BRIAN F. CLEM, Ph.D.

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A. Education

B.S.	Major: Biology, Minor: Chemistry, Centre College, Danville	06/2000
M.S.	Biochemistry and Molecular Biology, University of Louisville	05/2003
	Graduate School, Louisville	
Ph.D.	Biochemistry and Molecular Biology, University of Louisville	05/2005
	Graduate School, Louisville	

B. Academic Appointments:

Post-doctoral Scholar:	James Graham Brown Cancer Center	2005-2009

Department of Medicine University of Louisville

Assistant Professor: Department of Medicine (Term Track) 2009-2012

James Graham Brown Cancer Center

University of Louisville

Joint Appointment (Term Track), Department of 2010-2012

Biochemistry and Molecular Biology

Department of Medicine (Tenure Track) 2012-2013

James Graham Brown Cancer Center

University of Louisville

Joint Appointment (TenureTrack), Department of 2012-2013

Biochemistry and Molecular Biology

Primary Appointment (TenureTrack), Department 2013-present

of Biochemistry and Molecular Biology

Associate Scientist: James Graham Brown Cancer Center 2009-present

Full Member: Graduate Faculty, School of Medicine 2010-present

C. Other Positions

None

D. Board Certification and Licensure

N/A

E. Professional Memberships and Activities:

Judge, Jefferson County Public School Regional Science Fair Judge, Research! Louisville, University of Louisville Member, Molecular Targets Program, JGBCC Member, American Association for Cancer Research	2003 2006 2009-present 2010-present
F. Honors and Awards	
Travel Award from the American Society for Biochemistry and Molecular Biology	2003
Graduate Dean's Citation, University of Louisville John Richard Binford Award, Outstanding Performance in Graduate Studies, University of Louisville	2005 2005
2 nd Place poster award, Post-doctoral Division, James Graham Brown Cancer Center Retreat	2005
2 nd Place poster award, Post-doctoral Division, James Graham Brown Cancer Center Retreat	2007
1 st Place, Roger H. Herzig Junior Faculty Research Prize, James Graham Brown Cancer Center Retreat	2009
2nd Place, Poster Division , Ohio Valley Affiliates for Life Sciences (OVALS) 8 th Annual Conference	2010
Faculty Award, Potential for Major Clinical Application, ResearchLouisville!, University of Louisville	2010
Junior Faculty Research, James Graham Brown Cancer Center Retreat	2012
Junior Faculty Research, James Graham Brown Cancer Center Retreat	2013
G. Committee Assignments and Administrative Services	
Student Member , Biochemistry and Molecular Biology Department Graduate Executive Committee, University of Louisville	2002
Member, Distinguished Teaching Award Committee, University of Louisville	2003
Student Member, Health Science Center Medical Council, University of Louisville	2003-2005
Coordinator, Poa Pratensis JGBCC Molecular Targets Seminar Series Member, University of Louisville CEGIB Pilot Grant Review Committee Member, Brown Cancer Center Summer Research Internship Program Selection Committee	2008-2010 2010 2010-present
Voting Member , Brown Cancer Center Clinical Scientific Review Committee Member , Personnel Committee, Dept. Biochemistry and Molecular Biology	2012-present 2013-present

Member, Curriculum Committee, Dept. Biochemistry and Molecular Biology	2013-present
H. Journal Board Memberships / Peer Reviews	
Editorial Board Member, ISRN (Biochemistry) Ad hoc Reviewer, AICR, International Association for Cancer Research	2012-present 2014
I. Teaching	
Course Teaching: Teaching Assistant, Molecular Biology Graduate Course Lecturer, BIOC 675, Cancer Biology Course Lecturer, BIOC 647, Biochemistry II Course Director, Lecturer, BIOC611, Adv. Tech. in Bioch. and Mol. Biol.	2003 2012-present 2014 2014
Research/Laboratory Teaching:	
Ph.D. Students: Kaitlyn Wendland, Dept. Biochemistry James Bradley, Dept. Biochemistry Stephanie Metcalf	2013 2014 2014
Master Students: Miriam Reynolds, Dept. Biochemistry, University of Louisville	2011-2014
Residents: Umesh Goswami, M.B.B.S., University of Louisville	2007-2008
Medical Students: Whitney Goldsberry, University of Louisville	2011
Undergraduates: Janelle Fassbender, B.S., University of Louisville Harini Chenna, B.S., University of Louisville Adam Morrison, University of Louisville Margaret Means, Vanderbilt University Samantha Carlisle, University of Louisville Chelsea Rinnert, University of Louisville Brian Robertson, Hanover University Samantha Manning, University of Louisville Elizabeth Long, Hanover University Andrew Carroll, University of Louisville	2005-2006 2008 2009-2011 2010 2011 2012 2012 2013 2013 2013
High School Students: Student Science Fair Projects	2003-2004

