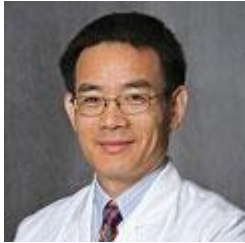


Meharry Cancer Summer Research Program

Mentor Project Descriptions/Research Project Areas

A. Basic/Translational Research



Zhenbang Chen, Ph.D.

The research in Dr. Zhenbang Chen's laboratory focuses on dysregulated signaling pathways in prostate cancer. His group has published several important discoveries on SKP2, androgen receptor (AR), ARF and MET essential oncogenic signaling in prostate cancer. Students in his laboratory will use cultured cells and animal models to explore molecular signaling pathways that influence prostate cancer growth and progression.

Recent Publications:

1: Cunningham D, Zhang Q, Liu S, Parajuli KR, Nie Q, Ma L, Zhang A, Chen Z, You Z. Interleukin-17 promotes metastasis in an immunocompetent orthotopic mouse of prostate cancer. *Am J Clin Exp Urol*. 2018 Jun 15;6(3):114-122.

2: Nangami GN, Sakwe AM, Izban MG, Rana T, Lammers PE, Thomas P, Chen Z, Ochieng J. Fetuin-A (alpha 2HS glycoprotein) modulates growth, motility, invasion, and senescence in high-grade astrocytomas. *Cancer Med*. 2016 Dec;5(12):3532-3543.

3: Lu W, Liu S, Li B, Xie Y, Izban MG, Ballard BR, Sathyanarayana SA, Adunyah SE, Matusik RJ, Chen Z. SKP2 loss destabilizes EZH2 by promoting TRAF6-mediated ubiquitination to suppress prostate cancer. *Oncogene*. 2017 Mar;36(10):1364-1373.

4: Xie Y, Lu W, Liu S, Yang Q, Goodwin JS, Sathyanarayana SA, Pratap S, Chen Z. MMP7 interacts with ARF in nucleus to potentiate tumor microenvironments for prostate cancer progression in vivo. *Oncotarget*. 2016 Jul 26;7(30):47609-47619.



Sanford Barsky, M.D.

The research of Dr. Barsky's laboratory is focused in the field of tumor biology and metastasis, particularly on discoveries underlying the mechanisms of metastatic progression of human breast cancer with a focus on inflammatory breast cancer, a disease that affects minorities and a disease with striking health care disparities. Recently the lab observed that inflammatory breast cancer produces lymphovascular emboli that bud into daughter emboli which eventually form micrometastases. Students working in Dr. Barsky's lab would study the molecular mechanisms involved in this phenomenon.

Recent Publications:

1: Modi AP, Nguyen JPT, Wang J, Ahn JS, Libling WA, Klein JM, Mazumder P, Barsky SH. Geometric tumor embolic budding characterizes inflammatory breast cancer. *Breast Cancer Res Treat.* 2023 Feb;197(3):461-478. doi: 10.1007/s10549-022-06819-6. Epub 2022 Dec 6. PMID: 36473978; PMCID: PMC9734724.

2: Nguyen C, Nguyen JPT, Modi AP, Ahmad I, Petrova SC, Ferrell SD Jr, Wilhelm SR, Ye Y, Schae D, Barsky SH. Use of constitutive and inducible oncogene containing iPSCs as surrogates for transgenic mice to study breast oncogenesis. *Stem Cell Res Ther.* 2021 May 27;12(1):301. doi: 10.1186/s13287-021-02285-x. PMID: 34044885; PMCID: PMC8162012.

3: Pandya R, Grace San Diego K, Shabbir T, Modi AP, Wang J, Dhahbi J, Barsky SH. The cell of cancer origin provides the most reliable roadmap to its diagnosis, prognosis (biology) and therapy. *Med Hypotheses.* 2021 Dec; 157:110704. doi: 10.1016/j.mehy.2021.110704. Epub 2021 Oct 13. PMID: 34688214.



Jamaine Davis, Ph.D.

