BIOGRAPHICAL SKETCH

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NAME: Zachary Levi Watson

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

POSITION TITLE: Instructor

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
University of North Florida, Jacksonville, FL	BS	07/2006	Biology
University of Florida, Gainesville, FL	PhD	11/2013	HSV-1 Epigenetics
University of Colorado, Aurora, CO	Postdoctoral	12/2016	HPV-Associated Cancer
University of Colorado, Aurora, CO	Postdoctoral	01/2019	Ovarian Cancer

A. Positions and Honors

Positions and Employment

2006-2013 Graduate Student, Molecular Genetics & Microbiology, Gainesville, FL
2014-2016 Postdoctoral Fellow, Immunology & Microbiology, Aurora, CO
2017-2018 Postdoctoral Fellow, Obstetrics & Gynecology, Aurora, CO
2019- Instructor, Obstetrics & Gynecology, Aurora, CO

Other Experience and Professional Membership

2010 BSL3 Science and Safety Course, Emory University, Atlanta, GA
2011-2016 Associate Member, American Society for Virology (ASV)
2018- Associate Member, American Association for Cancer Research (AACR)

Honors

2006-2008 University of Florida Grinter Fellowship
2008-2010 NIH Predoctoral Training Grant – Biodefense & Emerging Infectious Disease
2010 35th Annual Herpesvirus Workshop Travel Award
2011 36th Annual Herpesvirus Workshop Travel Award
2012 NIH Chromatin Control of Viral Infection Travel Award
2014-2016 NIH Postdoctoral Training Grant – Lung Head & Neck Cancer
2018 University of Colorado Postdoctoral Association Travel Award
2018 University of Colorado Cancer Biology Postdoc Symposium – Best Oral Presentation
2019 University of Colorado OB/GYN Research Retreat – Best Faculty Poster

B. Contributions to Science

1. Mortality due to ovarian cancer is mainly due to the growth of metastatic disease, which interferes with the normal function of organs within the peritoneal cavity. There is a significant knowledge gap as to how ovarian cancer cells gain the ability to exfoliate from the fallopian tube, survive in suspension, and metastasize to the peritoneum. To address this gap, I have contributed to several studies of ovarian cancer dissemination and identified epigenetic factors, metabolic adaptations, and autophagy regulators as contributing to anoikis resistance and survival in suspension.

a. *Wheeler LJ, ***Watson ZL**, Qamar L, Yamamoto TM, Sawyer BT, Sullivan KD, Khanal S, Joshi M, Ferchaud-Roucher V, Smith H, Vanderlindent LA, Brubaker SW, Caino CM, Kim H, Espinosa JM, Richer JK, Bitler BG. Multi-omic approaches identify metabolic and autophagy regulators important in ovarian cancer dissemination. *2019. iScience. doi: 10.1016/j.isci.2019.07.049.* ***Co-first authors.***
b. *Wheeler LJ, ***Watson ZL**, Qamar L, Yamamoto TM, Post MD, Berning AA, Spillman MA, Behbakht K, Bitler BG. CBX2 Identified as Driver of Anoikis Escape and Dissemination in High Grade Serous Ovarian Cancer. *2018. Oncogenesis. doi: 10.1038/s41389-018-0103-1.* ***Co-first authors.***

2. The use of Poly ADP-ribose polymerase inhibitors (PARPi) against recurrent ovarian cancer has made a positive impact on clinical outcomes. However, PARPi resistance is a major obstacle to management of this deadly disease. My goal is to examine epigenetic mechanisms of PARPi resistance and to identify novel biomarkers and druggable targets. Using PARPi-resistant cell lines and *in vivo* animal models, I have observed changes in specific histone modifications, as well as upregulation of histone methyltransferases (HMTs) and histone acetyltransferases (HATs). Knockdown of specific HMTs sensitizes PARPi-resistant cells to treatment and ablates DNA damage repair. Future directions include (1) RNA-Seq and ChIP-Seq analyses to identify genes that contribute to resistance, (2) examination of direct roles of HMTs and HATs in DNA damage repair, and (3) combinatorial treatments in animal models of ovarian cancer to eliminate or delay PARPi resistance and promote a more durable anti-tumor response.