Mary Richardson	2010
HaiHeng Cheav	2013
Veeresh Rai	2013, 2014
Ben Green	2014

Thesis Committees:

Department of Biochemistry:

M.S. Miriam Reynolds 2011-2014

Department of Pharmacology/Toxicology

M.S. Morgan Stathem 2014

J. Abstracts and Presentations

Oral Presentations, International/National:

10/18/06	"PFKFB3 and Tumor Metabolism: Targeting Mr. Embden and Mr. Meyerhoff's Accelerator" , Oral Presentation, 4 th International Conference on Tumor Cell Metabolism, Louisville, KY.
4/4/11	"Characterization of a Novel Small Molecule Antagonist of 6-Phosphofructo-2-Kinase (PFK-015) That Suppresses Glucose Metabolism and Tumor Growth", AACR 102 nd Annual Meeting, Orlando, FL – <u>Oral Presentation</u> (first author - presentation given by co-author Gilles Tapolsky)
11/15/11	"Loss of the retinoblastoma protein alters glucose and glutamine metabolism", AACR-NCI-EORTC International Conference: Molecular Targets and Cancer Therapeutics, San Francisco, CA – <u>Proffered Oral Presentation</u>
5/16/12	"Retinoblastoma protein regulation of glucose and glutamine metabolism", <u>Invited Speaker</u> , Banbury Conference – Energy Metabolism and the Cell Cycle, Cold Spring Harbor Laboratory, Lloyd Harbor, NY
1/31/13	"Preclinical Characterization of Antagonists of 6-Phosphofructo-2-Kinase that Suppress Glucose Metabolism and Tumor Growth", Invited Speaker, Target Cancer

Oral Presentations, Regional:

Metabolism Conference, Boston, MA

11/21/09	"Translating Metabolomics into Novel Cancer Therapeutics", <u>Invited Oral</u> Presentation, 1 st UL/UK Joint Symposium on Lung Cancer, Louisville, KY.
3/27/10	"Inhibition of Choline Kinase As a Novel Anti-Neoplastic Approach", Invited Oral Presentation, 2 nd UL/UK Joint Symposium on Lung Cancer, Lexington, KY

"Targeting Glycolysis as an Anti-Neoplastic Strategy", Department of Pharmaceutical Sciences, Invited Speaker, Host: Dr. Younsoo Bae, Department of Pharmaceutical Sciences, University of Kentucky, Lexington, KY
"RB and Tumor Metabolism", Department of Cancer and Cell Biology, Invited Speaker, Host: Dr. David Plas, University of Cincinnati, Cincinnati, OH
"Role for pRB in Regulating Tumor Metabolism and Potential Therapeutic Targets" Department of Cancer Biology, Invited Speaker, Host: Dr. Jun-Lin Guan, University of Cincinnati, Cincinnati, OH

Oral Presentations, University of Louisville:

