

5<sup>th</sup> International Conference on

# GLYCOBIOLOGY & GLYCOPROTEOMICS

&

3<sup>rd</sup> International Conference on

# MOLECULAR BIOLOGY & NUCLEIC ACIDS

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### Aberrant sialoglycan patterns facilitate 3D multicellular spheroid and xenograft tumor formation

Multicellular tumor spheroids are now at the forefront of cancer research, designed to mimic tumor-like developmental patterns *in vitro*. Tumor growth *in vivo* is known to be highly influenced by aberrant cell surface specific sialoglycan structures on glycoproteins. Aberrant sialoglycan patterns that facilitate spheroid formation are not well defined. Here, matrix-free spheroids from human breast, pancreatic and prostate cancer cell lines and their respective chemoresistant variants were generated using a unique cyclic Arg-Gly-Asp-D-Phe-Lys peptide modified with 4-carboxybutyl-triphenylphosphonium bromide (cyclo-RGDfK (TPP)) induced self-assembly platform. The cyclo-RGDfK(TPP) peptides mimic the natural extracellular matrices (ECM) protein's ability to induce cell aggregation via  $\alpha 5 \beta 1$  integrin. We used the cyclo-RGDfK (TPP) approach to biochemically induce cell aggregation and compaction, transmigrating monolayer cancer cells into tumor spheroids. MCF-7 and PANC-1 cells, and their drug-resistant cancer cell lines (MCF-7 TMX, PANC1-GemR) express different sialic acid content, which influenced their ability to form spheroids under cyclo-RGDfK (TPP)-induced self-assembly. Cancer cell aggregation and compaction correlate with the presence of  $\alpha$ -2,3- and  $\alpha$ -2,6-sialic acid cell surface residues to form spheroids under cyclo-RGDfK (TPP)-induced self-assembly and xenograft tumors. Removal or blockage of SA inhibited cell aggregation. Neuraminidase inhibitor, oseltamivir phosphate, enhanced cell aggregation and promoted compaction of cell aggregates. Future studies should build upon these findings and explore alternate and novel methods to target the cancer cell glycome and the unique sialylation patterns of the adhesion molecules involved in the spheroid formation and tumor progression.

### Biography

For the past 37 years, Dr Szewczuk is Full Professor of Immunology and Medicine, Queen's University, Kingston, Ontario Canada. Dr Szewczuk's recent research has focused on the role of glycosylation in receptor activation with a particular focus of Toll-like, nerve growth factor Trk, EGFR and insulin receptors. He has discovered a novel receptor-signaling platform and its targeted translation in multistage tumorigenesis.

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