Title: Further Decoding the Molecular Relationship Between Pancreatic Ductal Adenocarcinoma and Diabetes Mellitus

Authors: Russell Moreland, Anupam Dhasmana, PhD, Subhash Chauhan, PhD, Sheema Khan, PhD.

Affiliations: UTRGV School of Medicine, UTRGV School of Medicine South Texas Center of Excellence in Cancer Research

Background:

Pancreatic ductal adenocarcinoma (PDAC) is a devastating malignancy, especially as there are no current reliable methods of screening. A significant relationship between PDAC and Diabetes Mellitus (DM), specifically a new onset of diabetes mellitus (NOD). The molecular network of PDAC and new onset DM is not completely understood. We sought to investigate the molecular network of these two diseases with the ultimate goal of identifying potential biomarkers to aid in the screening of PDAC.

Methods:

We conducted a review for relevant articles concerning the molecular relationship between PDAC and DM. We compiled a list of 74 genes which have been implicated in the relationship between PDAC and DM. These genes were used for the construction of gene interaction network (GIN) by using GeneMANIA on the bases of genetic interactions, co-expression, co-localization, pathway, physical interactions, predicted interaction and shared protein domains. The GIN input file was imported in the cytoscape for the pathways enrichment analyses by using KEGG plugin. The cytoscape was used for the construction of the final GIN of both normal and cancer genes separately.

Results:

GIN and pathways enrichment analyses of genes known to be altered during NOD/DM and PDAC indicate their association with different pathways. in this study we have mentioned around 20 enriched pathways in the associated tables and figures which promptly show the direct and indirect association with pancreatic cancer. The major signaling pathways that were observed to be upregulated include NABA Matrisome, protein phosphorylation, metabolic processes and proteins upregulated as a result of hormone response. Out of all pathways, proteins that are more involved in metabolic processes were found most influenced.

Conclusion:

In conclusion, we have contributed to identifying the molecular network relating PDAC and DM. Our future aim is to investigate the genes associated in this pathway. We will use this data to design a panel for next generation sequencing in tissue samples of patients diagnosed with PDAC.