11/19/02	"XIAP Inhibits Apoptosis by Promoting Proteasome Degradation of Smac", Department of Biochemistry Seminar Series
5/13/04	"Inhibition of HIV Infection by Blocking Its Entry", Department of Biochemistry Seminar Series
07/13/06	"Pharmacological Inhibition of PFKFB3 Suppresses Tumor Growth", Poa Pratensis Molecular Targets Seminar Series.
07/8/08	"Targeting Metabolism to Fight Cancer", JGBCC Undergraduate Internship Seminar Series
12/4/08	"Sex, Violence, and Choline Kinase", Poa Pratensis Molecular Targets Seminar Series
7/14/09	"Fighting Cancer by Targeting Its Food", JGBCC Undergraduate Internship Seminar Series
11/6/09	"Translating Metabolomics into Novel Cancer Therapeutics", James Graham Brown Cancer Center Retreat
1/27/10	"Fighting Cancer by Targeting Its Food", JGBCC Outreach Program, Manual High School
3/10/11	"An Update on PFKFB3 Inhibitors – A Tale of Two Paths", JGBCC Molecular Targets Seminar
4/29/11	"Regulation of Tumor Metabolism by the Retinoblastoma Protein Family", Department of Ophthalmology & Visual Sciences Seminar Series
6/23/11	"Non-coding RNA transcript mediates p53 escape in Rb-mediated immortalization", JGBCC Molecular Targets Retreat
7/26/11	"Drug Design for New Cancer Therapies", JGBCC Undergraduate Internship Seminar Series

"Drug Design Towards New Cancer Therapies", JGBCC Undergraduate Internship Seminar Series
 "A Role for the Retinoblastoma Protein in Tumor Metabolism", Department of Pharmacology/Toxcicology Seminar Series
 "Cancer Initiation to Progression", JGBCC Summer Internship Seminar Series
 "Development of Small Molecule Inhibitors as Cancer Therapies", JGBCC Summer Internship Seminar Series
 "Can Metabolic Suppression Sensitize ER+ Breast Cancer to anti-Estrogen Therapy", Colloquia on Cancer Biology and Therapeutics Seminar Series

Poster Presentations, National/International:

Meeting, Washington D.C.

Poster Pres	entations, National/International:
6/8/03	"Identification of Steroidogenic Acute Regulatory Protein (StAR) Promoter DNA-binding and Associating Proteins by DNA-affinity Chromatography", Poster Presentation, Endocrine Society's 85th Annual Meeting Philadelphia, PA
06/14/04	"Sp3, mSin3A, and HDAC1/2 Functionally Repress Basal Transcription of The Steroidogenic Acute Regulatory Protein Gene Promoter", Poster Presentation, American Society for Biochemistry and Molecular Biology Annual Meeting Boston, MA
11/14/05	"Immortalization is Sufficient to Cause the Major Metabolic Alterations of Cancer", Poster Presentation, American Association for Cancer Research, NCI-EORTC International Conference, Philadelphia, PA
03/06/07	"Pharmacological Inhibition of 6-Phosphofructo-2-kinase Suppresses Tumor Growth", Poster Presentation, 4th International Conference on Tumor Microenvironment, Florence, Italy
10/22/07	"Small Molecule Inhibition of 6-Phosphofructo-2-Kinase Activity Suppresses Glycolytic Flux and Tumor Growth", Poster Presentation, AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, San Francisco, CA
06/28/08	"Inhibition of 6-Phosphofructo-2-Kinase Decreases Breast Cancer Growth", <u>Poster Presentation</u> , Department of Defense Era of Hope Meeting, Baltimore, MD
10/14/08	"Small Molecule Inhibition of 6-Phosphofructo-2-Kinase Decreases Breast Tumor Growth". Poster Presentation. AACR/JCA Chemical and Biological Aspects of Inflammation and Cancer, Ko Olina, HI
12/10/08	"Inhibition of 6-Phosphofructo-2-Kinase Suppresses Breast Cancer Growth In Vivo", Poster Presentation, San Antonio Breast Cancer Symposium, San Antonio, TX
2/08/09	"Inhibition of 6-Phosphofructo-2-Kinase Suppresses Breast Cancer Growth In Vivo", Poster Presentation, CDMRP, Breast Cancer Research Program, LINKS

