BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Liu, Bolin

eRA COMMONS USER NAME (credential, e.g., agency login): Bolin_Liu

POSITION TITLE: Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Beijing Medical University, Beijing, China	M.D.	07/1987	Medicine
Institute of Hematology, Chinese Academy of Medical Sciences and Peking Union of Medical Colleges, Tianjin, China	M.S.	07/1994	Molecular Biology
The University of Texas MD Anderson Cancer Center, Houston, TX	Postdoctoral	09/2002	Cancer Biology

A. Personal Statement

The major goal of our research programs is to elucidate the molecular mechanisms of drug resistance and tumor metastasis in the progression of breast cancer and non-small cell lung cancer. I have the expertise, leadership and motivation necessary to carry out the proposed works. I have a broad background in cancer biology, with specific training and expertise in Receptor Tyrosine Kinase (RTK) signaling, apoptosis, cell cycle, experimental therapeutics, noncoding RNAs (miRNAs and lncRNAs), and epigenetic regulation of gene expression. As PI or co-PI on several funded grants, I laid the groundwork for the proposed research by studying the mechanisms of drug resistance/tumor metastasis, and developing novel strategy targeting epigenetic mechanism involving in specific histone marks and/or histone modifiers for cancer treatment. I have successfully administered a number of research projects, collaborated with other researchers, and produced peer-reviewed publications from each project. I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget. The current application builds logically on the works published by my laboratory, and our novel preliminary data recently generated. My expertise and experience have prepared me to lead the proposed studies.

1. **Liu, B.**, Fan, Z., Alimova, I.N., Edgerton, S.M., and Thor, A.D. Metformin induces unique biological and molecular responses in triple negative breast cancer cells. ***Cell Cycle*** 2009;8: 2031-40
2. Deng, X., Wang, S., Deng, A., **Liu, B.,** Edgerton, S.M., Lind, S.E., Wahdan-Alaswad, R., and Thor, A.D. Metformin targets Stat3 to inhibit cell growth and induce apoptosis in triple negative breast cancers. ***Cell Cycle*** 2012;11(2): 367-376
3. Wang, S., Huang, J., Lyu, H., Lee, C-K, Tan, J., Wang, J., and **Liu, B.** Functional cooperation of miR-125a, miR-125b, and miR-205 in entinostat-induced downregulation of erbB2/erbB3

and apoptosis in breast cancer cells. ***Cell Death & Disease*** 2013; 4, e556; doi:10.1038/cddis.2013.79

4. Lyu, H., Wang, S., Huang, J., Wang, B., He, Z., and **Liu, B.** *Survivin*-targeting miR-542-3p overcomes HER3 signaling-induced chemoresistance and enhances the antitumor activity of paclitaxel against HER2-overexpressing breast cancer. ***Cancer Letters*** 2018; 420: 97-108

B. Positions and Honors

Positions and Employment

1994-1998	Visiting Scientist, Department of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX
2002-2006	Assistant Professor of Research, Department of Pathology, The University of Oklahoma Health Sciences Center (OUHSC), Oklahoma City, OK
2006-2007	Assistant Research Professor, Department of Pathology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO
09/07-06/15	Assistant Professor, Department of Pathology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO
07/15-10/18	Associate Professor, Department of Pathology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO
11/1/2018-	Professor, Department of Genetics, Stanley S. Scott Cancer Center, School of Medicine, LSU Health Sciences Center (LSUHSC), New Orleans, LA

