis	University of Miami	\$ 180,000	
Jie Wu	Modulation of ErbB Signaling and Lung Cancer by Shp2	Moffitt Cancer Center & Research Institute	\$ 180,000	
Antonis Zervos	A New Signaling Pathway in Myocardial Ischemic Injury	University of Central Florida	\$ 180,000	
Keith Pennypacker	GLG-302 as a Novel Treatment for Stroke	University of South Florida	\$ 100,000	

Lori Hazlehurst	Preclinical Testing of HM-27 in Lung Cancer Models	Moffitt Cancer Center & Research Institute	\$ 90,000
Lori Boules	Novel Therapy for Nicotine Addition in Alcholics	Mayo Clinic	\$ 99,856
Yiwen Li	A Method of Producing Recombinant RdCVF Protein	University of Miami	\$ 100,000
Jeffrey Goldberg	Functionalized Magnetic Nanoparticles as a Therapeutic Tool to Improve Axon Regneration After Stroke	University of Miami	\$ 100,000
Masanobu Komatsu	Development of Novel Lung-Targeted Biologics for Idiopathic Pulmonary Fibrosis	Sanford-Burnham Medical Research Institute	\$ 100,000

FLORIDA NATIONAL RESEARCH FUNDING DATA Florida's Rank in Funding, 2011¹

National Agency	Funding (in millions)	State Rank
National Institutes of Health	\$493	13
Centers for Disease Control and Prevention	\$305	4
National Science Foundation	\$150	13
Agency for Healthcare Research and Quality	\$1	25
Total	\$949	12

FL State Population (as of June 1, 2011): 18,801,310

State rank in population: 4

NIH Research Funding and Population of Selected States

State	2010 Census population (in millions) ²	NIH Funding in federal fiscal year 2012 (in millions) ³	Funding \$ Per capita
California	37.2	\$ 2,400	\$64.52
Texas	25.3	\$ 783	\$30.95
New York	19.3	\$ 1,536	\$79.59
Florida	18.8	\$ 493	\$18.40
Illinois	12.8	\$ 557	\$43.52
Pennsylvania	12.7	\$ 1,101	\$86.69
Ohio	11.5	\$ 504	\$43.83
Georgia	9.7	\$ 327	\$33.71
North Carolina	9.5	\$ 723	\$76.11

¹ Research America! Florida. Available at <u>http://www.researchamerica.org/florida</u>. Accessed August 7, 2012.

² U.S. Census Bureau. 2010 Census Data. Available at <u>http://2010.census.gov/2010census/data/</u>. Accessed August 7, 2012.

³ NIH Awards by Location & Organization. Available at <u>http://report.nih.gov/award/index.cfm#tab1</u>. Accessed August 7, 2012.

PUBLICATIONS REPORTED BY GRANTEES

The following list represents new publications in peer-reviewed journals and books reported between July 2011 and June 2012 based on funded research from King and Bankhead Coley Program research. Publication titles are presented in **bold** print.

A database of reaction monitoring mass spectrometry assays for elucidating therapeutic response in cancer. Remily-Wood ER, et.al. Proteomics Clin Appl. 2011; 5(7-8):383-96. doi: 10.1002/prca.201000115.

Monitoring a nuclear factor-kappaB signature of drug resistance in multiple myeloma. Xiang Y, Remily-Wood ER, et al. Mol Cell Proteomics. 2011; 10(11):M110.005520.

Expanding the use of real-time electromagnetic tracking in radiation oncology. Shah AP, Kupelian PA, Willoughby TR, Meeks SL. J Appl Clin Med Phys. 2011; 12(4):3590.

Analyzing the impact of intrafraction motion: correlation of different dose metrics with changes in target **D95%.** Waghorn BJ, Meeks SL, Langen KM. Med Phys. 20111; 38(8):4505-11.

Visualization of 3D volumetric lung dynamics for real-time external beam lung radiotherapy. Santhanam AP, et. al. Stud Health Technol Inform. 2011; 163:567-73.

An endorectal balloon reduces intra-fraction prostate motion during radiotherapy. Smeenk RJ, et al. Int J Radiat Oncol Biol Phus. 2012; 83(2):661-9.

The Importance of Hypoxia-regulated, RPE-targeted Gene Therapy for Chorodal Neovascularization. Smith GW, Dorey CK, Prentice H, Blanks J. Adv Med Biol. 2012; 723:269-77.

Hypoxia Responsive Vectors Targeting Astrocytes in Glioma. Biswal M, Prentice H and Blanks J. In Novel Therapeutic Concepts in Targeting Glioma. Book Chapter, Intech Publishing; 2012.

Chitin particles induce size-dependent but carbohydrate-independent innate eosinophilia. Kogiso M, Nishiyama A, et al. J Leukoc Biol. 2011; 90(1):167-76.

Induction of proinflammatory mediators by CHI3L1 is reduced by chitin treatment: Decreased tumor metastasis in a breast cancer model. Libreros S, et al. Int J Cancer. 2011; doi: 10.1002/ijc.26379. [Epub ahead of print].

Development of optimized AAV3 serotype vectors: mechanism of high-efficiency transduction of human liver cancer cells. Cheng B, Ling C, Dai Y, Lu Y, et al. Gene Ther. 2012; 19(4):375-84.

Induction of tolerance to factor VIII by transient co-administration with rapamycin. Moghimi B, et al. Thromb Haemost. 2011; Aug;9(8):1524-33. doi: 10.1111/j.1538-7836.2011.04351.x.

Nonredundant roles of IL-10 and TGF-β in suppression of immune responses to hepatic AAV-factor IX gene transfer. Hoffman BE, et al. Mol Ther. 2011,Jul;19(7):1263-72. doi: 10.1038/mt.2011.33. Epub 2011 Mar 8.

