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STUDY ON UNDERSTANDING INTERACTING PROTEINS ENCODED BY GENES VITAL FOR DIABETES PATHOLOGY IN HUMANS

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ABSTRACT: Diabetes, one of the major non-communicable diseases affecting people worldwide and threatening to turn India as its global epidemic capital, needs focused research. Since genes and proteins encoded by them lie at the basis of all physiological outputs (both in normal and diseased states), understanding their networks and the components involved in them can shed light into their mechanism of action under both situations. Such studies are also beneficial towards indentifying previously unknown interactions and target entities which can help in both diagnosis prognosis and treatment. This study was aimed towards identifying a few such interactions in context of genes which have been found to be important in diabetes in humans. Gene-gene interaction maps were generated which revealed novel interactions.

KEYWORDS: Non-communicable diseases, Diabetes, Gene interactions, Protein Interactions, Molecular makers.

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1.INTRODUCTION

The last several decades have seen a shift in the type of diseases that are primarily causing the greatest extent of morbidity and mortality among human beings. It has been observed that non-infectious, chronic non-communicable diseases (NCDs) are replacing infectious diseases in this context. Such a reversal in trend has resulted from several factors, including better treatment options including vaccination) for combating infectious diseases and change in lifestyle/behavioural patterns (including dietary habits, sedentary lifestyles, increasing physical inactivity and exposure to environmental

pollution) encouraging and supporting onset and progression of NCDs. Four major diseases are the major concerns among all NCDs, diabetes, cardiovascular diseases (including stroke and chronic obstructive diseases), respiratory diseases (including asthma and COPD) and cancers [1]. Estimates have indicated that NCDs will account for over 80-90% of deaths by the year 2020 [2-5].In an attempt to identify the main genes that are involved with/affected by diabetes, we carried out extensive research on available secondary data. We have previously reported our initial findings on eight genes which have been reported to be most involved in this context [accepted for publication]. Here we report the detailed findings on the interaction maps of six genes which have been identified to be most important with reference to diabetes pathology in humans.

2. MATERIALS AND METHODS

As mentioned previously, the initial identification of genes most relevant with reference to diabetes was performed from information based on secondary data gathered from various online resources and websites including:

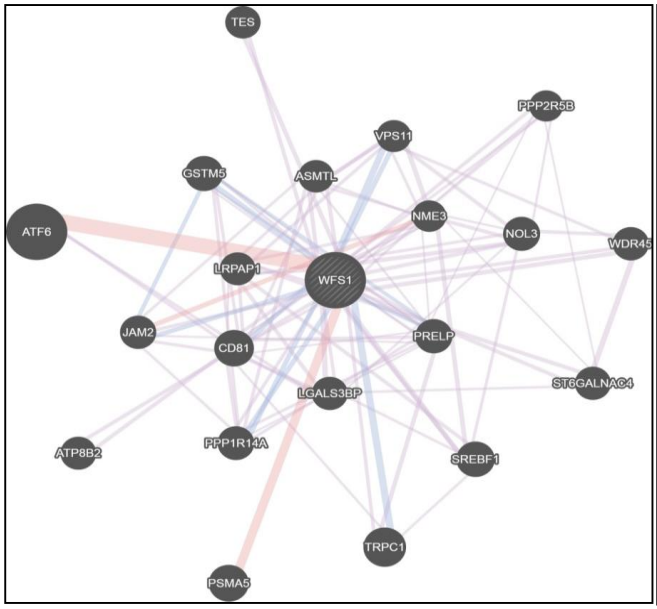
1. www.ncbi.nlm.nih.gov
2. genemania.org
3. en.wikipedia.org
4. www.genecards.com
5. www.healthline.com
6. www.scholar.google.co.in

The eight genes which were reported to be predominantly related to or affected by any type of diabetes were identified and further studies were carried out with the aim of identifying their interacting partners. These interaction maps were generated with help of GeneMANIA [6].