The Davis laboratory uses an interdisciplinary approach (biochemistry/biophysics, bioinformatics, cell and structural biology) to elucidate mechanisms of genomic maintenance and regulation in breast cancer. Their challenge is to understand how genomic and proteomic variations affect health, disease and drug response. To address this, the lab seeks to define how dysregulated

protein-protein interaction networks obtained from bioinformatics (patient data) influence disease. They also model these observations in cell systems to determine the best course of therapy for breast cancer patients. Students working with Dr. Davis and his team will use *in vitro* models of breast cancer to study the structure and function of proteins involved in DNA damage repair.

Recent Publications:

- 1: McIntosh DJ, Walters TS, Arinze IJ, Davis J. Arkadia (RING Finger Protein 111) Mediates Sumoylation-Dependent Stabilization of Nrf2 Through K48-Linked Ubiquitination. *Cell Physiol Biochem*. 2018;46(1):418-430.
- 2: Bhaumik P, Davis J, Tropea JE, Cherry S, Johnson PF, Miller M. Structural insights into interactions of C/EBP transcriptional activators with the Taz2 domain of p300. *Acta Crystallogr D Biol Crystallogr*. 2014 Jul; 70(Pt 7):1914-21.
- 3: Davis J, Wang J, Tropea JE, Zhang D, Dauter Z, Waugh DS, Wlodawer A. Novel fold of VirA, a type III secretion system effector protein from *Shigella flexneri*. *Protein Sci*. 2008 Dec; 17(12):2167-73.
- 4: Uppsten M, Davis J, Rubin H, Uhlin U. Crystal structure of the biologically active form of class Ib ribonucleotide reductase small subunit from *Mycobacterium tuberculosis*. *FEBS Lett*. 2004 Jul 02; 569(1-3):117-22.



Sakina Eltom, D.V.M, Ph.D.

The research in Dr. Eltom's laboratory overlaps molecular aspects of environmental toxicology and chemical carcinogenesis. One area of research explores molecular mechanisms involved in the signaling pathways of the aryl hydrocarbon receptor (AhR) in breast cancer. The second area of research involves the examination of the differential role of environmental chemicals on the etiology of breast cancer in pre-menopausal African American and Caucasian women. The overall objective of this study is to identify biological factors contributing to the ethnic variation in breast cancer and provide mechanistic data on the possible differential role of environmental chemicals on the biology of breast cancer. Students working within the Eltom laboratory will

use cell lines to study the biology of AhR and the effects of environmental chemicals on breast cancer.

Recent Publications:

1: Taha Z, Eltom SE. The Role of Diet and Lifestyle in Women with Breast Cancer: An Update Review of Related Research in the Middle East. *Biores Open Access*. 2018 May 1;7(1):73-80.

2: Ochieng J, Nangami GN, Ogunkua O, Miousse IR, Koturbash I, Odero-Marah V, McCawley LJ, Nangia-Makker P, Ahmed N, Luqmani Y, Chen Z, Papagerakis S, Wolf GT, Dong C, Zhou BP, Brown DG, Colacci AM, Hamid RA, Mondello C, Raju J, Ryan EP, Woodrick J, Scovassi AI, Singh N, Vaccari M, Roy R, Forte S, Memeo L, Salem HK, Amedei A, Al-Temaimi R, Al-Mulla F, Bisson WH, Eltom SE. The impact of low-dose carcinogens and environmental disruptors on tissue invasion and metastasis. *Carcinogenesis*. 2015 Jun;36 Suppl 1:S128-59.

3: Humphrey-Johnson A, Abukalam R, Eltom SE. Stability of the aryl hydrocarbon receptor and its regulated genes in the low activity variant of Hepa-1 cell line. *Toxicol Lett*. 2015 Mar 4;233(2):59-67.

4: Goode G, Pratap S, Eltom SE. Depletion of the aryl hydrocarbon receptor in MDA-MB-231 human breast cancer cells altered the expression of genes in key regulatory pathways of cancer. *PLoS One*. 2014 Jun 16;9(6):e100103.



Dana Marshall, Ph.D.

Dr. Dana Marshall's research focuses on identifying factors that contribute to the disparity in mortality between African-American males and their Caucasian counterparts. Her work includes the acquisition of clinical and demographic information from individuals treated for oral cancer at Nashville General Hospital at Meharry and in the Meharry Oncology Clinics. Patient tissues are evaluated molecularly for HPV as well as for other molecular clues predictive of outcome. She also works with cell lines, characterizing the role of Alpha2-HS glycoprotein (AHS2G) in enhancing metastatic properties of oral squamous cell carcinoma cells while also characterizing isoforms of human AHS2G using mass spectrometry.