- 2/25/13 **"Loss of Rb Function Enhances Glutamine Metabolism"**, <u>Poster Presentation</u>, Keystone Symposia Tumor Metabolism (X4), Keystone, CO
- 10/7/13 "Genetic Loss of the Rb Family Leads to Increased Glutamine Metabolism", <u>Poster</u> Presentation, 3rd International RB Meeting, Monterrey, CA
- 5/28/14 "Troglitazone Suppresses Tumor Cell Growth and Glutamine Metabolism through a PPAR-Independent Mechanism", Poster Presentation, Metabolism, Diet, and Disease Conference, Washington, DC

Poster Presentations, Regional:

- 2/25/10 Southern Society for Clinical Investigation Annual Meeting, New Orleans, LA Targeting Choline Kinase as an Anti-Neoplastic Approach
- 3/27/10 Joint UK/UofL Lung Cancer Conference, Lexington, KY
 - Small Molecule Targeting of Choline Kinase Decreases Tumor Growth In Vitro and In Vivo
 - 2. Requirement of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase Isoform 4 (PFKFB4) for Anchorage Independent Growth and Tumorigenesis
 - 3. Small Molecule Inhibition of 6-Phosphofructo-2-Kinase Activity Suppresses Glycolytic Flux and Tumor Growth
- 4/15/10 Ohio Valley Affiliates for Life Sciences (OVALS) 8th Annual Conference, Louisville, KY

Development of Small Molecule Inhibitors of Choline Kinase As a Novel Anti-Tumor Therapeutic Approach $-3^{\rm rd}$ Place Award Winner

4/14/11 Ohio Valley Affiliates for Life Sciences (OVALS) 9th Annual Conference, Cincinnati, OH

Characterization of a Novel Small Molecule Antagonist of 6-Phosphofructo-2-Kinase (PFK-015) That Suppresses Glucose Metabolism and Tumor Growth

Poster Presentations, University of Louisville:

11/09/02 Research! Louisville, University of Louisville

"Steroidogenic Acute Regulatory Protein (StAR) Promoter DNA-binding and Associating Proteins"

11/04/03 Research! Louisville, University of Louisville

"Cyclic Adenosine 3',5'-Monophosphate (cAMP) Enhances cAMP-Responsive Element Binding (CREB) Protein Phosphorylation and Phospho-CREB Interaction with the Mouse Steroidogenic Acute Regulatory (StAR) Protein Gene Promoter"

11/02/04 Research! Louisville, University of Louisville

"Sp3, mSin3A, and HDAC1/2 Functionally Repress Basal Transcription of The Steroidogenic Acute Regulatory Protein Gene Promoter"

09/14/05 JGBCC, University of Louisville Fourth Annual Retreat (The Olmstead)

- 1. "Pharmacologic Inhibition of 6-Phosphofructo-2-Kinase (PFKFB3) Suppresses Cancer Cell Proliferation"
- 2. "High Choline Kinase Activity is Essential for Neoplastic Proliferation"
- 3. "Nuclear Compartmentalization of a Key Regulator of Glycolysis, 6-Phosphofructo-2-Kinase (PFKFB3)"

05/15/06 JGBCC Molecular Targets Program Annual Retreat (The Brown Hotel)

- 1. Pharmacologic Targeting of 6-Phosphofructo-2-Kinase
- 2. The Inducible Isozyme of 6-Phosphofructo-2-Kinase Is an Essential Downstream Effector of the Oncogene Ras

11/29/06 JGBCC, University of Louisville Fifth Annual Retreat (The Olmstead)

- 1. Pharmacological Inhibition of 6-phosphofructo-2-kinase (PFKFB3) Suppresses Tumor Growth
- 2. The p16INK4a/Rb Family Pathway and Cancer Stem Cell Formation
- 3. Requirement of 6-phosphofructo-2-kinase/fructose-2,6- bisphosphatase- 4 (PFKFB4) for Anchorage Independent Growth and Tumorigenesis
- 4. PFKFB3 Interacts with C-RAF

11/28/07 JGBCC, University of Louisville Sixth Annual Retreat (The Olmstead)

- 1. Small Molecule Inhibition of 6-Phosphofructo-2-Kinase Activity Suppresses Glycolytic Flux and Tumor Growth
- 2. Requirement of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase- 4(PFKFB4) for Tumorigenesis
- 3. 6-Phosphofructo-2-Kinase (PFKFB3) Traffics to the Nucleus and Stimulates Cell Proliferation

