BIOGRAPHICAL SKETCH

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NAME: Ryu, Byungwoo

eRA COMMONS USER NAME (credential, e.g., agency login): bryu01

POSITION TITLE: Associate Scientist

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
Chonbuk National University, Republic of Korea	B.S.	03/1988	Chemistry
Oregon State University, Corvallis, OR	Ph.D.	05/1997	Biochemistry & Toxicology
National Cancer Institute, Bethesda, MD	Postdoctoral	07/1999	Molecular Biology
Johns Hopkins University, Baltimore, MD	Postdoctoral	09/2003	Cancer Biology

A. Personal Statement

My research experiences include biochemical analysis of chromatin modification associated with gene transcriptional activation and repression. I am also experienced in cancer biology by having studied genetic/epigenetic changes and gene expression profiles of pancreatic cancer and melanoma to detect and characterize cancer associated signaling pathways and biomarkers. My research interest is clinically relevant basic cancer research focused on molecular mechanisms of cancer metastasis and therapeutic/prophylactic strategy development.

The goal of this proposed study is to determine a chromatin repressive complex CoREST as a therapeutic target for melanoma and define molecular mechanisms. One of our collaborators, Dr. Philip Cole at the Johns Hopkins School of Medicine, has been developed a dual function small molecule inhibitor of CoREST complex, named as corin2 showing broad range of antitumor effect in NCI 60 cancer cell line screening. We will determine therapeutic efficacy of the compound *in vivo* and define mode of action mechanisms. To accomplish this goal, we will use chemical genetics approaches, melanoma animal model, and clinical tissue specimens to confirm that that the therapeutic strategy epigenetically targeting CoREST is relevant in human cancer.

For this exciting translational research proposal, I have formed a team devoted to this project with Dr. Philip Cole, a well-known medicinal chemist who synthesized the corin2 and its analogs and with Dr. Rhoda Alani, a clinician scientist and expert in cutaneous oncology and biomarker discovery. As a PI of this proposed project, I am fully aware the importance in the development of a realistic research plan, time line, budget, and frequent communications with our collaborators for successful outcomes of the proposed project. I have a research credential demonstrating that my expertise in cancer research focused on basic mechanism of malignant melanoma progression and biomarker discovery. I will be an effective PI for this very exciting project trying to address an unmet clinical demand, epigenetic anti-cancer drug development for durable clinical benefit.

B. Positions and Honors

Positions and Employment

2003-2007 Research Associate, Johns Hopkins University, Baltimore, MD
2007-2009 Instructor, Johns Hopkins University, Baltimore, MD

2009-2011 Assistant Professor, Nevada Cancer Institute, Las Vegas, NV
2011-2018 Assistant Professor, Boston University, Boston, MA
2018-present Associate Scientist, Hackensack University Medical Center, Hackensack, NJ
Associate Member, Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC

Professional Membership

1995-1997 Member, Society of Toxicology
2004-present Member, Society of Melanoma Research
2007-present Member, American Association of Cancer Research
2012-present Member, Society of Investigative Dermatology

Award

2014 Center for Nanoscience and Nanotechnology (CNN) Pilot Grant Award, Boston University
2010 ACS-IRG Pilot Research Grant Award, American Cancer Society
2006 The Howard Temin Award (K01), National Cancer Institute, National Institutes of Health

C. Contributions to Science

Molecular signatures and biomarker discovery for melanoma: Current practice in prognostic evaluation of melanoma largely relies on macroscopic histopathological features of affected lesions and immunohistochemical (IHC) analysis of tissue samples. These prognostic methods should be improved in terms of accuracy and easiness to use in clinical settings for patient classification and personalized treatment. I have been using gene expression profile analysis to discover molecular signatures associated with malignant melanoma progression and use them for the discovery of prognostic biomarkers for melanoma.