Recent Publications:

1: Appah EO, Ballard BR, Izban MG, Jolin C, Lammers PE, Parrish DD Jr, Marshall DR. A rapidly growing human papillomavirus-positive oral tongue squamous cell carcinoma in a 21-year old female: A case report. *Oncol Lett.* 2018 May;15(5):7702-7706.

2: Nangami G, Koumangoye R, Shawn Goodwin J, Sakwe AM, Marshall D, Higginbotham J, Ochieng J. Fetuin-A associates with histones intracellularly and shuttles them to exosomes to promote focal adhesion assembly resulting in rapid adhesion and spreading in breast carcinoma cells. *Exp Cell Res.* 2014 Nov 1;328(2):388-400.

3: Mandape SN, Marshall DR, Dent LL, Pratap S. Draft Genome Sequence of Multidrug-Resistant *Acinetobacter baumannii* Strain MMC4, Isolated from a Patient in Tennessee. *Genome Announc.* 2014 Feb 20;2(1). pii: e00051-14.

4: Thompson PD, Sakwe A, Koumangoye R, Yarbrough WG, Ochieng J, Marshall DR. Alpha-2 Heremans Schmid Glycoprotein (AHSG) modulates signaling pathways in head and neck squamous cell carcinoma cell line SQ20B. *Exp Cell Res.* 2014 Feb 15;321(2):123-32



Smita Misra, Ph.D.

Dr. Misra's research focuses on various aspects of breast carcinogenesis, particularly the gene expression regulation, posttranscriptional regulation of RNA and the molecular mechanisms of breast tumor growth, aggressiveness, progression to invasion and metastasis. The objective of this work is to understand the basis for the progression of breast cancer, with the aim to develop novel biomarkers for the detection and targeted therapies that may be useful in the development of chemotherapy and cure/control/eradication of breast cancer in particular along with other cancers. Students working with Dr. Misra would examine gene expression and RNA regulation within human breast cancer cells.

Recent Publications:

1: Walters TS, McIntosh DJ, Ingram SM, Tillery L, Motley ED, Arinze IJ, Misra S. SUMO-Modification of Human Nrf2 at K¹¹⁰ and K⁵³³ Regulates Its Nucleocytoplasmic Localization, Stability and Transcriptional Activity. *Cell Physiol Biochem*. 2021 Mar 27;55(2):141-159. doi: 10.33594/000000351. PMID: 33770425; PMCID: PMC8279473.

2: Ellison M, Mittal M, Chaudhuri M, Chaudhuri G, Misra S. The role of the redox/miR-6855-3p/PRDX5A axis in reversing SLUG-mediated BRCA2 silencing in breast cancer cells. *Cell Commun Signal*. 2020 Jan 27;18(1):15. doi: 10.1186/s12964-019-0493-5. PMID: 31987042; PMCID: PMC6986021.

3: Bailey CK, Mittal MK, Misra S, Chaudhuri G. High motility of triple-negative breast cancer cells is due to repression of plakoglobin gene by metastasis modulator protein SLUG. *J Biol Chem*. 2012 Jun 1;287(23):19472-86. doi: 10.1074/jbc.M112.345728. Epub 2012 Apr 11. PMID: 22496452; PMCID: PMC3365985.

4: Mittal MK, Singh K, Misra S, Chaudhuri G. SLUG-induced elevation of D1 cyclin in breast cancer cells through the inhibition of its ubiquitination. *J Biol Chem*. 2011 Jan 7;286(1):469-79. doi: 10.1074/jbc.M110.164384. Epub 2010 Nov 2. PMID: 21044962; PMCID: PMC3013006.



Siddharth Pratap, Ph.D.

Dr. Pratap is Director of Bioinformatics and Proteomics at Meharry Medical College. Dr. Pratap has collaborated with program mentors on cancer-focused genomics and proteomics research. He will serve as a co-research mentor for students performing cancer bioinformatics research projects and provide advice on the appropriate bioinformatics tools needed to complete each student's study.

