Bessi Qorri et al., J Glycobiol 2018, Volume 7
DOI: 10.4172/2168-958X-C2-014

Neuraminidase-1 and its role in multimodal therapy preventing chemotherapy resistance and metastasis in pancreatic cancer

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Pancreatic ductal adenocarcinoma (PDAC) represents the fourth leading cause of cancer-related deaths and this is attributed to the advent of metastatic disease, rendering curative surgery as an option in less than 25% of patients at diagnosis. PDAC is inherently resistant to current standard of care gemcitabine (Gem) chemotherapy, and its highly inflammatory microenvironment and extremely dense extracellular matrix (ECM) further exacerbate resistance and contribute to the aggressive, invasive and metastatic nature of the disease. We have previously reported that anti-viral oseltamivir phosphate (OP) inhibits the activing of neuraminidase-1 (Neu-1), preventing the cleavage of α-2,3 sialic acid residues, ultimately shutting down a novel signaling paradigm implicated in multistage tumorigenesis. Recent reports have described the overlapping effects of anti-diabetic metformin and non-steroidal anti-inflammatory drug acetylsalicylic acid (aspirin) in sensitizing malignant cells to chemotherapy and downregulating cell growth and inflammation. We propose that a combination therapy of OP, metformin and aspirin works synergistically to sensitize pancreatic cancer cells to Gem therapy, preventing metastasis, tumor angiogenesis and growth. Enzyme assays on live epidermal growth factor stimulated PANC-1 pancreatic cancer cells have revealed aspirin works in a manner similar to OP in inhibiting neuraminidase activity. Immunocytochemistry on PANC-1 cells and immunohistochemistry on paraffin-embedded tumor tissue samples from RAGxCy mice were stained and analyzed for markers of epithelial-to-mesenchymal transition (EMT) characteristic of metastatic disease. The multimodal therapy of OP, metformin and aspirin works synergistically to sensitize pancreatic cancer cells to chemotherapy, prevent metastasis, angiogenesis and tumor growth.

Biography

Bessi Qorri is a Trainee in the laboratory of Dr. Myron Szewczuk, Department of Biomedical and Molecular Sciences, Queen's University. She is a Scholar of the 2017 Terry Fox Research Institute Transdisciplinary Training Program in Cancer Research in collaboration with Dr. William Harless, MD, PhD in Clinical Oncology and with Dr. Cecile Malardier-Jugroot, Professor and Head of Chemical Engineering at the Royal Military College, on the self-assembly of novel polymeric nanotubes in the delivery of chemotherapeutic in the treatment of cancer. She is the First Co-Author of seven peer-reviewed published articles, a book chapter and on a review article on medicinal marijuana to Nature Reviews Drug Discovery (IF 57) under peer-review, Co-Editor on Springer series book on Metastatic Cancer and Contributing Co-Author of one peer-reviewed published article. Her research is on the role of anti-inflammatory agents in enhancing the sensitivity of chemotherapeutics against cancer.

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