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Exploring Protein interactions in Non-small-cell Lung cancer-associated Glycoproteins through Mass Spectrometry and StringDB

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Identification of glycans as potential biomarkers for cancer is a recent development in the field, with several studies reporting differential profiles of N-glycans among various cancers. High mortality in lung cancer is still an unresolved problem due to late detection/diagnosis and varying response to treatment regimens. Here we report glycomic profiling of A549, NCI-H23 (NSCLC) and CCD-Lu19 (normal lung tissue), glycoproteomic analysis of A549 non-small-cell lung cancer (NSCLC) cell lines using high-resolution mass spectrometry, and protein interaction network analysis of modified glycoproteins using StringDB to gain insights on the disease mechanisms involving protein glycosylation. We identified nine glycans that were differentially expressed in normal versus cancer cell lines and 124 proteins that were associated with these glycosylations, including the known cancer markers EGFR and CD44, ranging in the number of N-glycan modifications from 1 to 5. Hex(9) HexNAc(2), a high-mannose N-glycan, modifies the most number of proteins (n=105, unique=78). While HexNAc(4)Hex(5)Fuc(1), a complex hybrid-fucosylated N-glycan. The expanded protein interaction network for each of the glycan show enrichment for 5-7 cancer-related pathways including PI3K-Akt signaling, Pathways in cancer (KEGG: 05200), Proteoglycans in cancer (KEGG: 05205), micro-RNAs in cancer (KEGG: 05206) and non-small-cell lung cancer (KEGG: 05223), mostly via integrins, EGFR, EGF, CD44 and several other cell adhesion molecules. These results suggest the importance of glycans in mediating signaling cascades that are important in NSCLC. Further work is being done to validate these analyses and explore the utility of these glycans as possible cancer biomarkers for different NSCLC stages

Biography

Ruel Nacario received his Ph.D in Chemistry from the University of Toledo (USA) in 2005. From 2005-2007, he was a Postdoctoral Fellow with Prof. Todd Lowary at the University of Alberta, Canada, working in a collaborative total synthesis of arabinan-containing octadecasaccharide precursor and a docosanasaccharide proposed to be a common intermediate in mycobacterial cell wall biosynthesis. He then joined Nitto Denko Technical Corp (NDT) in California, USA, initially, as an Industrial Postdoctoral Fellow (2008) and then subsequently promoted to the Sr. Scientist (2009-2012) positions, working on the synthesis, purification and analysis of oligonucleotides in support of NDT's development of a delivery system and siRNA-based drug for treatment of liver fibrosis. He then returned to the Philippines and joined the University of the Philippines (2013-present) where he is currently an Associate Professor of Chemistry. His research interests span both Organic and Medicinal Chemistry.

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