Other Experience and Professional Memberships

1996-	Member, American Association for Cancer Research (AACR)
2005-	Member, American Association for the Advancement of Science (AAAS)
2010-	Member, Chinese Biological Investigators Society (CBIS)
2009-	Editorial Board Member, American Journal of Translational Research (AJTR)
2010-	Editorial Board Member, American Journal of Cancer Research (AJCR)
2010-	Editorial Board Member (Associate Editor), Biological Procedures Online (BPO)
2008, 2009	DOD-Breast Cancer Research Program (BCRP) Idea Award
2011-2017	Colorado Clinical and Translational Sciences Institute-CO Pilot Program
2012	DOD-Peer Reviewed Cancer Research Program-Blood Cancer Discovery Award
2012	DOD-Breast Cancer Research Program (BCRP) Postdoctoral Fellowship Award
2012	University of Maryland - Maryland Industrial Partnerships Program
2013	Medical Research Council, United Kingdom, Molecular & Cellular Medicine-Cancer Program
2014	The Health Research Board (HRB), Ireland, Health Research Awards
2015	DOD-Peer Reviewed Medical Research Program-Technology/Therapeutic Development Award (TTDA)
2016	Reviewer, Breast Cancer NOW, London, United Kingdom
02/2017	Reviewer (ad hoc), Developmental Therapeutics (DT) study section, NIH/NCI
03/2017	Mail reviewer, the Native American Cancer Prevention (NACP) NCI U54 grant - University of Arizona Cancer Center (UACC) and Northern Arizona University (NAU)
03/2017	Participating reviewer, study of the NIH review process led by Dr. Patricia G. Devine - University of Wisconsin-Madison
02/2018	DOD-Breast Cancer Research Program (BCRP) Breakthrough Award
02/2018	Reviewer (ad hoc), Developmental Therapeutics (DT) study section, NIH/NCI
03/2018	Reviewer (ad hoc), special panel ZRG1 OBT-D study section (R21s), NIH/NCI
10/2018	Reviewer (ad hoc), Developmental Therapeutics (DT) study section, NIH/NCI
10/2018	Reviewer (ad hoc), Tumor Progression and Metastasis (TPM) study section, NIH/NCI
01/2019	DOD-Breast Cancer Research Program (BCRP) Breakthrough Award

Honors and Awards

1999	Travel Award to AACR annual meeting, MD Anderson Cancer Center
2006	Award for Outstanding Research, Conference on ***Signaling Transduction Modulators in Cancer Therapy***, University of Colorado Cancer Center

07/09, 01/12 Special acknowledgements from the Department of Defense, Congressionally Directed Medical Research Programs (CDMRP)

2012 Award for Outstanding Lecture, 1st International Breast Cancer Symposium & 27th Annual Meeting of Korea Breast Cancer Society, Jeju, Korea

2014-2016 Merrit Award in Recognition of Outstanding Efforts as Co-Director of Cancer Biology Program Scientific Writing Course – Dept. of Pathology, University of Colorado AMC

C. Contribution to Science

1. Since I became an independent investigator in September 2007, the research activity in my laboratory has centered on the unique biology of erbB3 receptor in promotion of erbB2-driven (erbB2+) breast cancer. We have particularly focused on erbB3 signaling-mediated therapeutic resistance in erbB2+ breast cancer cells. A serious of articles published by my laboratory indicate that increased expression/activation of erbB3 results in drug resistance in the treatment of erbB2+ breast cancer. These publications further document that erbB3 receptor functions as the major cause of treatment failure in cancer therapy, thus provide a strong rationale to develop novel approaches targeting of erbB3 to effectively treat breast cancer patients with erbB2+ tumors.
    a. **Liu, B.**, Edgerton, S.M., Yang, X., Ordonez-Ercan, D., Kim, A., Mason, T.L., Alvarez, K.M., McKimmey, C.C., Liu, N., Thor, A.D. Low-dose Dietary Phytoestrogen Abrogates Tamoxifen Associated Mammary Tumor Prevention. ***Cancer Research*** 2005;65(3): 879-86
    b. **Liu, B.***, Ordonez-Ercan, D., Fan, Z., Edgerton, S.M., Yang, X., and Thor, A.D. Down-regulation of erbB3 abrogates erbB2-mediated tamoxifen resistance in breast cancer cells. ***International Journal of Cancer*** 2007;120: 1874-82 *Corresponding author
    c. Huang, X.P., Gao, L., Wang, S., McManaman, J.L., Thor, A.D., Yang, X., Esteva, F.J., and **Liu, B.** Heterotrimerization of the growth factor receptors erbB2, erbB3, and insulin-like growth factor-I receptor in breast cancer cells resistant to Herceptin. ***Cancer Research*** 2010;70(3):1204-14
    d. Wang, S., Huang, X., Lee, C-K., and **Liu, B.** Elevated expression of erbB3 confers paclitaxel resistance in erbB2-overexpressing breast cancer cells via upregulation of Survivin. ***Oncogene*** 2010;29: 4225-36