10/29/08 JGBCC, University of Louisville Seventh Annual Retreat (The Olmstead)

- 1. Inhibition of 6-Phosphofructo-2-Kinase Suppresses Breast Tumor Growth In Vivo
- 2. Small Molecule Targeting of Choline Kinase Decreases Tumor Growth *In Vitro* and *In Vivo*
- 3. Requirement of 6-Phosphofructo-2-Kinase/Fructose-2,6-Bisphosphatase-4 (PFKFB4) for Tumorigenesis
- 6-Phosphofructo-2-Kinase/Fructose-2,6-Bisphosphatase-3 (PFKFB3) Localizes to the Nucleus and Enhances Cyclin-Dependent Kinase Activity and the Phosphorylation of the Cell Cycle Inhibitor p27^{Kip1}
- 5. Selective Inhibition of Choline Kinase Interrupts Ras Signaling and Tumor Growth

11/6/09 JGBCC, University of Louisville Eighth Annual Retreat (The Olmstead)

- 1. P27 Is Required for Growth Defects and Apoptosis Caused by PFKFB3 Inhibition
- 2. Selective Inhibition of Choline Kinase Simultaneously Attenuates MAPK and PI3K/AKT Signaling
- 3. Small Molecule Targeting of Choline Kinase Decreases Tumor Growth In Vitro and In Vivo
- 4. Regulatory subunit Vb of cytochrome c oxidase is required for malignant

transformation

5. Requirement of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase Isoform 4 (PFKFB4) for Anchorage Independent Growth and Tumorigenesis

10/14/10 RESEARCH! Louisville, University of Louisville

- Small Molecule Targeting of Choline Kinase Decreases Tumor Growth In Vitro and In Vivo
 - Faculty Award Winner: Potential for Major Clinical Application

11/5/10 JGBCC, University of Louisville Ninth Annual Retreat (The Olmstead)

- 1. Micelle Encapsulation of the Glycolytic Inhibitor 3PO as a Therapeutic Delivery Formulation
- Small Molecule Targeting of Choline Kinase Decreases Tumor Growth In Vitro and In Vivo

10/10/11 RESEARCH! Louisville, University of Louisville

Loss of the Retinoblastoma Protein Alters Glucose and Glutamine Metabolism

10/28/11 JGBCC, University of Louisville Tenth Annual Retreat (The Olmstead)

- 1. Loss of the Retinoblastoma Protein Alters Glucose and Glutamine Metabolism
- 2. Glutathione Synthetase Is Required for the Anchorage Independent Growth of A549 Lung Adenocarcinoma Cells
- 3. Estradiol stimulates 6-phosphofructo-2-kinase (PFKFB3) expression and glycolysis by breast cancer cells
- Characterization of a novel small molecule antagonist (PFK-015) of 6-Phosphofructo-2-kinase/ fructose-2,6-bisphosphatase-3 (PFKFB3) that suppresses glucose metabolism and tumor growth

9/20/12 **RESEARCH!** Louisville, University of Louisville

Control of Glutamine Metabolism By the Tumor Suppressor Rb

10/26/12 JGBCC, University of Louisville 11th Annual Retreat

- 1. Control of Glutamine Metabolism By the Tumor Suppressor Rb
- 2. Stimulation of Glucose Metabolism by Estradiol Is Mediated by 6-Phosphofructo-2-Kinase (PFKFB3)
- 3. Troglitazone Decreases Glutaminolysis and Suppresses Proliferation in Cells Dependent on Glutamine Metabolism for Cell Growth
- 4. Targeting 6-Phosphofructo-2-Kinase (PFKFB3) as a Therapeutic Strategy Against Cancer
- Combined effects of choline kinase inhibition and suppression of PEMT on cell proliferation

