

4<sup>th</sup> World Congress on

# Breast Pathology and Cancer Diagnosis

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### Novel therapeutic target in multistage breast tumorigenesis

A novel organizational signaling platform linked to glycosylated receptor tyrosine kinases (RTK) (e.g., EGFR, TrkA, insulin) and TOLL-like (TLR) receptors is identified to regulate receptor activation process, all of which are known to play major roles in tumorigenesis. This signaling paradigm proposes that ligand, binding to its receptor on the cell surface induces a conformational change of the receptor, to initiate matrix metalloproteinase-9 (MMP-9) activation to induce neuraminidase-1 (Neu1). Activated Neu1 hydrolyzes  $\alpha$ -2,3-sialyl residues linked to  $\beta$ -galactosides, which are distant from the ligand binding sites. These findings predict a pre-requisite desialylation process by activated Neu1 enabling the removal of steric hindrance to receptor association. In addition, the relative levels of specific sialoglycan structures on the cell surface correlate with the ability of cancer cells to form avascular 3D multicellular tumor spheroids and *in vivo* xenograft tumors. Here, we have identified an innovative, promising and entirely new targeted therapy for cancer. Mammalian neuraminidase-1 (Neu1) in complex with matrix metalloproteinase-9 and G-protein coupled receptor, tethered to RTKs and TLRs is identified as a major target in the multi-stage of tumorigenesis. Pre-clinical studies support an entirely new cancer targeted therapy unaffected by mutations of growth factor receptors, involved in tumor neovascularization, chemo-resistance of tumors, immune-mediated tumorigenesis, and tissue invasion and metastasis.

### Biography

Myron R Szewczuk is currently working as Professor of Immunology, Department of Biomedical and Molecular Sciences and Medicine of Queen's University, Kingston, Ontario, Canada for the past 36 years. He received his BSc in Chemistry (University of Guelph), MSc in Biochemistry (Guelph), PhD in Immunochemistry (University of Windsor) and Post-doctoral training with Gregory Siskind, MD in Cellular Immunology at Cornell University Medical College, NYC. His recent research has focused on the role of glycosylation in receptor activation with a particular focus on TOLL-like, nerve growth factor Trk, EGFR and insulin receptors. He has discovered a novel receptor-signaling platform and its targeted translation in multi-stage of tumorigenesis.

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