a. **Watson ZL**, Yamamoto TM, McMellen A, Kim H, Hughes CJ, Wheeler LJ, Post MD, Behbakht K, Bitler BG. Histone methyltransferases EHMT1 and EHMT2 (GLP/G9A) maintain PARP inhibitor resistance in high grade serous ovarian carcinoma. *2019. Clin Epigenetics. doi: 10.1186/s13148-019-0758-2.*
b. Yamamoto TM, McMellen A, **Watson ZL**, Aguilera J, Ferguson R, Nurmemmedov E, Thakar T, Moldovan GL, Kim H, Cittelly DM, Joglar AM, Brennecke EP, Wilson H, Behbakht K, Sikora MJ, Bitler BG. Activation of Wnt signaling promotes olaparib resistant ovarian cancer. *2019. Mol Carcinog. doi: 10.1002/mc.23064.*
c. Bitler BG, **Watson ZL**, Wheeler LJ, Behbakht K. 2017. PARP inhibitors: Clinical utility and possibilities of overcoming resistance. *Gynecol Oncol 147:695-704.*

3. Herpes simplex virus type 1 (HSV-1) establishes latency within trigeminal ganglia (TG), and reactivation from the ophthalmic branch leads to recurrent corneal scarring and blindness. I demonstrated that the viral noncoding latency-associated transcript (LAT) epigenetically promotes reactivation. I designed a ribozyme targeting the LAT and delivered it into rabbit TG using an AAV vector, which I had previously demonstrated to transduce >90% of sensory neurons. The ribozyme knocked down LAT RNA levels and reduced HSV-1 reactivation by over 50%. This result represents an entirely novel therapeutic approach against previously untreatable HSV-1 reactivation.

a. **Watson ZL**, Ertel MK, Lewin AS, Tuli SS, Schultz GS, Neumann DM, and DC Bloom. 2016. Adeno-Associated Virus Vectors Efficiently Transduce Mouse and Rabbit Sensory Neurons Coinfected With Herpes Simplex Virus 1 Following Peripheral Inoculation. *Journal of Virology* 90(17):7894-901.
b. **Watson ZL**, Washington SD, Phelan DM, Lewin AS, Tuli SS, Schultz GS, Neumann DM, Bloom DC. 2018. In Vivo Knockdown of the Herpes Simplex Virus 1 Latency-Associated Transcript Reduces Reactivation from Latency. *J Virol 92(16). doi: 10.1128/JVI.00812-18.*
c. Washington SD, Edenfield SI, Lieux C, **Watson ZL**, Taasan SM, Dhummakupt A, Bloom DC, Neumann DM. 2018. Depletion of the insulator protein CTCF results in HSV-1 reactivation in vivo. *J Virol doi:10.1128/jvi.00173-18.*

Complete List of Published Work in My Bibliography
https://www.ncbi.nlm.nih.gov/myncbi/zachary.watson.1/bibliography/public/

C. Research Support

Ongoing Research Support

193527-ZW (Watson) 07/01/2019 – 06/30/2020
Cancer League of Colorado Research Grant
Targeting histone acetylation in PARP inhibitor-resistant ovarian cancer

Role: PI
Goals: This award provides funding to elucidate the relationship between histone acetyltransferases and the histone modification H3K14ac with DNA repair responses and PARP inhibitor resistance in ovarian cancers.

Completed Research Support

5T32CA174648 (Pyeon) 07/01/2014 – 06/30/2016
National Institutes of Health T32 Postdoctoral Fellowship
Training in Translational Research of Lung, Head and Neck Caner
Role: Postdoctoral Fellow
Goals: This award supported translational studies in lung, head and neck cancers. Specifically, this award supported my work in identifying ISGs that restrict early HPV infection, and also my work in developing a novel assay for DNA methylation as a biomarker of HPV-associated head and neck cancer prognosis.

5T32AI060527 (Bloom) 09/01/2008 – 07/31/2010
National Institutes of Health T32 Predoctoral Fellowship
Training in Biodefense and Emerging Infectious Diseases
Role: Graduate Student
Goals: This award supported basic and translational studies of numerous bacterial and viral pathogens. Specifically, this award supported my work in elucidating epigenetic mechanisms of HSV-1 latency and reactivation, and also my work in developing ribozymes against the HSV-1 LAT as a novel therapeutic strategy to prevent viral reactivation.