10/25/13 **JGBCC**, University of Louisville 12th Annual Retreat

- 1. Estradiol stimulates glucose metabolism via 6-phosphofructo-2-kinase (PFKFB3)
- 2. 6-Phosphofructo-2-Kinase (PFKFB3) Induces Autophagy as a Survival Mechanism
- 3. An anti-glycolytic small molecule inhibitor (PFK158) cooperates with a mutant B-RAF inhibitor (vemurafenib) to induce cell death in melanoma cells
- 4. Genetic Loss of the Rb Family Leads to Increased Glutamine Metabolism
- 5. Troglitazone Decreases Glutaminolysis and Suppresses Proliferation in Cells Dependent on Glutamine Metabolism for Cell Growth

6. Effect of Potential Phosphoserine Aminotransferase (PSAT1) Inhibitors on the Growth of Lung and Colon Cancer Cells

K. Patents

Issued United States Patents:

PFKB3 inhibitor for the treatment of a proliferative cancer

Inventors: Brian Clem, Jason Chesney, John O. Trent, Jason Meier, and Sucheta Telang United States Patent #8,088,385, issued January 3, 2012

Family of PFKFB3 Inhibitors With Anti-Neoplastic Activities

Inventors: Brian F. Clem, Gilles Tapolsky, Pooran Chand, John O. Trent, Sucheta Telang, Jason A. Chesney

United States Patent #8,557,823, issued October 15, 2013

Entered Phase I Clinical Trials, March 2014 - Clinical Trial.gov - NCT02044861

Submitted Patent Applications

Family of PFKFB3 Inhibitors With Anti-Neoplastic Activities

Inventors: Brian F. Clem, Gilles Tapolsky, Pooran Chand, John O. Trent, Sucheta Telang, Jason A. Chesney

European Patent Application serial no. 08 768 587.1; filed January 8, 2010.

Australian Patent Application serial no. 2008266856; filed January 18, 2010.

Japanese Patent Application serial no. (tbd); filed December 17, 2009.

Indian Patent Application serial no. 1100/DELNP/2010; filed February 17, 2010.

Small Molecule Inhibition of Choline Kinase Suppresses Tumor Growth

Inventors: Brian Clem, Jason Chesney, John O. Trent, Pooran Chand, and Sucheta Telang United States Provisional Patent Application serial no. 61/220,620; filed June 26, 2009

Novel Anti-Cancer Compounds

Inventors: Brian Clem, Jason Chesney, Pooran Chand, Gilles Tapolsky, Sucheta Telang, and John Trent

United States Provisional Patent Application serial no. 61/306,759; filed February 22, 2010

New Anti-Cancer Compounds and Methods to Treat Cancer

Inventors: Brian Clem and Gilles Tapolsky

United States Provisional Patent Application serial no. 61/324,441; filed April 15, 2010

L. Research Funding

Past Support:

1. Center for Genetics and Molecular Medicine Fellowship (*University of Louisville, Mentor: Barbara Clark, Ph.D.*)

Title: Transcriptional Regulation of StAR

Role: Principal Investigator

Period of Support: 05/01/02-4/31/03

Total Award: \$18,000

2. NIEHS T32 ES011564 Training Grant Fellowship (University of Louisville, Mentor: Barbara Clark, Ph.D.)

Title: Mechanisms of Transcriptional Regulation of the Mouse

Steroidogenic Acute Regulatory (StAR) Protein Gene Promoter

Role: *Project Investigator* Period of Support: 1/01/04-01/31/05

Total Award: \$20,000

3. Department of Defense Breast Cancer Multi-Disciplinary Post-doctoral Award

Title: <u>Targeting of Inducible 6-Phosphofructo-2-Kinase in Breast Cancer</u>

Role: Principal Investigator (100% Effort)

Period of Support: 05/01/06-04/30/09

Total Award: \$262,604 Total Direct Costs: \$262,604

4. 3P20RR018733-07S109 Center of Biomedical Research Excellence in Molecular Targets

Title: Administrative Supplement to Advance Translational

Research

Role: *Co-Investigator* (20%) for Projects 1+3

Period of Support: 10/01/09-09/30/11

Total Award: \$759,342

Projects 1+3

Direct Costs: \$398,983 (out of total Direct Costs of \$513,069)

2009-2010 Direct Costs: \$208,560 (out of total 2009-2010 Direct Costs of \$267,098)