Development of optimized AAV3 serotype vectors: mechanism of high-efficiency transduction of human liver cancer cells. Cheng B, et al. Gene Ther. 2011; Jul 21. doi: 10.1038/gt.2011.105. [Epub ahead of print].

Radiomics: Extracting more information from medical images using advanced feature analysis. Lambin P, et al. Eur J Cancer 2012; 48(4):441-6.

Molecular Characterization of kidney cancer: Association of Hyaluronic Acid Family with Histological Subtypes and Metastasis. Chi A, et al. Cancer 2012; 118(9):2394-402.

Chemokine and chemokine receptor expression in kidney tumors: molecular profiling of histological subtypes and association with metastasis. Gahan JC, et al. J Urol. 2012; 187(3):827-33.

Vascular Endothelial Growth Factor, Carbonic Anhydrase9, and Angiogenin as Urinary Biomarkers for Bladder Cancer Detection. Urquidi V, et al. Urology. 2012; 79(5):1185.e1-6.

Antagonism of CXCR7 attenuates chronic hypoxia-induced pulmonary hypertension. Sartina E, et al. Pediatr Res. 2012; 71(6):682-8.

Absence of Myocardial Thyroid Hormone Inactivating Deiodinase Results in Restrictive Cardiomyopathy in Mice. Ueta CB, et al. Mol Endocrinol. 2012; 26(5):809-18.

The Generation and Functional Characterization of Knock-In Mice Harboring the Cardiac-troponin I R21C Mutation Associated with Hypertrophic Cardiomyopathy. Wang Y, et al. J Biol Chem. 2012; 287(3):2156-67.

Myosin cross-bridges do not form precise rigor bonds in hypertrophic heart muscle carrying troponin t mutations. Midde K, et al. J Mol Cell Cardiol. 2011; 51(3):409-18.

Time resolved thermodynamics associated with diatomic ligand dissociation from globins. MiksovskaJ and Astudillo L. Thermodynamics/Book 1. 2011; ISBN 978-953-307-563-1.

Label-Free Electrochemical Imaging of Latent Fingerprints on Metal Surfaces. Qin G, Zhang M, Zhang T, Zhang Y, McIntosh M, Li Z, and Zhang X. Electroanalysis. 2012; 24(5):1027-32.

Regulation of p53 Stability and Apoptosis by a ROR Agonist. Wang Y, Solt LA, Kojetin DJ, Burris TP. PLoS One. 2012; 7(4):e34921.

Regulation of Circadian behavior and Metabolism by Synthetic REV-ERB Agonists. Solt LA, Wang Y, Banerjee S, Hughes T, Kojetin DJ, Lundasen T, Shin Y, Liu J, Cameron MD, Noel R, Yoo SH, Takahashi JS, Butler AA, Kamenecka TM, Burris TP. Nature. 2012; 485(7396):62-8.

Synthesis and SAR of tetrahydroisoquinolines as Rev-erbα agonists. Noel R, Song X, Shin Y, Banerjee S, Kojetin D, Lin L, Ruiz CH, Cameron MD, Burris TP, Kamenecka TM. Bioorg Med Chem Lett. 2012; 22(11):3739-42.

Structural and biophysical Insights into the Ligand Free Pitx2 Homeodomain and a Ring Dermoid of the Cornea Inducing Homeodomain Mutant. Doerdelmann T, et al.Kojetin DJ, Baird-Titus JM, Solt LA, Burris TP, Rance M. Biochemistry. 2012; 51(2):665-76.

¹H, ¹³C and ¹⁵N chemical shift assignments for the human Pitx2 homeodomain in complex with a 22-base hairpin DNA. Doerdelmann T, et al. Biomol NMR Assign. 2012; 6(1):79-81.

Identification of Akt Interaction Protein PHF20/TZP That Transcriptionally Regulates p53. Park S, Kim D, Dan HC, Chen H, Testa JR, Cheng JQ.. J Biol Chem. 2012; 287(14):11151-63.

Microfluidic extraction and stretching of chromosomal DNA from single cell nuclei for DNA fluorescence in situ hybridization. Wang X, Takebayashi S, et al. Biomed Microdevices. 2012; 14(3):443-51.

Development of optimized AAV3 serotype vectors: mechanism of high-efficiency transduction of human liver cancer cells. Cheng B, et al. Gene Ther. 2011; Jul 21. doi: 10.1038/gt.2011.105. [Epub ahead of print].

Protein disulfide isomerase-2 of Arabidopsis mediates protein folding and localizes to both the secretory pathway and nucleus, where it interacts with maternal effect embryo arrest factor. Cho EJ, Yuen CY, Kang BH, Ondzighi CA, Staehelin LA, Christopher DA. Mol Cells. 2011; 32(5):459-75.

Rural-urban difference in discussions of cancer treatment clinical trials. Vanderpool RC, Kornfeld J, Mills L, Byrne MM. Patient Educ Counts. 2011; 85(2):e69-74.

Design, synthesis and photoactivation studies of fluorous photolabels. Kumar A, Anderson J, and Manetsch R. Organic Bioorganic Chemistry. 2011; Sep 21;9(18):6284-92.

Fanconi anemia complementation group A (FANCA) protein has intrinsic affinity for nucleic acids with preference for single-stranded forms. Yuan F, et al. J Biol Chemistry. 2012; 287(7):4800-4807.

ATR-ATRIP Kinase Complex Triggers Activation of the Fanconi Anemia DNA Repair Pathway. Shigechi T, et al. Cancer Research. 2012; 72(5):1149-1156.

