BIOGRAPHICAL SKETCH

NAME: Bi-Dar Wang, Ph.D.

eRA COMMONS USER NAME: BWANGP

POSITION TITLE: Assistant Professor, Department of Pharmaceutical Sciences

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
National Taiwan University	B.S.	06/1992	Biology & Chemistry
National Taiwan University	M.S.	06/1994	Microbiology
National Taiwan University	Ph.D.	06/1997	Microbiology
Academia Sinica, Taiwan	Postdoctoral	07/1999-01/2002	Molecular Biology
National Institutes of Health	Visiting Fellow	02/2002-06/2006	Chromatin & Genome Biology

A. Personal Statement

Wang has extensive experiences (15 years) in the fields of functional genomics, molecular and cellular biology, biochemistry and bioinformatics. His research interests have been focusing on identification of genetic alterations and elucidation of molecular mechanism underlying cancer development and progression. Functional genomics, molecular and cellular biology approaches were employed in my previous studies to understand the molecular mechanism associated with cancer pathogenesis in *in-vitro* and *in-vivo* model systems.

In this proposed research project, Wang and colleagues plan to integrate genomics, molecular and cellular approaches to study the molecular mechanism of differential mRNA splicing in prostate cancers (PCa) derived from African American (AA) and European American (EA) patients. In the past years, Wang's research group applied a systems biology approach, combining the array-based analysis (exon, microRNA and SNP arrays), transcription factor mapping, microRNA-mRNA pairing and significant pathway analyses to identify the genome-wide genetic alterations and oncogenic pathways underlying the PCa disparities. In this proposed study, he hypothesized that the AA-specific/enriched splice variants of oncogenes and tumor suppressor genes play critical functional roles in promoting the PCa aggressiveness in AA population. Wang and colleagues aim to investigate the molecular basis of RNA splicing machinery (splicing factors and upstream microRNA regulation) in mRNA splice switching and aim to develop potential precision biomarkers and therapeutic targets in aggressive PCa.

The current proposal is logically built on Wang's prior research works in PCa disparities, cancer genomics/epigenetics and microRNA regulation in cancers. The strong leadership and environmental commitments at University of Maryland Eastern Shore (UMES) School of Pharmacy and the supporting collaborations (in the fields of cancer disparities, cancer genomics and epigenomics, RNA splicing, cancer diagnosis/pathogenesis from colleagues (at George Washington U, Georgetown U, Howard U, USDA, CPDR and NIH) will further ensure the success of this proposed project.

1. Wang, B.-D., Ceniccola, K., Hwang, S., Andrawis, R.,Horvath, A., Freeman, J.A., Knapp, S., Ching, T., Garmire, L., Patel, V., Garcia-Blanco, M.A., S.R., and Lee, N.H. (2016) Aberrant Alternative Splicing in African American Prostate Cancer: novel driver of tumor aggressiveness and drug resistance. ***Nature Communications*** (*In Press*).
2. Wang, B.-D., Yang, Q., Ceniccola, K., Bianco, F., Andrawis, R., Jarrett, T., Frazier, H., Patierno, S.R., and Lee, N.H. (2013) Androgen Receptor-Target Genes in African American Prostate Cancer Disparities. ***Prostate Cancer***. Article ID: 763569.

3. Wang, B.-D., Ceniccola, K., Yang, Q., Andrawis, R., Patel, V., Ji, Y., Rhim, J., Olender, J., Popratiloff, A., Latham, P., Patierno, S.R., and Lee, N.H. (2015) Identification and Functional Validation of Reciprocal microRNA-mRNA Pairings in African American Prostate Cancer Disparities. ***Clinical Cancer Res.*** 21:4970-4984 (highlighted by *Nature Rev. Urology,* 2015,12: 419).
4. Wang, B.-D., Kline, C.L., Pastor, D.M., Olson, T.L., Walsh, E., Frank, B., Luu, T., Sharma, A.K., Robertson, G., Weirauch, M.T., Patierno, S.R., Stuart, J.M., Irby, R.B., Lee, N.H. (2010) Prostate apoptosis response protein 4 sensitizes human colon cancer cells to chemotherapeutic 5-FU through mediation of an NFκB and microRNA network. ***Mol. Cancer*** 9:98