3. RESULTS AND DISCUSSION

Our previous studies have shown that the genes which have been reported to be related to or affected by diabetes include WFS1, Tcf712, SLC30A8, PPARG, KCNQ1, KCNJ11 and FTO. While Tcf712 was of mouse origin, PPARG of both human and mouse origin were found to be involved (Manuscript accepted for publication). Here we report the details about the interacting components of the six genes which are of human origin, namely WFS1, SLC30A8, PPARG, KCNQ1, KCNJ11 and FTO. WFS1is responsible for production of the protein wolframin. This protein is known to play role in the cellular balance of calcium [7-9]. The protein encoded by SLC30A8 gene acts as zinc efflux transporter and is involved with maintaining levels of zinc within intracellular vesicles [10-12]. PPARG gene encodes a protein which is part of the peroxisome proliferator-activated receptor family of nuclear receptors. It has been found to play role in the process of adipocyte differentiation [13-15]. The protein generated as translation product of the gene KCNQ1 is part of potassium channels. These channels are responsible for maintaining physiological concentrations of potassium ions thereby ensuring that electric signals are generated and maintained properly [16-18]. KCNJ11 too encodes a protein which

is part of a potassium channel. This channel is ATP-sensitive [19-21]. FTO gene encodes a nuclear protein which belongs to the AlkB related non-haem iron oxygenase superfamily. It is primarily involved with reversal of alkylated DNA and RNA damage [22-24]. The interaction map for all the genes were generated with the help of GeneMANIA as mentioned previously. Figure 1(a) shows the interactions for WFS1, Figure 1(b) for SLC30A8, Figure 1(c) for PPARG, Figure 1(d) for KCNQ1, Figure 1(e) for KCNJ11 and Figure 1(f) highlights the gene interactions for FTO.



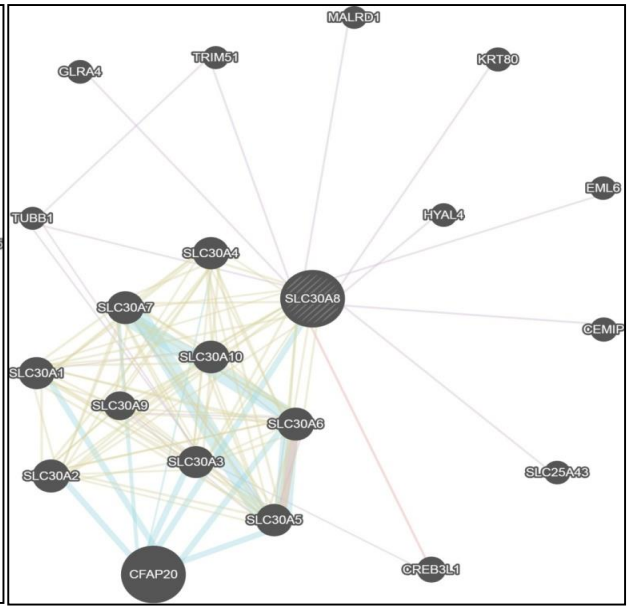
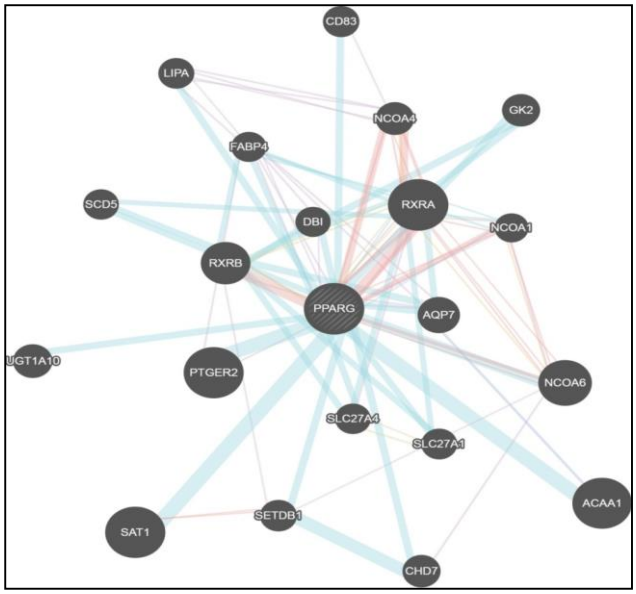


Figure 1 (a). Interaction map for gene WFS1Figure 1 (b). Interaction map for gene SLC30A8