Simultaneous Single-Molecule Mapping of Protein-DNA Interactions and DNA Methylation by MAPit. Pardo CE, et al. Curr Protoc Mol Biol. 2011; Chapter 21:Unit21.22

WIF1 is a frequent target for epigenetic silencing in squamous cell carcinoma of the cervix. Delmas AL, et al. Carcinogenesis 2011; 32(11):1625-33.

Multi-dye theranostic nanoparticle platform for bioimaging and cancer therapy. Singh AK, et al. Int J Nanomedicine. 2012; 7:2739-50.

TGF-beta antiproliferative effects in tumor suppression. Jahn SC, Law ME, Corsino PE, Law BK. Front Biosci (Schol Ed). 2012; 1:4:749-66.

MYC suppresses cancer metastasis by direct transcriptional silencing of $\alpha(v)$ and $\beta(3)$ integrin subunits. Liu H, et al. Nat Cell Biol. 2012; 14(6):567-74.

Synthesis of a diversifiable cis-dehydrodecalin scaffold based on meiogynin. Kim YB, Del Valle JR. A Tetrahedron Lett. 2011; 52:6396-8.

Cigarette smoking is associated with a dose-response effect in clopidogrel-treated patients with diabetes mellitus and coronary artery disease: results of a pharmacodynamic study. Ueno M, et al. JACC Cardiovasc Interv. 2012; 5(3):293-300.

Hyperactive EGF receptor, Jaks and Stat3 signaling promote enhanced colony-forming ability, motility and migration of cisplatin-resistant ovarian cancer cells. Yue P, et al. Oncogene. 2012; 31(18):2309-22.

Alpha B-crystallin, an effector of unfolded protein response, confers anti-VEGF resistance to breast cancer via maintenance of intracrine VEGF in endothelial cells. Ruan Q, Han S, Jiang WG, Boulton ME, Chen ZJ, Law BK, Cai J. Mol Cancer Res. 2011; 9(12):1632-43.

Inhibition of Foxo transcriptional activity prevents muscle atrophy during cachexia and induces hypertrophy. Reed SA, Sandesara PB, Senf SM, Judge AR. FASEB J. 2012; 26(3):987-1000.

MGMT Inhibition Restores ERa Functional Sensitivity to Anti-Estrogen Therapy. Bobustuc GC, et al. Mol Med. 2012.

Combination of temozolomide and O6- Benzylguanine inhibit breast cancer growth. Jeudy S, Srivenugopal KS, Konduri SD. Cancer Res. 2012; 72(8 Supplement):3721.

Activation of Notch1 signaling in stromal fibroblasts inhibits melanoma growth by upregulating WISP-1. Shao H, et al. Oncogene. 2011; 30(42):4316-26.

Inhibition of tumor angiogenesis and melanoma growth by targeting vascular E-selectin. Liu ZJ, Tian R, Li Y, An W, Zhuge Y, Livingstone AS, Velazquez OC. Ann Surg. 2011; 254(3):450-6.

Convergent synthesis and discovery of a natural product-inspired paralog-selective Hsp90 inhibitor. Jeso V, et al. Org Lett. 2011; 13(19):5108-11.

Is surgical resection superior to transplantation in the treatment of hepatocellular carcinoma? Koniaris LG, et al. Ann Surg. 2011; 254(3):527-37.

Ethics and the law: is there common ground on informed consent for disparities in hospital outcomes? Housri N, et al. Ann Intern Med. 2011; 16;155(4):260-4.

Deep sequence analysis of non-small cell lung cancer: integrated analysis of gene expression, alternative splicing, and single nucleotide variations in lung adenocarcinomas with and without oncogenic KRAS mutations. Kalari KR, et al. Front Oncol. 2012; 2:12.

Matrix metalloproteinase-10 is required for lung cancer stem cell maintenance, tumor initiation and metastatic potential. Justilien V, et al. PLoSOne. 2012; 7(4):e35040.

Matrix metalloproteinase-10 (MMP 10) interaction with tissue inhibitors of metalloproteinases TIMP-1 and TIMP-2: binding studies and crystal structure. Batra J, et al. J Biol Chem. 2012; 287(19):15935-46.

Protein kinase C iota regulates pancreatic acinar-to-ductal metaplasia. Scotti ML, Smith KE, Butler AM, Calcagno SR, Crawford HC, Leitges M, Fields AP, Murray NR. PLoS One. 2012; 7(2):e30509.

Protein kinase C iota as a therapeutic target in alveolar rhabdomyosarcoma. Kikuchi K, et al. Oncogene. 2012; 2012.46.

Correction of metabolic abnormalities in a rodent model of obesity, metabolic syndrome, and type 2 diabetes mellitus by inhibitors of hepatic protein kinase C-1. Sajan MP, et al. Metabolism. 2012; 61(4):459-69.

Protein kinase Cα promotes cell migration through a PDZ-dependent interaction with its novel substrate discs large homolog 1 (DLG1). O'Neill AK, et al. J Biol Chem. 2011; 286(50):43559-68.

Matrix metalloproteinase-10 promotes Kras-mediated bronchio-alveolar stem cell expansion and lung cancer formation. Regala RP, et al. PLoS One. 2011; 6(10):e26439.

Protein kinase C iota in the intestinal epithelium protects against dextran sodium sulfate-induced colitis. Calcagno SR, et al. Inflamm Bowel Dis. 2011; 17(8):1685-97.

Protein kinase C iota regulates pancreatic acinar-to-ductal metaplasia. Scotti ML, Smith KE, Butler AM, Calcagno SR, Crawford HC, Leitges M, Fields AP, Murray NR. PLoS One. 2012; 7(2):e30509.

Protein kinase C iota as a therapeutic target in alveolar rhabdomyosarcoma. Kikuchi K, et al. Oncogene. 2012; onc.2012.46.