B. Positions and Honors

Positions and Employment

1993, 1995	*Teaching Assistant*, Microbiology/Electron Microscopy, National Taiwan University
1995.7	*Visiting Pre-doctoral Fellow*, Purdue University, West Lafayette, IN
1997.7-1999.5	*Science & Technology Officer, Second Lieutenant* (military service), Taiwan
1999.6-2002.1	*Postdoctoral Fellow*, Institute of Molecular Biology, Academia Sinica, Taiwan.
2002.2-2006.6	*Visiting Fellow*, NIH/NICHD, National Institutes of Health, Bethesda, MD
2006.7-2009.11	*Senior Research Scientist*, Department of Biochemistry & Molecular Biology, the GW Cancer Institute, GWUMC, Washington, DC.
2013.1	*Guest Lecturer*, Neuropharmacology and Medicinal Chemistry Module, School of Pharmacy, University of Maryland Eastern Shore, MD
2009.12-2016.1	*Assistant Research Professor*, Department of Pharmacology & Physiology, The George Washington University Medical Center, Washington, DC.
2016.2-current	*Adjunct Assistant Professor,* Department of Pharmacology & Physiology, The George Washington University Medical Center, Washington, DC
2016.2-current	*Assistant Professor,* Department of Pharmaceutical Sciences, School of Pharmacy, University of Maryland Eastern Shore (UMES), Princess Anne, MD.

Awards/Honors/Committees/Activities

2007-present	*Active Member*, American Association for Cancer Research
2001	*Cooperative Postdoctoral Training Award*, selected by National Science Council (NSC, Taiwan) and MD Anderson Cancer Center (US)
2001	*National Research Grant Recipient in Genomic Medicine*, NSC, Taiwan
2002-2006	*NIH Visiting Fellowship Award*, National Institutes of Health, MD
2006	*NIH Fellows Award for Research Excellent (FARE)*, NIH
2014.11-present	*Editorial Board*, Journal of Addiction and Neuropharmacology.
2017.2- present	*Editorial Board,* Archives of Natural and Medicinal Chemistry.

C. Contribution to Science

1. **Genomics in prostate cancer disparities**

In recent years, I have been involved in the studies for identifying genetic risk elements associated with PCa disparities in AA and EA men. PCa is the most frequently diagnosed and second most common cause of cancer deaths among American men, and AA men have highest incidence and mortality rates compared to other ethnic groups. By applying gene profiling, computational analysis and genetic/epigenetic approaches, we have demonstrated that microRNA-mRNA interaction, gene methylation, and differential activation of cancer signaling (e.g. up-regulated AR signaling and EGFR/PI3K/AKT signaling in AA) may associate with the PCa disparities between AAs and EAs. Currently, we are investigating the in-vitro and invivo functional roles of the population-specific splice variants in the AA and EA PCa cell lines, and in PCa xenograft and metastasis mouse models.

a. Wang, B.-D., Ceniccola, K., Hwang, S., Andrawis, R.,Horvath, A., Freeman, J.A., Knapp, S>, Ching, T., Garmire, L., Patel, V., Garcia-Blanco, M.A., S.R., and Lee, N.H. (2016) Aberrant Alternative Splicing in African American Prostate Cancer: novel driver of tumor aggressiveness and drug resistance. ***Nature Communications*** (*In Press*).
b. Wang, B.-D., Ceniccola, K., Yang, Q., Andrawis, R., Patel, V., Ji, Y., Rhim, J., Olender, J., Popratiloff, A., Latham, P., Patierno, S.R., and Lee, N.H. (2015) Identification and Functional Validation of Reciprocal microRNA-mRNA Pairings in African American Prostate Cancer Disparities. ***Clinical Cancer Res.*** 21:4970-4984.
c. Wang, B.-D., Yang, Q., Ceniccola, K., Bianco, F., Andrawis, R., Jarrett, T., Frazier, H., Patierno, S.R., and Lee, N.H. (2013) Androgen Receptor-Target Genes in African American Prostate Cancer Disparities. ***Prostate Cancer***. Article ID: 763569.
d. Devaney, J.M., Wang, S., Furbert-Harris, P., Apprey, V., Ittmann, M, Wang, B.-D., Olender, J., Lee, N. H., Kwabi-Addo, B. (2015) Genome-wide differentially methylated genes in prostate cancer tissues from African-American and Caucasian men. ***Epigenetics*** 10:319-28.
e. Kwabi-Addo, B., Wang, S., Chung, W., Jelinek, J., Issa, J.-P., Lee, N.H., Patierno, S., Wang, B.-D., Ittmann, M. (2010) Identification of differentially methylated genes in normal prostate tissues from African American and Caucasian Men. ***Clinical Cancer Res****.* 16:3539-3547.