5. University of Louisville Advanced Translational Award

Title: Pre-Clinical Testing of 3-(3-Pyridinyl)-1-(4-Pyridinyl)-2-Propen-1-One

In Autoimmunity

Role: Co-Investigator

Period of Support: 06/01/10-05/31/11 (no cost extension: 4/30/12)

 Total Award:
 \$96,192

 Total Direct Costs:
 \$94,306

 2010-2011 Direct Costs:
 \$94,306

6. Sponsored Research Grant (Un-restricted) – Advanced Cancer Therapeutics

Title: Pre-Clinical Analysis of 3PO and CK37 Derivatives

Role: Co-Investigator (1%)
Period of Support: 08/01/10-04/30/12

Total Award: \$224,661 Total Direct Costs: \$149,823 2010-2011 Direct Costs: \$74,838

7. Commonwealth of Kentucky Lung Cancer Research Program Grant

Title: Novel Small Molecular Inhibitors of Choline Kinase as a Therapeutic

Strategy against Lung Cancer

Role: *Principal Investigator* (10% effort)
Period of Support: 11/01/09-10/31/12 – no cost extension

 Total Award:
 \$150,000

 Total Direct Costs:
 \$136,364

 2011-2012 Direct Costs:
 \$38,528

8. 8P20GM103482-10 Center of Biomedical Research Excellence in Molecular Targets (Principal

Investigator: Donald Miller)

Role: *Project Leader* (40%)
Period of Support: 10/01/08-06/30/13
Total Award: \$11,038,973
2012-2013 Direct Costs: \$168,619

9. 1 R43 CA165300-01 (NCI) Center for Scientific Review Special Emphasis Panel

Small Business: Cancer Drug Development and Therapeutics (PI: Gilles Tapolsky, Advanced Cancer

Therapeutics)

Title: PFK-015: An inhibitor of PFKFB3 to treat Glioblastomas

Role: Project Investigator (Sub-contract)

Period of Support 10/1/12-6/30/13 Total Award: \$115,000

2012-2013 Direct Costs: \$33,500 (sub-contract to UofL)

Current Support:

1. 1R01CA149438 (NCI, PI: Chesney)

Title: Activation of Cyclin-Dependent Kinases by Fructose-2,6-

Bisphosphate

Role: Co-Investigator (10%)

Period of Support: 4/01/11-3/31/16
Total Award: \$1,552,500
2014-2015 Direct Costs: \$207,500

This grant funds the characterization of fructose-2,6-bisphosphate as a novel allosteric regulator of cyclin dependent kinases and cell cycle progression.

2. 1R01CA166327 (NCI)

Title: Regulation of Tumor Metabolism by Retinoblastoma Protein

Role: Principal Investigator (20%)

Period of Support 6/1/13-5/31/18
Total Award: \$1,095,000
2014-2015 Direct Costs: \$130,000

This grant will characterize metabolic pathways and downstream mediators regulated by the retinoblastoma protein in MEF cells, mouse transgenic and human tumors.

3. RSG 13-139-01 (American Cancer Society)

Title: Control of Glucose and Glutamine Metabolism by the

Retinoblastoma Protein

Role: Principal Investigator (25%)

Period of Support 7/1/13-6/30/17
Total Award: \$720,000
2014-2015 Direct Costs: \$150,000

This grant will fund an examination of the role of Rb in regulating glucose and glutamine metabolism in lung cancer.

4. 1P30GM106396 (Pilot Grant: Molecular Targets Phase III CoBRE grant: NIH)

Title: Targeting Phosphoserine Aminotransferase (PSAT1) in the

Treatment of Lung Cancer

Role: Principal Investigator (5%)

Period of Support 11/1/13-6/30/15

Total Award: \$150,000 2014-2015 Direct Costs: \$75,000

Pending Support:

1. R21 CA194894-02 (NCI, PI: Clem)

Title: Targeting Phosphoserine Aminotransferase in Squamous Cell Lung

Cancer

Role: Co-Investigator (10%)

Period of Support 4/1/15-3/31/17
Total Award: \$412,500
Direct Costs / year: \$125,000