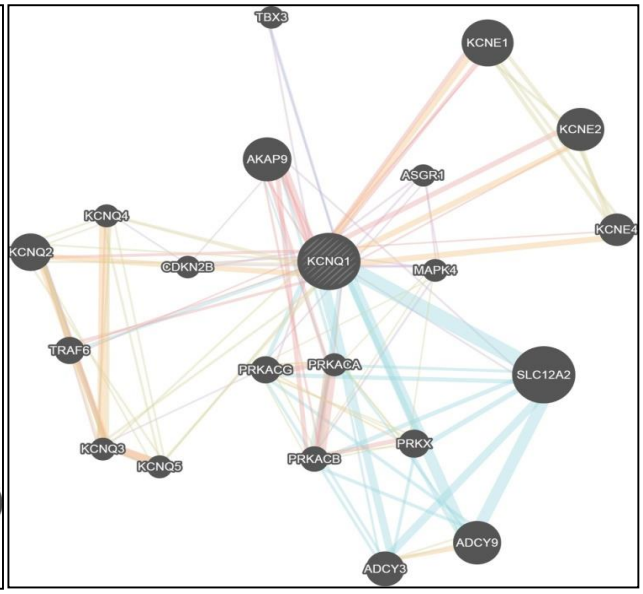


Figure 1 (c). Interaction map for gene PPARG Figure 1(d). Interaction map for gene KCNQ1

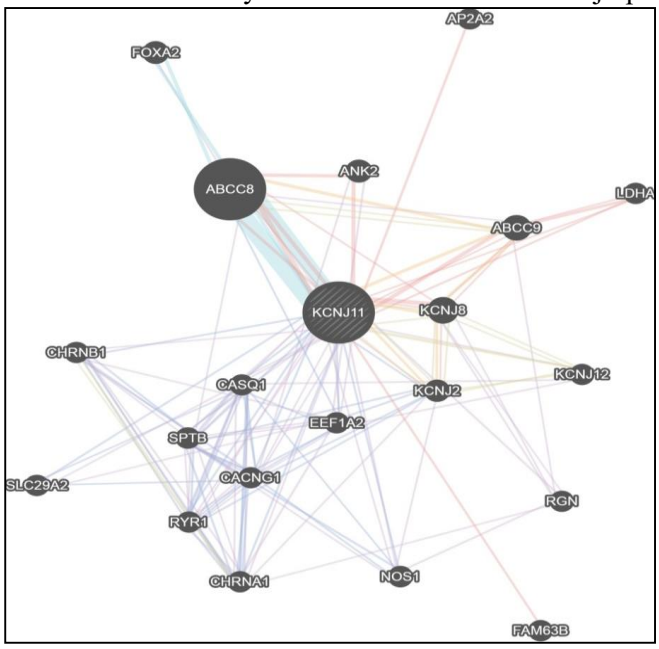


Figure 1 (e). Interaction map for gene KCNJ11

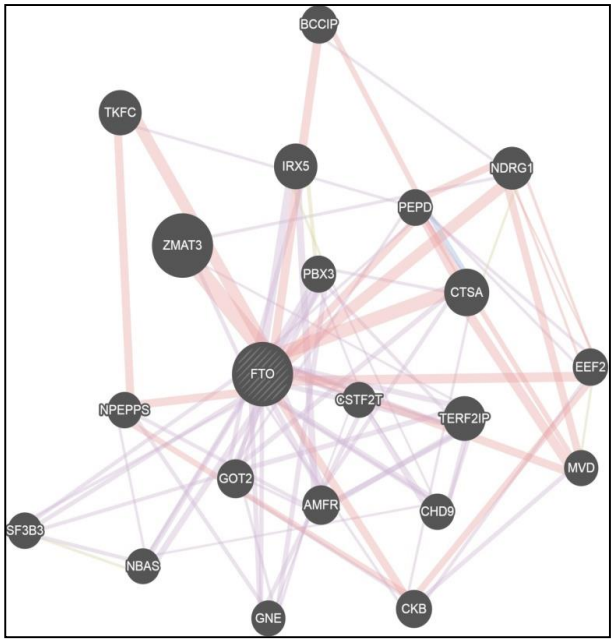


Figure 1 (f). Interaction map for gene FTO

- Physical interaction-67.64%
- Co-expression-13.50%
- Predicted-6.35%
- Co-localization-6.17%
- Pathway-4.35%
- Genetic interactions-1.40%
- Shared protein domains-0.59%

Weighted percentages of different color coded sections of (a) to (f)

4. CONCLUSION

The current study focused on the role of interplay between a few genes in disease pathology of diabetes, a major non-communicable disease affecting a significant proportion of the population. Generation of interaction maps for each of these genes resulted in identification of novel candidate genes which were previously not reported to be involved in this disease [25-27]. Further studies aimed towards understanding the exact mechanisms of the interactions between them can be helpful in getting a clearer picture of the physiological manifestations that are observed [28-30].

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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