Undergraduate Research Symposium May 17, 2013 Mary Gates Hall

Online Proceedings

SESSION 2L

CANCER MECHANISMS

Session Moderator: Michael Lagunoff, Microbiology
271 MGH
3:45 PM to 5:15 PM

* Note: Titles in order of presentation.

Elucidating the Interaction Between Long-Distance Chromosomal Interactions within the 8q24 Risk Locus and the Myc Oncogene
Srilatha Madhuri (Madhuri) Popuri, Senior, Biochemistry
Mentor: Tony Krumm, Radiation Oncology

Genome-wide association studies indicate that the sequence polymorphism rs6983267 located in the 8q24 risk locus correlates with increased risk for colorectal, prostate, breast and ovarian cancers. This region is particularly interesting because it is located in a 'gene desert' in which no expressed genes are known; however, several reports suggest that it functions as an enhancer that regulates the expression of the Myc oncogene located more than 300 kilobases away from rs6983267. The enhancer region also contains a binding site for CTCF, a factor known for its contributions to long-distance chromosomal interactions and gene regulation. Here, we aim to elucidate the specific function of CTCF located close to the rs6983267 sequence variation in DLD1-colorectal cells. We test the hypothesis that the CTCF element at the 8q24 risk region is required for a physical interaction between the enhancer of the 8q24 risk locus and the Myc gene. This hypothesis predicts that deletion of the CTCF binding site will yield reduced Myc expression. In our study we introduced a series of genomic modifications with recombinant adeno-associated virus (rAAV) to generate site-specific deletions and to examine CTCF's role in long-range chromosomal interactions at the 8q24 locus. Mutant cell lines were developed with modifications on either one or both 8q24 alleles in the colorectal cancer cell line DLD1. Cell growth characteristics, gene expression and chromosome conformation capture (3C) experiments will be performed to better understand the functional and physical interaction between the 8q24 risk locus and the Myc gene.

POSTER SESSION 3

Balcony, Easel 122
2:30 PM to 4:00 PM

Dose Distribution Measurements of an Experimental Proton Pencil Beam
Christopher K. (Chris) Mochizuki, Senior, Physics: Biophysics
Mentor: Eric Ford, Radiation Oncology

Treating tumors with radiation requires a trade-off between the necessary dose to eliminate the tumor and the quantity which the healthy tissue can withstand. Radiation therapy with protons allows for a large amount of dose to be delivered to the target area while only delivering a relatively small amount of dose to the surrounding healthy tissue. Utilizing this new method guarantees improved patient safety and treatment success. At the UW Department of Radiation Oncology, a proton cyclotron is being refined to provide a unique system for laboratory experiments in radiation. The purpose of these measurements was to gain further insight into dose distribution of the beam, its lateral spread through air, and its dose delivery efficiency into biological medium. Gafchromic EBT3 film, utilized in conjunction with a rectangular water phantom to simulate biological tissue, measured various characteristics of the beam. When exposed to the beam, the film darkend due to energy-catalyzed cross linking of the polymer. The opacity change in the film was calibrated against a known dose from a clinical beam. Using the film, the dose of the beam was measured at incremental depths leading up to, and behind, the Bragg peak. From the data acquired, it was discovered that the EBT3 film has an under-response of up to 30% dose within the Bragg peak, likely due to effects of linear energy transfer. Under-response of the EBT3 film is prohibitive for measuring absolute Bragg peak dose values, but the relative dose distributions obtained from these experiments provides important insight into the accuracy of Monte Carlo simulations for proton pencil beams.

POSTER SESSION 4

Balcony, Easel 127
4:15 PM to 5:45 PM

An *in vitro* Assay for Quantifying DNA Damage Effects in an Experimental Proton Radiotherapy Beam

Jonathan Robert (Jonathan) Hanisch, Junior, Pre-Health Sciences
Mentor: Jing Zeng, Radiation Oncology
Mentor: Geoffrey Linn, Radiation Oncology
Mentor: Jeffrey Schwartz, Radiation Oncology
Mentor: Eric Ford, Radiation Oncology

Proton radiation therapy is an emerging modality for the treatment of cancer. Clinical use of protons is growing around the world because of their favorable energy deposition patterns in tissues, but many unknowns remain in terms of the radiobiology of proton radiotherapy. Therefore, more preclinical research is needed. To this end the UWMC is developing a first-of-its kind experimental proton beam specifically designed for preclinical laboratory studies. The goal of this experiment is to compare biological endpoints of DNA damage and repair to radiation dose deposition patterns of the proton beam. As the proton beam passes through tissues it loses energy exponentially. At the end of its track it reaches very high levels of linear energy transfer, LET, i.e. – the energy deposited per unit length. We hypothesize that cells within high-LET regions of the beam are subject to more DNA damage. A549 lung cancer cells were grown to confluence in chamber slides, irradiated with protons or ^{1}37Cs gamma rays (control), and fixed in methanol at 0, 15, 30, 60, 120, and 1440 minutes post-irradiation. DNA double-strand breaks were indirectly measured by immunohistochemical staining for γH2AX, a histone protein modified at sites of double strand breaks. The resulting biodosimetric assay will provide valuable information concerning DNA damage as a function of varying LET. Future work will extend the results to an *in vivo* model of mouse brain tissue with the goal of analyzing normal tissue toxicity in high-LET regions of the proton beam. This research has implications for current cancer treatment planning by, for example, avoiding proton beams directed at an organ at risk, or correcting normal tissue toxicity tolerances currently accepted by the academic community.