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Specific sialoglycan structures on the cell surface correlate with the ability of cancer cells to form avascular multicellular 3D tumor spheroids and *in vivo* xenograft tumors

Multicellular 3D tumor spheroid (MTS) formation in cancer research has been designed to mimic tumor-like developmental patterns *in vitro*. Tumor growth and invasion is known to be highly influenced by aberrant cell surface-specific sialoglycans on cell surface glycoproteins. Aberrant sialoglycan patterns that facilitate MTS formation have not been well defined. To evaluate the role of sialylation of cancer cell surfaces in spheroid formation, we used the cyclo-RGDfK (TPP) approach to biochemically induce cell aggregation and compaction, transmogrifying monolayer cancer cells into tumor spheroids. The cyclo-RGDfK (TPP) peptide-based platform causes specific biochemical alterations of cell surface receptors inducing self-assembly in monolayer cell cultures into 3D MTS by facilitating cell-cell recognitions, interactions and adhesion. Matrix-free spheroids from breast MCF-7 and pancreatic PANC1 cancer cell lines and their respective tamoxifen (TMX) and gemcitabine (Gem) resistant variants formed tight spheroids while all PANC1 cells formed loose aggregates. MCF-7 and PANC1 cells and their drug-resistant variants expressed different sialic acid (SA) content on their cell surfaces. α-2,3- and α-2,6-sialic acid surface residues facilitated spheroid formation under cyclo-RGDfK(TPP)-induced self-assembly. Pretreatment with α-2,3-SA specific Maackia amurensis (MAL-II) lectin, α-2,6-SA specific Sambucus nigra (SNA) lectin and exogenous α-2,6-SA specific neuraminidase (Vibrio cholerae) dose dependently reduced spheroid volume. Oseltamivir phosphate (OP) treatment enhanced cell aggregation and compaction forming spheroids. PANC1 and MDA-MB231 xenograft tumors from untreated and OP-treated RAGxCγ double mutant mice expressed significantly higher levels of α-2,3-SA over a-2,6-SA. The present report provides evidence for the important role of specific sialoglycan structures expressed on cancer cells to form avascular multicellular tumor spheroids and *in vivo* xenograft tumors. 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 spheroid formation and tumor progression.

Biography

M R Szewczuk is a Full Professor of Immunology and Medicine at Queen's University, Kingston, Ontario, Canada. His current research is focusing on the role of glycosylation in receptor activation with a particular focus on alternate new active tumor targeting drug delivery systems.

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