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Fucosylation is contributing to the formation of multicellular tumor spheroids generated from prostate cancer cells

Regina-Veronicka Kalaydina
Queen's University, Canada

Aberrant cell surface glycan alterations such as glycosylation have been linked to a variety of cancers. These findings have warranted a deeper investigation into whether fucosylation may play a role in prostate cancer, which affects roughly 1.1 million people worldwide. Fucosylation is a type of cell surface glycosylation that involves the transfer of an L-fucose from a GDP-fucose to an acceptor substrate. Additionally, Asapargine N-linked glycans are typically the target of core fucosylation. Overexpression of Fucosyltransferase-8 (Fut-8), which catalyzes an α-1,6 fucose transfer and is responsible for "core fucosylation", has been detected in aggressive prostate cancers with high Gleason scores. With the growing use of multicellular tumor spheroids (MTS) to study complex interactions in the tumor microenvironment, prostate spheroids (or prostaspheres) constitute a good three-dimensional model for studying the role of fucosylated proteins in tumor formation. Prostaspheres can be generated from DU145 and PC3 prostate cancer cell lines using the cyclo-RGDfK(TPP) peptide, a novel method that enables rapid, inexpensive and true spheroid formation. I have shown that DU145 prostate cancer cells express core fucose with immunochemistry (ICC) using the Aspergillus oryzae lectin (AOL), which binds core fucose residues. Using a lectin inhibition assay, I have also shown that pre-treating prostaspheres generated from DU145 prostate cancer cells with AOL result in the formation of spheroids with a reduced volume. Therefore, in addition to the previously established role of sialylation in MTS formation, fucosylation is also likely contributing to prostate tumor formation. The role of glycosylation in tumor spheroid formation is an emerging yet poorly understood area of research that can enhance our understanding of the mechanisms behind tumor growth in humans. Novel applications of glycobiology to the recent advancements in MTS with the advent of the cyclo-RGDfK(TPP) peptide method give rise to the possibility of optimizing current MTS models.

Biography

Regina-Veronicka (Nicka) is a trainee in Prof. Szewczuk's lab. She has a special interest in optimizing the multicellular tumor spheroid (MTS) model developed by her colleagues. Her research explores how different types of glycosylation may be contributing to prostasphere tumor formation. She has shown that prostate cancer cells are highly fucosylated and that blocking core fucosylation in prostaspheres results in the formation of spheroids with a reduced volume. In addition to her work with MTS, Nicka is also investigating whether fucosylation may be involved in metastasis in pancreatic cancer.

nicka.kalaydina@queensu..ca

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