Correction of metabolic abnormalities in a rodent model of obesity, metabolic syndrome, and type 2 diabetes mellitus by inhibitors of hepatic protein kinase C-1. Sajan MP, et al. Metabolism. 2012; 61(4):459-69.

Caffeine induces beneficial changes in PKA signaling and JNK and ERK activities in the striatum and cortex of Alzheimer's transgenic mice. Zeitlin R, et al. Brain Res. 2011; 1417:127-36.

Cotinine enhances the extinction of contextual fear memory and reduces anxiety after fear conditioning. Zeitlin R, et al. Behav Brain Res. 2012;228(2):284-93.

Identification of an Akt interaction protein, PHF20/TZP, that transcriptionally regulates p53. Park S, Kim D, Dan HC, Chen H, Testa JR, Cheng JQ. J Biol Chem. 2012; 287(14):11151-63.

Monitoring a nuclear factor-\kappaB signature of drug resistance in multiple myeloma. Xiang Y, et al. Mol Cell Proteomics. 2011; 10(11):M110.005520.

High resolution of microRNA signatures in human whole saliva. Patel RS, Jakymiw A, Yao B, Pauley BA, Carcamo WC, Katz J, Cheng JQ, Chan EK. Arch Oral Biol. 2011; 56(12):1506-13.

MicroRNA processing and binding site polymorphisms are not replicated in the Ovarian Cancer Association Consortium. Permuth-Wey J, et al. Ca Epidemiol Biomarkers Prev. 2011; 20(8):1793-7.

IKBKE protein activates Akt independent of phosphatidylinositol 3-kinase/PDK1/mTORC2 and the pleckstrin homology domain to sustain malignant transformation. Guo JP, et al. J Biol Chem. 2011; 286(43):37389-98.

Phase 1 pharmacokinetic and pharmacodynamic study of tricirbine phosphate monohydrate, a small-molecule inhibitor of AKT phosphorylation, in adult subjects with solid tumors containing activated AKT. Garrett CR, et al. Invest New Drugs. 2011; 29(6):1381-9.

Cyclosporine-A as a neuroprotective agent against stroke: its translation from laboratory research to clinical application. Osman MM, et al. Neuropeptides. 2011; 45(6):359-68.

Immediate, but not delayed, microsurgical skull reconstruction exacerbates brain damage in experimental traumatic brain injury model. Glover LE, Tajiri N, Lau T, Kaneko Y, van Loveren H, Borlongan CV. PLoS One. 2012; 7(3):e33646.

A Step-Up Approach for Cell Therapy in Stroke: Translational Hurdles of Bone Marrow-Derived Stem Cells. Glover LE, et al. Transl Stroke Res. 2012; 3(1):90-98.

Amniotic fluid stem cells: a promising therapeutic resource for cell-based regenerative therapy. Antonucci I, et al. Curr Pharm Des. 2012; 18(13):1846-63.

Toward personalized cell therapies: autologous menstrual blood cells for stroke. Rodrigues MC, et al. J Biomed Biotechnol. 2011; 2011:194720.

Expression of the antiapoptotic protein survivin in colon cancer. Hernandez JM, et al. Clin Colorectal Cancer. 2011; 10(3):188-93.

Metabolic Syndrome and Colorectal Cancer: Is Hyperinsulinemia/Insulin Receptor-Mediated Angiogenesis a Critical Process? Liu JJ, et al. J Clin Oncol. 2011; 29:2011(suppl;abstr e14004).

Acquired and intrinsic BRAF inhibitor resistance in BRAF V600E mutant melanoma. Fedorenko IV, Paraiso KH, Smalley KS. Biochem Pharmacol. 2011; 1;82(3):201-9.

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FOLLOW-ON FUNDING AWARDS REPORTED BY GRANTEES

The following list represents **\$33.89 million** in additional single and multi-year awards reported from July 2011-June 2012 by current and past grantees from projects funded by the James and Esther King and Bankhead-Coley Program. Grants are presented in alphabetical order by last name of the Grantee.

Bannister, Thomas. BC, (2010, NIR), "Targeting Slx 16a/Mct Lactate transporters in cancer Therapeutics." National Institutes of Health and National Cancer Institute, \$390,000.00.

Bannister, Thomas. BC, (2010, NIR), "Identification and optimization of inhibitors of the LAT1 essential amino acid transporter as anti-breast cancer therapeutic agents." Department of Defense, \$75,000.00.

Barrientos, Antoni. King Special, (2009, Florida RC1), "Mitochondrial Dysfunction in Neurodegeneration and Compensatory Apporaches." National Institutes of Health, National Institute on Aging, \$1,520,595.00.

Blaydes Ingersoll, Susan. BC, (2009, NIR), "Non-coding and MicroRNA Molecular Screening for Potential Biomarkers of Ovarian Cancer Risk." Ovarian Cancer Alliance of North Florida, \$25,000.00.

Borlongan, Cesar. King, (2010-11, RPG), "Battlefield-Related injury Translational Research, Post-Traumatic Disease and Disability - Veterans Re-Integration Strategy." DOD, \$1,500,000.00.

Borlongan, Cesar. King, (2010-11, RPG), "Blood Brain Barrier Repair in Cell Therapy for Stroke." National Institutes of Health, \$2,200,000.00.

Brown, Kevin. BC, (2009, NIR), "Interplay of Epigenetic Mechanisms in Gene Silencing." National Institutes of Health, \$1,501,940.00.

Diaz, Francisa. King, (2008-09, NIR), "Cellular and Molecular Consequences of Respiratory Chain Defects in Neurons." National Institutes of Health, \$1,673,440.00.

Guldiken, Rasim. BC, (2010, NIR), "EAGER: A Surface Acoustic Wave Device for High-Resolution Atherosclerotic Plaque Inspection." National Science Foundation, \$199,908.00.