Recent Publications:

1: Olokpa E, Mandape SN, Pratap S, Stewart MV. Metformin regulates multiple signaling pathways within castration-resistant human prostate cancer cells. *BMC Cancer*. 2022 Sep 29;22(1):1025. doi: 10.1186/s12885-022-10115-3. PMID: 36175875; PMCID: PMC9520831.

2: Wiley K, Findley L, Goldrich M, Rakhra-Burris TK, Stevens A, Williams P, Bult CJ, Chisholm R, Deverka P, Ginsburg GS, Green ED, Jarvik G, Mensah GA, Ramos E, Relling MV, Roden DM, Rowley R, Alterovitz G, Aronson S, Bastarache L, Cimino JJ, Crowgey EL, Del Fiol G, Freimuth RR, Hoffman MA, Jeff J, Johnson K, Kawamoto K, Madhavan S, Mendonca EA, Ohno-Machado L, Pratap S, Taylor CO, Ritchie MD, Walton N, Weng C, Zayas-Cabán T, Manolio TA, Williams MS. A research agenda to support the development and implementation of genomics-based clinical informatics tools and resources. *J Am Med Inform Assoc.* 2022 Jul 12;29(8):1342-1349. doi: 10.1093/jamia/ocac057. PMID: 35485600; PMCID: PMC9277642.

3: Beasley HK, Widatalla SE, Whalen DS, Williams SD, Korolkova OY, Namba C, Pratap S, Ochieng J, Sakwe AM. Identification of MAGEC2/CT10 as a High Calcium-Inducible Gene in Triple-Negative Breast Cancer. *Front Endocrinol (Lausanne).* 2022 Mar 10;13:816598. doi: 10.3389/fendo.2022.816598. PMID: 35355564; PMCID: PMC8959981.



Amos Sakwe, Ph.D.

Dr. Sakwe's research focuses on the molecular basis of cancer progression, metastasis and chemoresistance. His laboratory uses molecular and cell biology, and biochemical techniques as well as animal models of breast cancer to study the role of calcium binding and calcium activated proteins in breast cancer progression and metastasis. The laboratory is also interested in drug discovery techniques to identify drugs that attenuate the progression of breast cancer. Students working in the Sawke laboratory will use human cell lines and other *in vitro* models to study breast cancer progression and metastasis.

Recent Publications:

1: Ochieng J, Nangami G, Sakwe A, Rana T, Ingram S, Goodwin JS, Moyo C, Lammers P, Adunyah SE. Extracellular histones are the ligands for the uptake of exosomes and hydroxyapatite-nanoparticles by tumor cells via syndecan-4. *FEBS Lett.* 2018 Oct;592(19):3274-3285.

2: Wang L, Widatalla SE, Whalen DS, Ochieng J, Sakwe AM. Association of calcium sensing receptor polymorphisms at rs1801725 with circulating calcium in breast cancer patients. *BMC Cancer*. 2017 Aug 2;17(1):511.

3: Nangami GN, Sakwe AM, Izban MG, Rana T, Lammers PE, Thomas P, Chen Z, Ochieng J. Fetuin-A (alpha 2HS glycoprotein) modulates growth, motility, invasion, and senescence in high-grade astrocytomas. *Cancer Med*. 2016 Dec;5(12):3532-3543.

4: Koumangoye RB, Nangami GN, Thompson PD, Agboto VK, Ochieng J, Sakwe AM. Reduced annexin A6 expression promotes the degradation of activated epidermal growth factor receptor and sensitizes invasive breast cancer cells to EGFR-targeted tyrosine kinase inhibitors. *Mol Cancer*. 2013 Dec 19;12(1):167.



Anil Shanker, Ph.D.

The central focus of Dr. Anil Shanker's laboratory is to understand the molecular mechanisms of intratumoral functional cross-talk between T lymphocytes and natural killer (NK) cells. They are also invested in dissecting the mechanisms of immunomodulation by the proteasome inhibitor bortezomib, Notch ligands, and neurotransmitters in adoptive T cell/NK cell transfer settings in an effort to optimize lymphocyte effector function for cancer therapy. His laboratory is also interested in identifying common functional immune signatures and specifying Notch and lymphocyte repertoires in racial and ethnic minorities that could correlate with strong anti-tumor responses. Students working in Dr. Shanker's laboratory will use *in vitro* and *in vivo* models of cancer to explore these different aspects of cancer immunology.