2. We show that the anti-erbB3 antibody MM-121 is effective to overcome drug resistance and significantly enhance Herceptin- and paclitaxel-induced growth inhibition and/or apoptosis in erbB2+ breast cancer cells. The class I HDAC inhibitor, entinostat selectively induces apoptosis in erbB2+ breast cancer cells via downregulation of erbB3. Mechanistic studies reveal that entinostat elicits a profound effect on suppression of erbB3 protein translation via induction of miR-125a, miR-125b, and miR-205. Our data not only identify a novel epigenetic strategy targeting of erbB3 to enhance erbB2-targeted therapy, they also provide a strong rationale for a recently initiated clinical trial determining the activity of entinostat combined with lapatinib in breast cancer patients that are erbB2+ and progressed on Herceptin.
    a. Huang, X.P., Gao, L., Wang, S., Lee, C-K, Ordentlich, P., and **Liu, B.** HDAC inhibitor SNDX-275 induces apoptosis in erbB2-overexpressing breast cancer cells via downregulation of erbB3 expression. ***Cancer Research*** 2009; 69(21):8403-8411
    b. Wang, S., Huang, J., Lyu, H., Cai, B., Yang, X., Li, F., Tan, J., Edgerton, S.M., Thor, A.D., Lee, C-K., and **Liu, B.** Therapeutic targeting of erbB3 with MM-121/SAR256212 enhances antitumor activity of paclitaxel against erbB2-overexpressing breast cancer. ***Breast Cancer Research*** 2013, **15**:R101; doi:10.1186/bcr3563
    c. Huang, J., Wang, S., Lyu, H., Cai, B., Yang, X., Wang, J., and **Liu, B.** The anti-erbB3 antibody MM-121/SAR256212 in combination with trastuzumab exerts potent antitumor activity against trastuzumab-resistant breast cancer cells. ***Molecular Cancer*** 2013; 12:134
    d. Lyu, H., Huang, J., He, Z., and **Liu, B.** Targeting of HER3 with functional cooperative miRNAs enhances therapeutic activity in HER2-overexpressing breast cancer cells. ***Biological Procedures Online*** 2018; 20:16

3. With a team of collaborators, I directly documented that metformin, the most commonly used drug in type II diabetes, exhibited antitumor activity against breast cancer. We discovered that metformin potently induced apoptosis in triple-negative breast cancer (TNBC) cells. This unique activity of metformin against TNBC drew a lot of attention in breast cancer research. Dr. M-C Hung at MD Anderson Cancer Center commented on our findings, which was published as News & Views in ***Cell Cycle***. We further showed that metformin exerted more profound inhibitory effects on Herceptin-resistant breast cancer cells. We believe that metformin is particularly efficacious in the treatment of TNBCs and erbB2+ breast cancers that are resistant to Herceptin. Our ongoing collaborative effort with Dr. Thor's laboratory is to elucidate the mechanism through which metformin selectively promotes TNBC cells undergoing apoptosis.
    a. Alimova, I.N., **Liu, B.**, Fan, Z., Edgerton, S.M., Dillon, T., Lind, S.E., and Thor, A.D. Metformin inhibits breast cancer cell growth, colony formation and induces cell cycle arrest *in vitro.* ***Cell Cycle*** 2009;8: 909-15
    b. **Liu, B.**, Fan, Z., Alimova, I.N., Edgerton, S.M., and Thor, A.D. Metformin induces unique biological and molecular responses in triple negative breast cancer cells. ***Cell Cycle*** 2009;8: 2031-40
    c. **Liu, B.,*** Fan, Z., Edgerton, S.M., Yang, X., Lind, S.E., and Thor, A.D.***** Potent anti-proliferative effects of metformin on trastuzumab-resistant breast cancer cells via inhibition of erbB2/IGF-1 receptor interactions. ***Cell Cycle*** 2011;10 (17): 2959-66 *Corresponding authors
    d. Lyu, H., Yang, X., Edgerton, S.E., Thor, A.D., Wu, X., He, Z., and **Liu, B.** The erbB3- and IGF-1 receptor-initiated signaling pathways exhibit distinct effects on lapatinib sensitivity against trastuzumab-resistant breast cancer cells. ***Oncotarget*** 2016;7(3): 2921-2935
4. In collaboration with others, I have also studied the antitumor activity of entinostat in multiple myeloma (MM) and the therapeutic potential of Survivin inhibition in acute myeloid leukemia (AML). Entinostat synergistically enhances melphalan-induced DNA damage responses and apoptosis in MM cells; and cladribine, a well-known purine nucleoside analog, exhibits therapeutic potential against MM. Our data suggest that epigenetic approach or targeting of Survivin is a novel strategy to enhance therapeutic efficacy against MM or AML, respectively. Our findings contributed to a patent application "Treatment of multiple myeloma", in which I am a co-Inventor.
    a. Lee, C-K., Wang, S., Huang, X., Ryder, J., and **Liu, B.** HDAC Inhibition Synergistically Enhances Alkylator-induced DNA Damage Responses and Apoptosis in Multiple Myeloma Cells. ***Cancer Letters*** 2010;296: 233-40
    b. Huang, J., Lyu, H., Wang, J., and **Liu, B.** MicroRNA regulation and therapeutic targeting of Survivin in cancer. ***American Journal of Cancer Research*** 2015;5(1):20-31.
    c. Huang, J., Lyu, H., Wang, J., and **Liu, B.** Influence of survivin-targeted therapy on chemosensitivity in the treatment of acute myeloid leukemia. ***Cancer Letters*** 2015;366:160-72
    d. Wang, B., Lyu, H., Pei, S., Song, D., Ni, J., and **Liu, B.** Cladribine in combination with entinostat synergistically elicits anti-proliferative/anti-survival effects on multiple myeloma cells. ***Cell Cycle*** 2018; 17:985-996