M. Publications

Peer-Reviewed Research Publications:

- 1. **Clem, B.F.**, Hudson, E., Clark, B.J. Cyclic Adenosine 3',5'-Monophosphate (cAMP) Enhances cAMP-Responsive Element Binding (CREB) Protein Phosphorylation and Phospho-CREB Interaction with the Mouse Steroidogenic Acute Regulatory (StAR) Protein Gene Promoter. *Endocrinology*.146(3):1348-1356. 2005. PMID: 15550512
- 2. **Clem, B.F.**, Clark, B.J. Association of the mSin3A-histone deacetylase 1/2 Co-Repressor Complex with the Mouse Steroidogenic Acute Regulatory Protein Gene. *Molecular Endocrinology*. 20(1): 100-113. 2006. PMID: 16109738
- 3. **Clem, B.F.**, Telang, S., Clem, A., Yalcin, A., Meier, J., Simmons, A., Rasku, M., Arumugam, S., Dean, W.L., Eaton, J., Lane, A., Trent, J.O., and Chesney, J. Small Molecule Inhibition of 6-Phosphofructo-2-Kinase Activity Suppresses Glycolytic Flux and Tumor Growth. *Mol. Cancer Therapeutics*, 7(1):110-20, 2008. PMID: 18202014
- 4. Liu, Y., El-Naggar, S., **Clem B.**, Chesney. J., Dean, D.C. The Rb/E2F pathway and Ras activation regulate RecQ helicase gene expression. *Biochemical Journal*, 412(2):299-306, 2008. PMID: 18215118
- 5. Thornburg, J., Nelson, K., **Clem, B. F.**, Lane, A., Arumugam, S., Simmons, A., Eaton, J. W., Telang, S. and Chesney, J. Targeting Aspartate Aminotransferase in Breast Cancer. *Breast Cancer Research*, 10(5):R84, 2008. PMCID: 2614520

- 6. Liu Y., Clem, B. F., Zuba-Surma, E., El-Naggar, S., Telang, S., Jenson, A.B., Ratajczak, M., Chesney, J., and Dean, D. C. Mouse Fibroblasts Lacking RB1 Function Form Spheres and Undergo Reprogramming to a Cancer Stem Cell. *Cell Stem Cell*, Apr 3; 4(4):336-47, 2009. PMCID: 2743858
- 7. Yalcin, A., Clem, B.F., Simmons, A, Lane, A., Nelson, K., Clem, A., Brock, E., Siow, D., Wattenburg, B., Telang, S., and Chesney, J. Activation of Cyclin-Dependent Kinases By Fructose-2,6-Bisphosphate. *Journal of Biological Chemistry*, Sep. 4;284(36):24223-32, 2009. PMCID: 2782016
- 8. Yalcin, A., **Clem, B.F.**, Makoni, S., Clem, A., Nelson, K., Thornburg, J., Siow, D., Lane, A.N., Brock, S.E., Goswami, U., Eaton, J.W., Telang, S., and Chesney, J. Selective Inhibition of Choline Kinase Simultaneously Attenuates MAPK and PI3K/AKT Signaling. *Oncogene*, Jan 7;29(1):139-49, 2010. PMID: 19855431
- 9. **Clem, B.F.**, Clem, A.L., Yalcin, A., Goswami, U., Telang, S., Trent, J.O., and Chesney, J. A Novel Small Molecule Antagonist of Choline Kinase-α That Simultaneously Suppresses MAPK and PI3K/AKT Signaling. *Oncogene*. Jul 28;30(30):3370-80, 2011. PMCID: 3136659
- Telang, S., Rasku, M.A., Clem, A.L., Carter, K., Klarer, A.C., Badger, W.,R. Milam, R.A. Rai, S.N., Pan, J., Gragg, H, Clem, B.F., McMasters, K.M., Miller, D.M., and Chesney, J. Phase II Trial of the Regulatory T Cell-Depleting Agent, Denileukin Diffitox, in Patients with Unresectable Stage IV Melanoma. BMC Cancer. Dec 13; 11:515, 2011. PMCID: 3293785
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