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Aberrant sialylation patterns to evaluate the efficacy of a novel multimodal combination treatment of cancer

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The heterogeneity of tumors is well-documented and multimodal therapeutic targeting of these specific heterogeneous subpopulations is an area of intense research interest. We propose applying a novel multimodal targeted therapy in an effort to disable cancer stem cells and overcome chemoresistance. To investigate the efficacy of combinatorial therapy, RAGxCy double mutant mice (lacks T, B and NK cells) were injected with pancreatic PANC-1 cancer cells. When a palpable tumor was formed, the animals were treated with chemotherapy alone or combination multimodal therapy. Preliminary data have shown a difference in the proliferative capacity of cultured primary tumor and liver metastatic cells (collected at the time of necropsy and subsequently cultured until confluent) of treated versus untreated cohorts. Upon initial flow cytometry analysis of sialic acid expression levels, cells of chemotherapy treated animals demonstrated a higher percentage of α-2, 6-sialic acid expression when compared with cells of untreated and combination treatment animals. A more aggressive cancer phenotype may be selected for, by chemotherapy which can be overcome by our multimodal drug cocktail. Cultured cells' ability to form spheroids was also assessed as a means to further characterize the biological differences in cells treated with different regimens. Surprisingly, animals treated with chemotherapy lost the ability to form spheroids, while animals treated with multimodal therapy maintained their adhesion capability. While additional characterization is required, our proposed treatment regimen is capable of overcoming the challenges that are currently observed in the clinic including chemoresistance and selection of cancer stem cells.

Biography

Manpreet Sambi is currently a PhD Trainee under the direct supervision of Dr. Myron R Szewczuk in the Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Canada and co-supervision of Dr. William Harless—MD, PhD—certified Medical Oncologist and CEO of Encyt Technologies, Inc., Sydney to work on therapeutic targeting cancer stem cells (CSC). To do this, she is working towards characterizing and understanding the mechanisms of cancer stem cell activation and proliferation. This knowledge will improve the potency of conventional chemotherapeutic treatment options with aspirin, metformin and oseltamivir phosphate in a multimodal targeted approach.

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