

BIOINFORMATICS SEMINAR

DARIA GAYKALOVA

Assistant Professor of Otolaryngology – Head and Neck Surgery
Assistant Professor of Oncology

JOHNS HOPKINS MEDICAL INSTITUTIONS

THE ROLE OF CHROMATIN REORGANIZATION AND ALTERNATIVE SPLICING EVENTS IN HEAD AND NECK CANCER DEVELOPMENT

My group focuses on the analysis of alternative splicing events (ASE) in head and neck squamous cell carcinoma and the role of this process on cancer development and progression. Previous work has shown that ASEs are prevalent in HNSCC, but further validation is needed to understand the regulation of this process and its role in these tumors. As of today, we have applied modern computational methodologies, that detected biologically relevant ASEs, and we validated the individual splice isoforms using in vitro qRT-PCR using our HNSCC samples and in silico validation using TCGA cohort. Further evaluation of chromatin modification revealed that ASEs strongly correlated with the cancer-specific distribution of acetylated lysine 27 of histone 3 (H3K27ac). Subsequent epigenetic treatment of HNSCC cell lines with JQ1 (inhibitor of H3K27ac-recognising BRD proteins) induced not only the downregulation of cancer-specific ASE isoforms, but also the cell proliferation inhibition. The cell line with higher ASE expression also showed more significant growth inhibition after JQ1 treatment. This study confirmed several novel cancer-specific ASEs in HNSCC and provided evidence for the role of chromatin modifications in the regulation of alternative splicing in HNSCC. This highlights the role of epigenetic changes in the oncogenesis of HNSCC, which represents a unique, unexplored target for therapeutics that can alter global post-transcriptional change.

BIOGRAPHY

As a cancer biologist with a background in pharmacology, the ultimate goal of Dr. Gaykalova is to develop novel cancer therapies, particularly for tumor types that lack effective disease-specific treatment options, such as human papillomavirus-related head and neck squamous cell carcinoma (HPV+ HNSCC). She heads the translational laboratory, which defines the functional role of epigenetics in the regulation of expression of canonical and alternatively spliced transcripts. Her team had recently characterized the landscape of the cancer-specific alternative splicing events (ASE) in HPV+ HNSCC and defined their potential role in cancer formation. Moreover, the preliminary data in her group suggest that chromatin, and in particular, enhancers, have a regulatory role in the expression of cancer-specific ASE isoforms. Dr. Gaykalova supposes that both of these processes (splicing and chromatin remodeling) can be therapeutically controlled. Such potential therapeutic strategy can form the basis for the development of effective disease-specific therapeutics for this the most rapidly growing disease, as well as other virus-related and non-related solid tumors.



CBCB
SEMINAR
2/17/2020

3:30 PM
DELAWARE
BIOTECHNOLOGY
INSTITUTE
Room 102

bioinformatics.udel.edu