1. Eisenstein A, Panova IP, Chung HJ, Goldberg LJ, Zhang Q, Lazova R, Bhawan J, Busam KJ, Symanowski JT, Alani RM, **Ryu B**. Quantitative Assessment of Neuropilin-2 as a Simple and Sensitive Assay for Spitzoid Melanocytic Lesions. Melanoma Res., 2018 Feb;28(1):71-75. PMC5805139
2. Rossi M, Tuck J, Kim OJ, Panova I, Symanowski JT, Mahalingam M, Riker AI, Alani RM, **Ryu B**. Neuropilin-2 Gene Expression Correlates with Malignant Progression in Cutaneous Melanoma. Br J Dermatol. 2014 Aug;171(2):403-8. PMID: 24359286.
3. Kim HE, Symanowski JT, Samlowski EE, Gonzales J, **Ryu B**. Quantitative measurement of circulating lymphoid-specific helicase (HELLS) gene transcript: a potential serum biomarker for melanoma metastasis. Pigment Cell Melanoma Res. 2010 Dec; 23(6):845-8. PMCID: PMC3192016.
4. **Ryu B**, Kim DS, Deluca AM, Alani RM. Comprehensive expression profiling of tumor cell lines identifies molecular signatures of melanoma progression. PLoS One. 2007; 2(7):e594. PMCID: PMC1895889.

Epigenetic modulations of chromatin and gene expression: Aberrant histone modification and DNA methylation patterns are hallmark of cancer. Small molecules targeting those chromatin modulating enzymes and proteins may have therapeutic values for cancer treatment. I have contributed studies illustrating that p300/CBP, a histone acetyltransferase (HAT), could be an effective epigenetic target for malignant melanoma treatment.

5. Kalin JH, Wu M, Gomez AV, Song Y, Das J, Hayward D, Adejola N, Wu M, Panova I, Chung HJ, Kim E, Roberts HJ, Roberts JM, Prusevich P, Jeliazkov JR, Roy Burman SS, Fairall L, Milano C, Eroglu A, Proby CM, Dinkova-Kostova AT, Hancock WW, Gray JJ, Bradner JE, Valente S, Mai A, Anders NM, Rudek MA, Hu Y, **Ryu B**, Schwabe JWR, Mattevi A, Alani RM, Cole PA. Targeting the CoREST Complex with Dual Histone Deacetylase and Demethylase Inhibitors. Nature Commun. 2018 Jan 4;9(1):53. PMCID: PMC5754352
6. Yan G, Eller MS, Elm C, Larocca CA, **Ryu B**, Panova IP, Dancy BM, Bowers EM, Meyers D, Lareau L, Cole PA, Taverna SD, Alani RM. Selective Inhibition of p300 HAT Blocks Cell Cycle Progression, Induces Cellular Senescence, and Inhibits the DNA Damage Response in Melanoma Cells. J Invest Dermatol. 2013 Oct; 133(10):2444-52. PMCID: PMC4380234.
7. **Ryu B**, Fletcher TM, Baumann CT, Warren BS, Fragoso G, John S, Hager GL. Structure and dynamic properties of a glucocorticoid receptor-induced chromatin transition. Mol Cell Biol. 2000 Sep; 20(17):6466-75. PMCID: PMC86121.

8. Su GH, Sohn TA, **Ryu B**, Kern SE. A novel histone deacetylase inhibitor identified by high-throughput transcriptional screening of a compound library. Cancer Res 2000 Jun 15; 60(12): 3137-42. PMID: 10866300.

Stromal-tumor interaction and invasive cancer development: It is known that tumor microenvironment plays significant roles in malignant tumor growth, metastasis, and drug resistance to targeted therapy. I discovered gene signatures induced by stromal-tumor interaction and molecular pathways associated with invasive cancer development and therapy resistance in pancreatic adenocarcinoma and melanoma.