2. ***In-vitro*** **and** ***in-vivo*** **functional study of novel signaling proteins in tumors**

By applying genomics, molecular/cellular biology and biochemistry approaches, I have involved in the studies for identification of novel tumor suppressor genes/oncogenes and oncogenic activation in cell lines and in animal models. The finding included the identification of PAR-4/NFkB/miRNA signaling in colon cancer, Id2-TGFβ crosstalk in neuroblastoma, novel tumor suppressor glucagon receptor in HCC, and Na^+-channel activated MAPK signaling in colon cancer. The following studies were initiated in our lab or reflected the collaboration based on my genomics/bioinformatics/biochemistry expertise.

a. Wang, B.-D., Kline, C.L., Pastor, D.M., Olson, T.L., Walsh, E., Frank, B., Luu, T., Sharma, A.K., Robertson, G., Weirauch, M.T., Patierno, S.R., Stuart, J.M., Irby, R.B., Lee, N.H. (2010) Prostate apoptosis response protein 4 sensitizes human colon cancer cells to chemotherapeutic 5-FU through mediation of an NFκB and microRNA network. ***Mol. Cancer*** 9:98.
b. House, C.D., Wang, B.D., Cennicola, K., Williams, R.,Olender, J., Patel, V., Gutkind, J.S., Hales, T., Lee, N.H. (2015) Voltage-gated Na^+ Channel Activity Increases Colon Cancer Transcriptional Activity and Invasion Via Persistent MAPK Signaling. ***Scientific Reports*** 5:11541.
c. Chakrabarti, L., Wang, B.-D., Lee, N.H., and Sandler A.D. (2013). A mechanism linking Id2-TGFβ crosstalk to reversible adaptive plasticity in neuroblastoma. ***PLOS ONE*** 8(12):e83521.

3. **Functional identification of deregulated microRNA in cancers and other diseases**

MiRNAs are small regulatory RNAs of ~21-25 nucleotides in length that complementarily target mRNAs to inhibit translation and/or promote mRNA degradation, and dysfunction of microRNAs have been implicated in the pathogenesis in diseases such as cancers, neurological disorders and other diseases. By applying microRNA array analysis and computational analyses, we have identified differentially expressed microRNAs in human prostate cancer, colon cancer and neurological disorder. The functional roles of these deregulated microRNAs were validated in cell lines and/or animal models for understanding their functional roles in diseases. The following studies reflected the original finding in our lab or collaborations based on my expertise in functional microRNA genomics.

a. Wang, B.-D., Kline, C.L., Pastor, D.M., Olson, T.L., Walsh, E., Frank, B., Luu, T., Sharma, A.K., Robertson, G., Weirauch, M.T., Patierno, S.R., Stuart, J.M., Irby, R.B., Lee, N.H. (2010) Prostate apoptosis response protein 4 sensitizes human colon cancer cells to

chemotherapeutic 5-FU through mediation of an NFκB and microRNA network. ***Mol. Cancer*** 9:98