Guldiken, Rasim. BC, (2010, NIR), "Large Stroke Microscale Actuators Based on Electrowetting." National Science Foundation, \$354,121.00.

Hare, Joshua. King, (2009, Shared Instrument), "Cell Based Therapy for Non-Ischemic Dilated Cardiomyopathy." National Institutes of Health, \$4,284,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument),"A Molecular Basis Accounted for the Malignant Features of Breast Cancer Cells." DOD, \$114,750.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Mystatin Family Signaling in Burn-Injury Related Muscle Wasting." National Institutes of Health–National Institute of General Medical Sciences, \$370,080.00.

Hu, Jennifer. BC, (2006, Shared Instrument),"A Novel Assay to Detect Multiple Viral Gene Expression in Cancer." Women's Cancer Association at University of Miami, \$50,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Regulation of Melanoma Heterogeneity and Metastasis by Stromal Fibroblasts in Tumor Microenvironment." Women's Cancer Association at University of Miami, \$50,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Investigator of Novel Breast Cancer Resistance Mechanisms to ERBB2-Targeted Therapies." Women's Cancer Association at University of Miami, \$50,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument),"Role of Immunity in Efficacy of Chemotherapy Plus Trastuzumab." National Institutes of Health / Subcontract Mayo Clinic, \$15,962.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Novel Hedgehog and WNT Inhibitors for Treatment of Lung Cancer." Women's Cancer Association at University of Miami, \$50,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Effects of Cellular Mammary Stem Cells and how Mammary Stem Cells Change with Populations Aging." Breast Cancer Research Foundation, \$223,000.00.

Hu, Jennifer. BC, (2006, Shared Instrument), "Nonapoptotic Function of Caspase-6 in Promoting Mammary Carcinogenesis." Department of Defense/Congressionally Directed Medical Research Programs, \$114,750.00.

Judge, Andrew. BC, (2009, NIR) "FoxO signaling and skeletal muscle atrophy." National Institutes of Health/National Cancer Institute/ NIAMS, \$1,621,385.00.

Koomen, John. BC, (2006, Shared Instrument,) "Microenvironment Mediated Drug Resistance in Melanoma." National Cancer Institute, \$346,525.00.

Lee, David. King, (2010-11, RPG), "Culturally Specific Interventions and Acculturation in African American Smokers." National Institutes of Health, \$1,554,093.00.

Lewin, Alfred. King Special, (2009, Shared Instrument) "Counter-balancing the Renin-angiotensin System with Ang (1-7)/ACE2 - A Novel Mechanism and Therapy for Diabetic Retinopathy." American Diabetes Association, \$345,000.00.

Lewin, Alfred. King Special, (2009, Shared Instrument), "Arresting Migration in Photoreceptors: Mechanism/Function." National Institutes of Health/National Eye Institute, \$1,465,000.00.

Lewin, Alfred. King, Special, (2009, Shared Instrument), "Vision Research Core." National Institutes of Health/National Eye Institute, \$2,922,493.00.

Lewin, Alfred. King Special, (2009, Shared Instrument), "RNA Replacement Therapy for adRP." Foundation Fighting Blindness, \$300,000.00.

Lewin, Alfred. King Special, (2009, Shared Instrument), "Ocular Renin Angiotensin System in Pathogenesis of Diabetic Retinopathy." National Institutes of Health/National Eye Institute, \$1,098,750.00.

Li, Wei. King, (2010-11, TTF), "Anti-retinal autoantibodies as AMD biomarkers." American Health Assistance Foundation, \$100,000.00.

Grant. BC, (2010, TSP), "MyxomaVirotherapy for Treatment of Hematological Malignancies." Climb for Cure Foundation, \$10,000.00.

Ning, Shunbin. BC, (2010, NIR), "Targeting an oncogenic miRNA by IRFs promotes survival of tumor virus-transformed cells." American Society of Hematology, \$150,000.00.

Pal, Tuya. BC, (2010, RPG), "Breast cancer genetics research and education in African Americans team expanding reach - B-GREATER." Florida Breast Cancer Foundation, \$9,999.00.

Pal, Tuya. BC, (2010, RPG), "Behavioral and Emotional Impact of BRCA testing In African Americans (BENITA)." American Cancer Society, \$903,000.00.

Radisky, Evette. King, (2008-09, NIR), "Engineering an MMP-9 Inhibitor for Enhanced Anticancer Therapeutic Potential." Fraternal Order of Eagles Pilot Project, \$40,000.00.

Riley, Richard. BC Special, (2009, Shared Instrument), "Mitochondrial Dysfunction in Neurodegeneration and Compensatory Approaches." National Institute of Aging, \$302,466.00.

Salihu, Hamisu. King, (2010-11, RPG), "Delineating the genetic pathway for folate-induced fetal brain growth among smoking mothers participating in a randomized clinical trial." University of South Florida, Office of Research & Innovation, \$25,000.00.

Shibata, Yoshimi. BC, (2006, Shared Instrument),"IL-10, Inflammation, and Selective Inhibition of Neovascularization." National Institutes of Health, \$212,050.00.

Shibata, Yoshimi. BC, (2006, Shared Instrument),"Molecular Mechanisms of Oxidative Stress Resistance in an Animal Model of Aging without Senescence." National Institutes of Health/National Institute on Aging, \$213,413.00.

Srivastava, Arun. BC, (2006, Shared Instrument), "Oral Therapy for Hemophilia A." National Institutes of Health, \$3,575,350.00.

Srivastava, Arun. BC, (2006, Shared Instrument), "Oral Immune Modulatory Therapy Using Antigens Bioencapsulated in Plant Cells." National Institutes of Health, \$1,832,808.00.

