Abstract ID:- 142

Abstract Topic:- Statistical genetics and genetic epidemiology

Abstract Title:- Comparative gene co-expression network analysis: Insights into key genes and pathways associated with healthy and prediabetic phenotypes.

Presenting author name :- Shriyansh Srivastava

Presenting author institute:- Indian Institute of Technology Gandhinagar

Co-authors name:- Ashutosh Srivastava, Madhulika Dixit

Co-authors institute:-Indian Institute of Technology Gandhinagar, Indian Institute of Technology Madras

Aims:-Type 2 diabetes mellitus (T2DM) is a metabolic disorder, with its onset defined by a precursor pre-diabetic state. While several studies have been conducted to identify the key genes and pathways involved in T2DM disease progression, the molecular mechanisms in the pre-diabetic state remain largely unknown. In addition, the underlying changes upon transition from healthy to pre-diabetic phenotype are poorly understood. Therefore, the study aimed to determine the regulatory network differences between healthy and prediabetic conditions and understand the changes upon oral glucose load.

Methods:- Weighted gene co-expression network analysis (WGCNA) was performed on the publicly available microarray dataset GSE153837 to identify gene network modules associated with healthy (NGT) and pre-diabetic (PD) phenotypes in fasting and 2-hour post load glucose conditions. The modules were correlated with clinical trait data to identify modules of interest. Lastly, downstream analyses were performed on modules of interest to determine the hub genes and pathways associated with different phenotypes.

Results:- We found that modules (gene clusters with similar expression) across conditions (NGT /PD: Fasting and 2-hour post load glucose) correlated with clinical traits differently. Based on the correlation between module eigengenes and clinical traits such as fasting glucose, fasting insulin, 2-hour post load glucose, 2-hour post load insulin, and HOMA-IR levels, we identified modules of interest in different conditions. A comparative analysis of hub genes and gene ontology revealed differences in regulatory pathways. Genes TSPAN32, AP3M1, SPOCD1, PARVB, WRB and ZNRD1, ERCC3, EIF2B4, IL10, TMEM17 were identified as hub genes in NGT and PD fasting states, respectively. Genes ZNF33B, IPO13, C1orf69, FAM115A, USP49 and JMJD8, SLFN5, PMPCA, ZNF483, PIP5K2B were reported as hub genes in NGT and PD 2-hour post load glucose state, highlighting the transcription regulator activity (GO:0140110), catalytic activity (GO:0003824), and binding (GO:0005488) as key molecular functions regulated by these genes. The biological processes involved with hub genes were biological regulation (GO:0065007), cellular process (GO:0009987), localization (GO:0051179), and metabolic process (GO:0008152). Intergrin and interleukin signaling pathways were associated with hub genes PARVB and IL10.

Conclusions:- Our study revealed differences in hub genes and pathways that change upon PD phenotype and glucose load. Future studies would focus on identifying preserved modules and comparative analysis with T2DM datasets.

Keywords:- gene regulatory network, WGCNA, prediabetes, PBMCs, oral glucose load