Recent Publications:

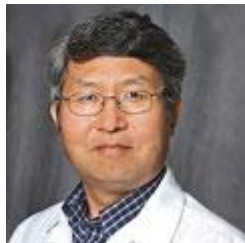
1: Shanker A, Thounaojam MC, Mishra MK, Dikov MM. Innate-Adaptive Immune Crosstalk 2016. *J Immunol Res*. 2017;2017:3503207.

2: Uzhachenko R, Boyd K, Olivares-Villagomez D, Zhu Y, Goodwin JS, Rana T, Shanker A, Tan WJ, Bondar T, Medzhitov R, Ivanova AV. Mitochondrial

proteinFus1/Tusc2 in premature aging and age-related : critical roles of calcium and energy homeostasis. *Aging (Albany NY)*. 2017 Mar 26;9(3):627-649.

3: Pellom ST Jr, Singhal A, Shanker A. Prospects of combining adoptive cell immunotherapy with bortezomib. *Immunotherapy*. 2017 Mar;9(4):305-308.

4: Pellom ST Jr, Dudimah DF, Thounaojam MC, Uzhachenko RV, Singhal A, Richmond A, Shanker A. Bortezomib augments lymphocyte stimulatory cytokine signaling in the tumor microenvironment to sustain CD8+T cell antitumor function. *Oncotarget*. 2017 Jan 31;8(5):8604-8621.



Deok-Soo Son, D.V.M., Ph.D.

The laboratory of Dr. Son examines the role of proinflammatory chemokines on the progression of ovarian cancer and the link between obesity and breast cancer. Students working in this laboratory will have an opportunity to study chemokine networks in models of human ovarian cancer in order to determine which chemokines can be used as biomarkers and therapeutic targets. In a second project, the Son lab has identified a proinflammatory chemokine profile linking obesity and breast cancer. Students working on this project will perform experiments designed to define the roles of obesity-promoted proinflammatory chemokines on the progression of breast cancer.

Recent Publications:

1: Ignacio RMC, Lee ES, Wilson AJ, Beeghly-Fadiel A, Whalen MM, Son DS. Chemokine Network and Overall Survival in TP53 Wild-Type and Mutant Ovarian Cancer. *Immune Netw*. 2018 Aug 13;18(4):e29.

2: Ignacio RMC, Gibbs CR, Lee ES, Son DS. The TGF α -EGFR-Akt signaling axis plays a role in enhancing proinflammatory chemokines in triple-negative breast cancer cells. *Oncotarget*. 2018 Jun 29;9(50):29286-29303.

3: Johnson J Jr, Pajarillo E, Karki P, Kim J, Son DS, Aschner M, Lee E. Valproic acid attenuates manganese-induced reduction in expression of GLT-1 and GLAST with concomitant changes in murine dopaminergic neurotoxicity. *Neurotoxicology*. 2018 Jul;67:112-120.

4: Ignacio RMC, Dong YL, Kabir SM, Choi H, Lee ES, Wilson AJ, Beeghly-Fadiel A, Whalen MM, Son DS. CXCR2 is a negative regulator of p21 in p53-dependent and independent manner via Akt-mediated Mdm2 in ovarian cancer. *Oncotarget*. 2018 Jan 15;9(11):9751-9765.



LaMonica Stewart, Ph.D.

Dr. Stewart's laboratory studies signaling pathways activated by the peroxisome proliferator activated receptor (PPAR γ). Her laboratory also studies interactions between the androgen receptor signaling pathway and PPAR γ in human prostate cancer cells. Students working in Dr. Stewart's laboratory will use human prostate cancer cell lines to explore how PPAR γ agonists and the anti-diabetic drug metformin regulate prostate cancer growth and progression.