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/bolin.liu.1/bibliography/47189926/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

1 R01 CA201011 (Liu) 09/01/2016-08/31/2021
NIH/NCI
ErbB3-miRNA axis in tumor metastasis of erbB2-positive breast cancer
The goal of this project is to define miR-203 and miR-542-3p as the key mediators of erbB3 signaling to enhance metastatic potential of erbB2+ breast cancer cells by upregulating the EMT markers; and

identify novel strategy/agents inhibiting erbB3 to prevent or attenuate erbB2+ breast cancer metastasis.
Role: PI

Completed Research Support (in the last 3 years)

25A3253
Mainline Bioscience LLC (Liu) 12/18/2015-12/31/2018
Development of peptide CXCR4-antagonist for cancer treatment
The goal of this project is to identify the peptide antagonists of CXCR4 with therapeutic potential against triple negative breast cancer (TNBC) and non-small cell lung cancer (NSCLC).
Role: PI

1R03CA181918-01 (Liu) 02/12/2014-01/31/2016
NIH/NCI
Survivin-targeting miRNAs in erbB3 promotion of erbB2-positive breast cancer
The major goal of this project is to elucidate the molecular basis of erbB3/PI-3K/Akt signaling-dependent upregulation of Survivin, and to determine the antitumor activity of miR-542-3p-replacement therapy in combination with chemotherapy against erbB2+ breast cancer.
Role: PI

ELSA U. PARDEE FOUNDATION (Liu) 10/01/2013-12/31/2015
The erbB3-targeting miRNAs in breast cancer chemotherapy
The goal of this project is to determine whether targeting of erbB3 with the two miRNA-cluster will significantly potentiate the antitumor activity of paclitaxel against erbB2+ breast cancer *in vitro* and *in vivo*.
Role: PI

The AEF Bridge Funding (Liu) 01/01/2012-03/31/2015
University of Colorado Denver School of Medicine
Mechanism of ErbB3 signaling in therapeutic resistance of cancer treatment
This bridge fund provides necessary support to elucidate the molecular mechanism of erbB3 signaling-mediated drug resistance in cancer treatment.
Role: PI

The Front Range Ride Award (Liu) 03/01/2013-02/28/2015
University of Colorado Cancer Center
ErbB3 upregulation of Survivin in erbB2 positive breast cancer
The goal of this project is explore the molecular mechanism of erbB2/erbB3 signaling-induced upregulation of Survivin, and define the efficacy of MM-121 in overcoming paclitaxel resistance against erbB2+ breast cancer.
Role: PI