Name: Yousef Alharbi

Email: yalharbi@wisc.edu

Major Professor: Dr. Manish Patankar

Degree Objective: Ph.D. Endocrinology and Reproductive Physiology

Background: BS in Veterinary Medicine, Qassim University, Saudi Arabia

MS in Molecular and Cell Biology, Quinnipiac University, Connecticut

Graduate Researcher in Biochemistry in the Department of Pathology, School of Medicine, Yale University, Connecticut

Current Research Project:

My research focus is on studying the molecular mechanism of two novel chemotherapeutic drugs that inhibit proliferation and mediate death of high grade serous ovarian cancer. The first drug is a new class of antibody conjugated drug referred to as Extracellular Drug Conjugate (EDC) which induces apoptosis and autophagy of ovarian cancer cells at low concentration (IC50 2.5nM). The EDCs are composed of modified cardiac glycoside (CEN-09) conjugated to the antibody through chemical linker. The antibody selectively binds to molecules such as dysadherin that form complex with the Na+/K+-ATPase, and this complex is overexpressed in cancer cells as compared to normal cells. The antibody binding to Dysadherin allows the attached drug (CEN-09) to bind to Na/K-ATPase, presumably interfering with the membrane potential and hence causing apoptotic death of cancer cells. The second classes of drugs that I am investigating are natural compounds. One of these compounds is plumbagin, a small molecule agent extracted from the root of the plant, plumbago. Plumbagin inhibits the proliferation of the cancer cells at an IC50 of 3 micromolar. Plumbagin induces cell death through generation of reactive oxygen species (ROS). Generation of ROS after the treatment caused activation of Bax and Bak leading to loss of the mitochondrial membrane potential and eventually releasing cytochrome-c and activating caspase-3. 1mM of N-Acetyl Cysteine (ROS inhibitor) abrogates the toxicity of plumbagin. I am investigating if cancer cells can compensate and attenuate the activity of plumbagin by activating Nrf-2, a transcription factor that is the master regulator of anti-oxidant responses. Activation of Nrf-2 is likely a chemoresistance mechanism that will compromise the cytolytic activity of plumbagin. I am testing the activities of plumbagin in mouse as well as canine models of cancer. This data will be used to promote the use of plumbagin as an agent for treatment of ovarian cancer.

Honors:

Saudi Government Scholarship for graduate studies in the United States

Publications:

Yousef Alharbi, Mildred Felder, Amruta Nayak, Tom Beres, Timothy Stein, Arvinder Kapur, Manish S. Patankar (2017) Plumbagin induces Apoptosis via reactive oxygen species in Dog cancer cells. (*manuscript in preparation to be submitted to Oncology Reports*)

Book Chapter

Yousef Alharbi, Manish Patankar, Rebecca Whelan (2017) Antibody Based Therapy for Ovarian Cancer in book titled: Ovarian Cancer Immunotherapy. Ed: Samir Farghaly, Oxford University Press, (Exact publication date is not available at this time).

Presentations:

Selected for Oral Presentation: Yousef Alharbi, Arvinder Kapur, Mildred Felder, Manish Patankar; Antibody-conjugated Cardiac Glycosides: Potent Agents for Treatment of Ovarian Cancer. Endocrinology and Redproductive Physiology Annual Symposium (Jun-2015).

Oral Presentation: Yousef Alharbi, Arvinder Kapur, Mildred Felder, Manish Patankar; Antibody-conjugated Cardiac Glycosides: Potent Agents for Treatment of Ovarian Cancer. Endocrinology and Redproductive Physiology Seminar (Aug-2015) and (Sep-2016).

Teaching and Mentorship:

Mentor for UW-Madison undergraduate students Emmalee Kent, Nicole Gregorich and Samantha Mindlin.