b. Wang, B.-D., Ceniccola, K., Yang, Q., Andrawis, R., Patel, V., Ji, Y., Rhim, J., Olender, J., Popratiloff, A., Latham, P., Patierno, S.R., and Lee, N.H. (2015) Identification and Functional Validation of Reciprocal microRNA-mRNA Pairings in African American Prostate Cancer Disparities. ***Clinical Cancer Res.*** 21:4970-4984.
c. Tapocik, J.D., Luu, T.V., Mayo, C.L., Wang, B.-D., Doyle, E., Lee, A.D., Lee, N.H., and Elmer, G.I. (2012) Neuroplasticity, axonal guidance, and microRNA genes are associated with morphine self-administration behavior. ***Addiction Biol.*** 18(3):480-495.
d. Wang, Z., Ceniccola, K., Florea, L., Wang, B.-D., Lee, N.H., Kumar, A. (2015) Viral non-coding RNA inhibits HNF4α expression in HCV associated hepatocellular carcinoma. ***Infect Agent Cancer*** 10:19.
e. Tapocik, J.D., Ceniccola, K., Mayo, C.L., Schwandt, M.L., Solomon, M., Wang, B.-D., Luu, T.V., Olender J., Harrigan T., Maynard, T.M., Elmer, G.I. and Lee, N.H. (2016) MicroRNAs Are Involved in the Development of Morphine-Induced Analgesic Tolerance and Regulate Functionally Relevant Changes in Serpini1. ***Front. Mol. Neurosci.*** 9:20. doi: 10.3389/fnmol.2016.00020

4. **Chromosome structure and function in cell cycle control**

Accumulating evidences suggested that dysfunction of chromosome structures/functions are involved in the development of human diseases, including cancers. Mutations of chromosome organizers, condensin and cohesin, have been implicated in different types of cancers. Previously, I have applied genetic screening, functional genomics, molecular and cellular biology approaches to elucidate the molecular links between condensin and chromosome dynamics (including chromosome transcription, replication and segregation). The following studies were achieved based on my expertise in chromatin biology, epigenetics and functional genomics.

a. Wang, B.-D.**,** Eyre D., Lichten, M., Basrai, M. and Strunnikov, A.V. (2005). Condensin binds distinct and specific chromosomal sites in the *S. cerevisiae* genome. ***Mol. Cell. Biol.*** 25:7216-7225. PMCID: PMC1190225
b. Wang, B.-D., Yong-Gonzalez, V. and Strunnikov, A.V. (2004) Cdc14p/FEAR pathway controls segregation of nucleolus in *S. cerevisiae* by facilitating condensin targeting to rDNA chromatin in anaphase. ***Cell Cycle*** 3: 960-967 (*Cover Image*). PMCID: PMC2673102
c. Wang, B.-D.**,** Butylin P., and Strunnikov, A. V. (2006). Condensin function in mitotic nucleolar segregation is regulated by rDNA transcription. ***Cell Cycle*** 5:2260-2267. PMCID: PMC3225123
d. Wang, B.-D., Butylin, P., and Strunnikov, A.V. (2008). Transcriptional homogenization of rDNA repeats in the episome-based nucleolus induces genome-wide changes in the chromosomal distribution of condensin. ***Plasmid*** 59:45-53. PMCID: PMC2366798

5. **Mitochondrial dysfunctions in cancers and neurological diseases**

Dysfunction of mitochondria has been implicated in diseases such as cancer, neurological disorders, obesity, diabetes and aging. Previously, we have applied mitochondrial-focused microarrays to investigate mitochondria-associated gene expression profiles in diseases. Our analyses led to the identification of deregulated anti-apoptotic genes, neuron function and survival genes in cancers and neurological disorder such as PTSD. The following studies were initiated at GW and reflected my expertise in mitochondrial genomic and identification of molecular targets in cancers.

a. Zhang, Q., Wu, J., Nguyen, A., Wang, B.-D.**,** He, P., Rennert, O. M., and Su, Y. A. (2008) Molecular mechanisms of differential apoptosis between human melanoma cell lines

UACC903 and UACC903(+6) revealed by mitochondria-focused cDNA microarrays. ***Apoptosis*** 13:993-1004.

