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THE CENTRE FOR BLOOD RESEARCH

The Centre for Blood Research Seminar Series

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LSC 3 | 12:00 - 1:00PM

Jessica Kalra, PhD

Associate Member, Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, British Columbia, Canada.

Staff Scientist, Department of Experimental Therapeutics, BC Cancer Research Center, Vancouver, British Columbia, Canada.

Instructor, Department of Biology and Health Sciences, Langara College, Vancouver, British Columbia, Canada.

"Developing circRNA signatures as a biomarker for the early diagnosis of Pancreatic Carcinoma"

At the time of diagnosis, pancreatic ductal adenocarcinoma (PDAC) is typically advanced and incurable. Current research has concentrated on finding tumor markers for early detection while the cancer is still localized and amenable to therapy, however, these markers remain elusive. We believe that exonic circular RNAs (circRNA) will act as a novel set of diagnostic/prognostic biomarkers for cancer and specifically PDAC. CircRNAs found in mammalian cells, are backsplice variants of transcripts that are derived from approximately 15% of actively transcribed genes. The prevalence, stability and cell-specific expression patterns of circRNAs suggest that they could be exploited as an indirect or surrogate readout of transcriptional activity in normal and diseased states. We propose that aberrantly expressed genes in transformed cells such as cancer cells produce different types of circRNAs that become enriched in tumor-secreted exosomes. Our team has established a novel method for the isolation of circRNAs from RNA in exosomes. We propose to expand on this research by inventorying the total circRNA from PDAC exosomes using RNA-seq methods. RNA samples from tumor cells, exosomes from the conditioned media of tumor cell lines, xenografts, patient derived xenografts, animal serum and serum from patients will be used to enrich for circRNAs and subsequently be subject to RNA-seq in order to characterize circRNAs associated with the diseased state. Our hypothesis is that exosomal circRNA expression patterns are specific to different stages/types of PDAC and therefore can be used in disease sub-typing and prognosis. The use of routine screening for cancer in its early stages has been shown to significantly impact patient outcomes and reduce the mortality associated with aggressive and metastatic disease. We hope to demonstrate that specific circRNAs can be extracted from the exosomes of body fluid and used as a non- or minimally invasive, clinically relevant biomarker and screening tool for those cancers where early diagnosis remains problematic such as PDAC.

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