Sugrue, Stephen. BC, (2006, Shared Instrument), "AGAP2 Regulates Membrane Trafficking and Migration of Glioblastoma Cells." National Institutes of Health, \$192,024.00.

Thompson, E. Aubrey. BC, (2010, RPG), "MicroRNAs In Lobular Involution and Breast Cancer." National Institutes of Health/National Cancer Institute, \$255,500.00.

Wang, Liyong. King, (2010-11, NIR), "Vitamin D Concentration, Genetic Modifiers, and Parkinson Disease." National Institutes of Health, \$983,365.00

Yu, Hong-Guo. BC, (2008, NIR), "Mechanism of spindle pole body duplication and separation in yeast meiosis" National Science Foundation, \$675,000.00.

PROGRAM PERFORMANCE OUTCOMES

Florida Statistics:

- In 2011, cancer surpassed heart disease as the leading cause of death in the state of Florida accounting for almost **23.8** percent of all deaths
- Cancer was the leading cause of death for individuals aged 45-84 accounting for **30.8** percent of the total deaths in this age group

James & Esther King:

- \$196.8m received in follow-on funding
- 2,376 new jobs created, for every research job in Florida
- **66%** of Florida investigators completing King grants have earned additional, non-state funds based on their finding, averaging \$700,000 each
- More than **250** scientists at **22** different institutions throughout the state have led King Program projects, aided by hundreds more graduate and post-doctoral students
- **860** peer-reviewed journals
- 1,331 scientific presentations on grant findings
- 18 early partnership's created between academic researchers and small businesses
- Among 8 early partnership projects, 5 have formed new Florida companies and brought **\$13.8M** in additional external funding
- \$16.62M awarded for Collaboration Grants
- National recognition for State Science and Technology Institute (SSTI) as the winner of its 2009 Excellence in Tech-Based Economic Development

Florida Statistics:

- In 2011, cancer surpassed heart disease as the leading cause of death in the state of Florida accounting for almost **23.8** percent of all deaths
- Cancer was the leading cause of death for individuals aged 45-84 accounting for **30.8** percent of the total deaths in this age group

William "Bill" Bankhead, Jr., & David Coley:

- **\$140.5M** in follow-on funding has been awarded directly related to Coley grants
- **1,600** new jobs created (for every research job in Florida, 2.12 new jobs are created)
- **755** people working on cancer projects
- 410 peer-reviewed journal articles on the findings of their sponsored projects
- 272 researchers invited to give presentation at scientific meetings on their research
- 48 new investigators have launched independent cancer research careers in Florida
- Provided funds to **154** senior researchers who, in addition to their own work, employ and train lab professionals and students
- Provided Collaboration Research grants resulting in more than **70** researchers meeting monthly as a team to concentrate on an aggressive form of breast cancer
- 37 Health Disparities projects in two years
- 62% of grants in 2010 classified as translating laboratory discoveries

Appendix A



Richard J. Bookman, Ph.D. Senior Advisor for Program Development and Science Policy

State Surgeon General John Armstrong, M.D. Florida Department of Health 2585 Merchants Row Blvd. Tallahassee, FL 32399

October 26, 2012

Dear Dr. Armstrong,

Thank you for participating in the September 26th meeting of the Department's Biomedical Research Advisory Council (BRAC). Your leadership was welcomed and energizing. We fully concur that the time is ripe to move forcefully to improve health through biomedical research and to lessen the impact of disease, particularly cancer.

As a result, a subcommittee meeting to respond to your charge was organized, noticed, and held on October 12th. This letter reflects that dialogue as well as full BRAC review, revisions and approval of the work performed by the subcommittee.

WHAT WE HEARD

We heard loud and clear that you want to **take bold action** to create a "Florida System of Cancer Care", designed and built to serve all Floridians, a system founded upon the best available science and protocols for treatment, and one which will continuously improve through outcomes-based measures and feedback.

We agree that it is appropriate to align the Bankhead-Coley Cancer Research Program (covering all cancers regardless of cause) and the King Biomedical Research Program (all tobacco-related illnesses including cancer caused by tobacco) to the new, broader vision of cancer care and treatment you have articulated. In a number of important scientific and healthcare delivery respects, **cancer can provide a model** by which we can work to address other preventable disease, including cardiovascular disease, lung disease, and stroke.

The members of the BRAC see both real value as well as the economic necessity to **focus and to coordinate our efforts** both within the Department of Health and across the state. Our work to date has been influenced by our proactive collaborations with DoH's Office of Minority Affairs, the universitybased technology transfer directors, FLCURED, and BioFlorida. To extend this, we have reached out to CCRAB and will work together with them and other stakeholders going forward.

We also heard your request that the BRAC **develop a research agenda** to support the Florida System of Cancer Care. This agenda is to ask specific research questions relevant to Florida, to establish goals

and dates, and to seek proposals that address those questions. Incorporated into the agenda will be incentives for inter-institutional and interdisciplinary collaboration. <u>We want to assure you, we can create focused Requests for Applications (RFAs) designed around this vision and these goals.</u>

WHAT WE DID

The attached document, "BRAC's Research Agenda in Support of Florida's System of Cancer Care", puts forward a range of research activities. We have consulted broadly with colleagues both in Florida and around the country from patient advocacy groups, big pharma, academia, venture capital, non-profits, health policy think tanks and others to take advantage of their expertise and diverse perspectives. It reflects BRAC's best effort in the time since we met. The agenda provides background, suggested principles for research grants, and a three-pronged approach – Infrastructure, Talent, and Problem-Focused RFAs.