Recent Publications:

- 1: Olokpa E, Moss PE, Stewart LV. Crosstalk between the Androgen Receptor and PPAR Gamma Signaling Pathways in the Prostate. *PPAR Res*. 2017; 2017:9456020.
- 2: Olokpa E, Bolden A, Stewart LV. The Androgen Receptor Regulates PPAR γ Expression and Activity in Human Prostate Cancer Cells. *J Cell Physiol*. 2016 Dec;231(12):2664-72.
- 3: Bolden A, Bernard L, Jones D, Akinyeke T, Stewart LV. The PPAR Gamma Agonist Troglitazone Regulates Erk 1/2 Phosphorylation via a PPAR γ -Independent, MEK-Dependent Pathway in Human Prostate Cancer Cells. *PPAR Res*. 2012; 2012:929052.
- 4: Akinyeke TO, Stewart LV. Troglitazone suppresses c-Myc levels in human prostate cancer cells via a PPAR γ -independent mechanism. *Cancer Biol Ther*. 2011 Jun 15; 11(12):1046-58.

B. Clinical/Community-Based Research



Maureen Sanderson, M.P.H., R.D., Ph.D. Dr. Maureen Sanderson has a background in cancer epidemiology, with specific training and expertise in breast cancer, prostate cancer, human papillomavirus (HPV) related cancers, lung cancer, and cancer survivorship. Much of her research has been conducted as community based participatory research. Students who work with Dr. Sanderson will design, conduct, and interpret epidemiologic studies that focus on the causes of and means of preventing cancer.

Recent publications:

- 1: Sanderson M, Aldrich MC, Levine RS, Kilbourne B, Cai Q, Blot WJ. Neighbourhood deprivation and lung cancer risk: a nested case-control study in the USA. *BMJ Open*. 2018 Sep 10;8(9):e021059.
- 2: Patel K, Inman W, Giske J, Johnson O, Brown E, Kanu M, Theriot R, Sanderson M, Hull P, Hargreaves M. A Community-Driven Intervention for Improving Biospecimen Donation in African American Communities. *J Racial Ethn Health Disparities*. 2018 Feb;5(1):15-23.
- 3: Sanderson M, Canedo JR, Khabele D, Fadden MK, Harris C, Beard K, Burrell M, Pinkerton H, Jackson C, Mayo-Gamble T, Hargreaves MK, Hull PC. Pragmatic trial of an intervention to increase human papillomavirus vaccination in safety-net clinics. *BMC Public Health*. 2017 Feb 2;17(1):158.
- 4: Canedo JR, Miller ST, Schlundt D, Fadden MK, Sanderson M. Racial/Ethnic Disparities in Diabetes Quality of Care: the Role of Healthcare Access and Socioeconomic Status. *J Racial Ethn Health Disparities*. 2018 Feb;5(1):7-14.



Flora Ukoli, M.D., M.P.H. The research of Dr. Flora Ukoli focuses on developing culturally appropriate prostate cancer education interventions particularly for low-income and low-education populations that will improve the level of knowledge about prostate cancer and positively impact attitude to early detection. A second area of interest is to investigate dietary exposures that might contribute in some way to the high prostate cancer risk and burden observed in African-Americans. Students working with Dr. Ukoli will have the opportunity to perform community-based participatory research and epidemiological studies to determine the effect of diet and gene-environment interactions on prostate cancer risk.

Recent Publications:

- 1: Williams JR, Yeh VM, Bruce MA, Szetela C, Ukoli F, Wilkins CH, Kripalani S. Precision Medicine: Familiarity, Perceived Health Drivers, and Genetic Testing Considerations Across Health Literacy Levels in a Diverse Sample. *J Genet Couns.* 2018 Aug 13. doi: 10.1007/s10897-018-0291-z. [Epub ahead of print]
- 2: Zhou YE, Buchowski MS, Liu J, Schlundt DG, Ukoli FA, Blot WJ, Hargreaves MK. Plasma Lycopene Is Associated with Pizza and Pasta Consumption in Middle-Aged and Older African American and White Adults in the Southeastern USA in a Cross-Sectional Study. *PLoS One.* 2016 Sep 1;11(9):e0161918.
- 3: Sanderson M, Fowke JH, Lipworth L, Han X, Ukoli F, Coker AL, Blot WJ, Hargreaves MK. Diabetes and prostate cancer screening in black and white men. *Cancer Causes Control.* 2013 Oct;24(10):1893-9.
- 4: Ukoli FA, Patel K, Hargreaves M, Beard K, Moton PJ, Bragg R, Beech D, Davis R. A tailored prostate cancer education intervention for low-income African Americans: impact on knowledge and screening. *J Health Care Poor Underserved.* 2013 Feb;24(1):311-31.