b. Su, Y. A., Wu, J., Zhang, Q., Zhang, L., Su, M. D., He, P., Wang, B.-D., Lee, H., Webster, M. J., Traumatic Stress Brain Study Group, Rennert, O. M., Ursano, R. J. (2008). Dysregulated mitochondrial genes and networks with drug targets in postmortem brain of patients with posttraumatic stress disorder (PTSD) revealed by human mitochondria-focused cDNA microarrays. ***Int. J. Biol. Sci.*** 4:223-235.
c. Wang, B.-D.**,** Rennert, O.M., and Su, Y.A. (2008) Mitochondrial oxidative phosphorylation, obesity and diabetes. ***Cell Science Reviews*** 4:57-81.
d. Zhang, Q, Chen Y., Wang, B.-D.**,** He, P., and Su, Y.A. (2007) Differences in Apoptosis and Cell Cycle Distribution between Human Melanoma Cell Lines UACC903 and UACC903(+6), before and after UV Irradiation. ***Int. J. Biol. Sci.*** 3:342-348.

List of Selected Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1t_3dtp6OmE5V/bibliography/46169228/public/?sort=date&direction=descending

D. Research Support

Ongoing Research Support

PC121975 DOD CDMRP PCRP Lee (PI)
Differential splicing of oncogenes and tumor suppressor genes in African and Caucasian American populations: contributing factor in prostate cancer disparities.
The goal of this project is to clone and functionally characterize the population-specific splice variants of oncogenes and tumor suppressor genes in African and Caucasian American prostate cancer specimens. *In vitro* molecular techniques and *in vivo* xenograft and metastasis mouse models have been employed to study the functional roles of population/race-specific splice variants in PCa aggressiveness.
Role: **Co-Investigator**

NCI R01 CA204806-01A1 Lee (PI)
Consequences and Mechanism of aberrant splicing in African American prostate cancer disparities.
The goal of this study is to investigate the functional impacts of the alternative splice variants in AA and EA PCa patients. Short splice variants of *PIK3CD* and *FGFR3*, overexpressed in AA PCa, have been shown to contribute to the aggressive cancer phenotypes in *in-vitro* and *in-vivo* PCa models. We aim to provide a mechanistic framework of population-associated splicing factors, differential mRNA splicing and PCa phenotypes in AA and EA populations.
Role: **Sub-Award PI**

DoD W81XWH-14-1-0569 Patierno (PI)
Validation and Interrogation of Differentially Expressed and Alternatively Spliced Genes in African-American Prostate Cancer.
This study aims to understand the molecular mechanisms underlying the more aggressive prostate cancer biology in African American men. We are performing experiments to elucidate the relationship of genetic/epigenetic and post-transcriptional factors with prostate cancer disparities between AA and EA patients. Novel splice switching oligonucleotides (SSOs) will be used to correct the aberrant splicing leading to AR-V7 and to inhibit EGFR isoforms.
Role: **Co-Investigator**

Completed Research Support

CTSI-CN Rapid Response Funding Solicitation Lee (Lead PI)

CTSI-Children's National Medical Center (CTSI-CN)
Differences in Splicing of Oncogenes and Tumor Suppressor Genes between African and Caucasian Americans.
The goal of this study is to employ RNA-seq technology to identify differential splicing patterns of selected oncogenes/tumor suppressive genes in PCa specimens from AA and EA patients.
Role: **Co-PI**

IRG-08-091-01 Wang (PI)
American Cancer Society Institutional Research Grant for Junior Faculty
Genomic analysis of biological pathways associated with cancer health disparities.
The goal of this study is to compare the mRNA and microRNA expression profile, alternative splicing patterns and CNVs between AA and EA PCa patients.
Role: **PI**

NCI U01 CA116937
DC city-wide patient navigation research program (supplement) Patierno (PI)
The goal of this project is to utilize genomic and molecular biology approaches to identify the aberrant genetic elements associated with PCa disparities in AA and EA populations. Affymetrix exon and SNP arrays were applied to identify the gene expression, splice variations, SNPs, and CNVs in the two populations.
Role: **Co-Investigator**