As you know, healthcare and the world of biomedical research are changing rapidly. As we prepared our recommendations to support the Florida System of Cancer Care, we felt it was important to try a) "to skate to where the puck will be", to **seize emerging opportunities** in cancer care and research, and b) to factor in Florida's specific needs and opportunities. Florida is what the US will look like in the next 20 years. Our diversity gives us the opportunity to <u>provide national research and clinical care leadership</u> to understand how such diversity may impact cancer etiology and disease outcomes. Florida can be ahead of the curve, **addressing transformative research questions** in a way that only Florida can.

The options described in the Research Agenda may have value either individually or taken together; however, the 13 ideas, if only seen as pieces, fail to be responsive to your call for a clear, simple, bold, and ambitious goal. Aligned, each can complement what we think is a unifying theme: personalization of medicine is the future and a patient's genome is the key.

WHAT WE PROPOSE:

The overarching goal is, by 2025, to offer the genome sequencing option to all Floridians who present with a cancer diagnosis.

It's a way of saying "If you're a Floridian and you're diagnosed with cancer, you can have your cancer genome sequenced."

It's a way of saying to the people of Florida "Cancer in Florida just got personal."

It's a way of saying to the world that "<u>Florida</u> is a cancer care destination" – or even more strongly, "Florida is <u>the</u> cancer care destination."

Such individualized analysis not only personalizes cancer diagnosis and treatment, but also increasingly makes it **more effective – both for outcomes and cost – in all of Florida's diverse communities**. This sequencing effort will need to be carefully ramped up, likely starting in selected clinical trials to ensure consistent approaches, and should include the malignant genome, epigenomics, as well as the patient's normal genome.

Much collaborative effort is needed on protocols, data infrastructure, training, ethics, privacy, patient/community education and engagement, and getting <u>all</u> healthcare professionals ready to handle the data. A project like this **brings the Cancer Centers together with community oncologists** and primary care networks. The project will **spur economic development** through building the first industrial scale clinical genomics platform in the US. It may take us 10 years of planning, infrastructure

construction, and resource development to stand this effort up. But, **setting the goal now and getting to work immediately** on planning and implementation is something that we can do. The sooner we commit to this goal, the sooner Florida's cancer patients and their families will start to benefit. **NEXT STEPS**

As you stated, the BRAC is uniquely positioned to help make Florida a more attractive environment for biomedical researchers and those who fund them (public and private) and, in so doing, to make Florida a better place for patients to receive the most advanced and effective care.

Thank you for including us in your vision and on your team. With a signal from you, and in consultation with CCRAB and other stakeholders, we will start to craft the RFAs to take the first important steps to make this ambitious goal a reality.

Sincerely,

Richard J. Bookman, Ph.D. Chair, and on behalf of Florida Biomedical Research Advisory Council

cc: CCRAB - Dr. Thomas George, Chair

BRAC's Research Agenda in support of The Florida System of Cancer Care

BRAC BACKGROUND: For more than a decade, the BRAC, supported by outstanding Department of Health staff and a dedicated contractor, has accumulated substantial experience in the design and running of research grant programs. Our efforts have won awards and national recognition. Our grant programs have been approved by the NCI as a funding source that counts towards NCI standards for research intensity. Also, our procedures pay scrupulous attention to any potential conflicts of interest, issues which now are bedeviling the cancer efforts in Texas. Finally, we have a proven return on investment of more than \$2.5-to-\$1 for getting federal research dollars as follow-on funding.

We therefore feel confident that we can contribute a proven system and operating procedures to produce calls for applications, create peer review criteria, run an unconflicted peer review process, make award recommendations in a blinded fashion based on merit, rigorously track progress of awardees, and utilize various outcome measures for continuous program improvement.

From our history, certain principles have evolved and we would like to share those before detailing our suggestions.

PRINCIPLES FOR FLORIDA BIOMEDICAL RESEARCH GRANT PROGRAMS:

- 1. *Competition* Funds should be awarded through merit-based competition with proposal review carried out by out-of-state, unconflicted peer reviewers.
- 2. Alignment and leverage Florida's cancer research programs need to be agile and responsive to the environment (e.g., NIH funding, partnership opportunities, evolving FDA regulations, etc.).
- 3. Collaboration Discovery is accelerated by rewarding people for working together, whether within or across institutions, disciplines or borders.
- 4. Accountability Florida's grant programs should use clear outcome measures such as follow on funding, translation of research, IP, startups, workforce development, reductions in morbidity and mortality, etc. as outcome measures.
- 5. Openness and transparency Grant competitions should be open to all Florida-based investigators, institutions, and companies. And, importantly, results of publicly funded research should be made available to the public. Data sharing serves the patient's interest.

This last principle is worth some extra attention. Clinical data, collected as part of the Florida System of Cancer Care, represent an important source of information for further knowledge creation. Re-use of such data for research purposes should be encouraged, open to all, including through partnerships with the private sector – both large and small. Similarly, translational and clinical research data need to be made broadly available, consistent with and mindful of intellectual property considerations. The mantra: "re-useful is the new useful" should inform our policy in this area, as it is increasingly doing with federal agencies, big pharma, the Institute of Medicine, and various patient advocacy groups. Transparency to avoid real or perceived conflicts of interest is an important required element.

We believe a three-pronged approach to competitive grant funding -- general infrastructure, talent, and problem-focused research projects -- will be highly effective as a means of driving a focused cancer research program to enhance cancer care in Florida, to support the big goal, and to improve cancer outcomes significantly.

RESEARCH COMPONENTS TO SUPPORT THE FLORIDA SYSTEM OF CANCER CARE

I. INFRASTRUCTURE COMPONENT

1. Clinical Research Data Platforms:

Platforms are enablers and data are the fuel for innovation. Our ability to capture detailed patient data, from the behavioral to the molecular, is increasing. Advances in genomics and related data-intensive sciences are emerging as keys to the challenge of personalized cancer diagnostics and therapeutics.