9. Hwang S, Kim HE, Min M, Raghunathan R, Panova IP, **Ryu B**. Epigenetic Silencing of SPINT2 Promotes Cancer Cell Motility via HGF-MET Pathway Activation in Melanoma. J Invest Dermatol. 2015 Apr 24. Doi: 10.1038/jid.2015.160. [Epub ahead of print] PMID: 25910030.
10. Stine MJ, Wang CJ, Moriarty WF, **Ryu B**, Cheong R, Westra WH, Levchenko A, Alani RM. Integration of genotypic and phenotypic screening reveals molecular mediators of melanoma-stromal interaction. Cancer Res. 2011 Apr 1; 71(7):2433-44. PMCID: PMC3070809.
11. **Ryu B**, Jones J, Hollingsworth MA, Hruban RH, Kern SE. Invasion-specific genes in malignancy: SAGE comparisons of primary and passaged cancers. *Cancer Res* 2001 Mar 1; 61(5): 1833-8. PMID: 11280733.
12. Iacobuzio-Donahue CA, **Ryu B**, Hruban RH, Kern SE. Exploring the host desmoplastic response to pancreatic carcinoma: gene expression of stromal and neoplastic cells at the site of primary invasion. Am J Pathol. 2002 Jan; 160(1):91-9. PMCID: PMC1867150.

Gene expression profiles of pancreatic cancer: In early years, before the microarray technique was widely available, SAGE (serial Analysis of Gene Expression) was a possible option to look into a real-time snapshot of global gene expression patterns in cancer. I used the SAGE technique to generate gene expression profiles of pancreatic cancer and identified gene signatures and molecular pathways that are associated with malignant pancreatic cancer development.

13. **Ryu B**, Jones J, Blades NJ, Parmigiani G, Hollingsworth MA, Hruban RH, Kern SE. Relationships and differentially expressed genes among pancreatic cancers examined by large-scale serial analysis of gene expression. Cancer Res. 2002 Feb 1; 62(3):819-26. PMID: 11830538.
14. **Ryu B**, Kern SE. The essential similarity of TGF-beta and activin receptor transcriptional responses in cancer cells. Cancer Biol Ther. 2003 Mar-Apr; 2(2):164-70. PMID: 12750556.
15. Iacobuzio-Donahue CA, Maitra A, Olsen M, Lowe AW, van Heek NT, Rosty C, Walter K, Sato N, Parker A, Ashfaq R, Jaffee E, **Ryu B**, Jones J, Eshleman JR, Yeo CJ, Cameron JL, Kern SE, Hruban RH, Brown PO, Goggins M. Exploration of global gene expression patterns in pancreatic adenocarcinoma using cDNA microarrays. Am J Pathol. 2003 Apr; 162(4):1151-62. PMCID: PMC1851213.
16. Argani P, Iacobuzio-Donahue CA, **Ryu B**, Goggins M, Rosty C, Wilentz RE, Murugesan SR, Kaushal M, Leach SD, Jaffee EM, Yeo CJ, Cameron JL, Kern SE, and Hruban RH. Mesothelin is expressed in the vast majority of adenocarcinomas of the pancreas: Identification of new cancer marker by serial analysis of gene expression (SAGE). *Clin Cancer Res* 2001 Dec; 7(12): 3862-8. PMID: 11751476.

Also, please see a full list of my published works as found in a publically available digital database at the http://www.ncbi.nlm.nih.gov/sites/myncbi/byungwoo.ryu.1/bibliography/41156426/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIH, NCI, 1R01CA212639-01A1 Ryu (PI) 9/1/17-8/31/22
Targeting Transcriptional Co-repressor CoREST Complex in Melanoma
Project goal is to evaluate functional roles of CoREST complex in tumor development and determine therapeutic efficacy of Corin, a small molecule dual-action inhibitor of CoREST, to overcome melanoma targeted therapy.

Completed Research Support:

V Foundation Feinberg and Cole, (Multi-PI)/ Ryu (Co-investigator) 10/1/14-9/30/17
Translational Research Grant
Epigenetic Detection and Chemoprevention of Skin Cancer

The goal of this research is to evaluate a novel small molecule compound inhibiting histone modification complex CoREST in an animal model.

LabCorp, Inc. Industry Sponsored Research Ryu (PI) 7/1/14-9/31/15
Novel Biomarkers for Melanoma
These studies seek to evaluate the utility of genes associated with melanoma tumor microenvironmental crosstalk as biomarkers for melanoma.