The state is in a unique position to forge and to force a **shared**, **standards-based cancer research data platform across the state**. Such a platform may be developed based on phased requirements for interoperability, for example. It might build upon the base of DoH's existing Florida Cancer Data System. With necessary privacy protections, aggregated patient-level data can accelerate evaluation and refinement of new treatment protocols.

This type of initiative can attract outside partners including federal (e.g, NIH, PCORI, AHRQ, CMS), public/private partnerships (e.g., Project DataShare,

DataLiquidityCoalition.Org), NGOs (e.g, Sage Bionetworks, Cancer Commons), or private (e.g., GSK's new open data initiative.)

Importantly, these clinical research data platforms, enhanced with 'omics' data, can ignite the virtuous cycle of bed-to-bench-to-bed information flow.

2. Shared Core Facilities:

Certain assays, whether in support of laboratory research or as part of hi-tech clinical tests, require expensive cutting edge equipment, trained experts to operate, and adherence to strict QA/QC standards. Core facilities often require partial subsidy in order to operate at research scale and provide general access to a diverse set of users. Any state support for **core facilities** should avoid duplication, **promote sharing**, and require **high standards for data reproducibility**. The robust core facilities and integrated research programs of the CTSA Programs at UF and UM and the cancer research cores at Florida's cancer centers can serve as seeds for state investment and statewide expansion. Further, earlier state investments in infrastructure, such as those for expression profiling and genomics, should be leveraged.

3. Clinical Trial Cooperation and Recruitment:

A number of steps can be taken to **increase cancer clinical trials participation** in Florida. Master affiliation agreements between collaborative research and clinical trial sites, centralized data safety monitoring oversight resources, and reciprocity agreements among the various IRBs would all help to expedite the initiation of new clinical trials at many sites. These agreements should be part of a framework among cancer research organizations that make it possible to test new therapeutic ideas rapidly in a conflict-free manner. Lastly, the availability of community-informed clinical trial navigators for cancer patients as part of a statewide trials matching program will increase patient understanding and trial enrollment from all of Florida's diverse communities.

II. TALENT COMPONENT

- 4. As our cancer efforts become better defined, it is certain that additional talent will accelerate our efforts. The Florida cancer effort could provide a portion of the resources needed for research institutions to accomplish cluster hires of teams of experts. Such institutional grants should require matching funds and utilize the 5 year funding window that FBRP statutes now permit. An open question is whether the cluster can have or should be required to have a multi-institutional base.
- 5. The BRAC strongly supports a continued focus on **support for young investigators**. While some of these may be hired in the context of a cluster hire program, many will not. Such support helps to level the playing field by making all of Florida's institutions more competitive with wealthier ones with respect to start-up funds. These future stars of

cancer care and research, representing diverse backgrounds and training, need our support - particularly at a time of declining federal dollars for cancer research.

- 6. Cancer clinical trials need to be conducted throughout the state and we need to expand the clinical research workforce. There are numerous specialist roles beyond the MDs, RNs, and PhDs. Job training programs, recognition of all healthcare professionals as key cancer team members, consistent standards for credentialing, and curriculum development for health professional schools are needed. This training effort is a win/win for both patients and for economic development through job creation. Cancer centers and medical schools should provide leadership for this and content can be deployed through community colleges and online methods. Collaboration with FLASCO can help to achieve this goal.
- 7. The molecular evidence seems increasingly clear: if you've seen one patient's cancer, you've seen one patient's cancer. Our comprehensive system of cancer care needs to take the diversity of Florida's population and communities into account. An approach to cancer screening and prevention in one neighborhood might be ineffective in another. We therefore need to **train and deploy community engagement specialists** as part of the system approach.
- 8. An increasing number of clinical practice areas are discovering the benefits of interprofessional education (IPE), forging strong teams of healthcare professionals. A curriculum development grant to support IPE training programs in next-gen cancer care will positively impact patients, cancer care, and the clinical research effort.

III. PROBLEM-FOCUSED COMPONENT

- 9. The data we have on hand today are clear: we have significant disparities in cancer outcomes based on various factors such as socioeconomic status, race, ethnicity, place of residence, etc. Some of the largest and earliest improvements in statewide cancer outcomes can be achieved through focused **projects to reduce cancer disparities**. The state is in a unique position to drive this effort and to demonstrate improvement towards health equity, setting an example for other states to follow.
- 10. Given the diversity of Florida's population, we know that one size doesn't fit all. We need to understand more about the specific needs of different communities and how best to engage people in those communities with respect to cancer prevention, screening and care. A focused RFA to **develop models for community engagement** can provide needed examples for emulation in other parts of Florida.
- 11. As our lives, and particularly our health, become increasingly digitized, issues of privacy and confidentiality may appear threatened. Since more and better data are so key to the evolution of Florida's system of cancer care, we need to address the intersection of ethics, privacy and electronic health records. A modest, focused RFA can generate ideas to guide policy and practice.
- 12. As Florida's biomedical researchers create new knowledge, some of it may be appropriate for commercialization and therefore require patent protection. But the complexity of biology has proven repeatedly that single patents rarely generate new drugs. Rather, it is bundles of IP that are more likely to be attractive for venture funding. We should consider funding a project to **explore different models of IP pooling** and continue our innovative 'feasibility' grants in partnership with the technology transfer directors.
- 13. Investigator-initiated research is an important element of a balanced research portfolio. Basic and translational research projects should focus on key molecular mechanisms, pathway elucidation, therapeutic obstacles or potential targets. We would suggest that this might be focused on a subset of cancers of high prevalence or cancer disparities in Florida such as lung, breast, prostate, and colorectal.