Diabetes mellitus, often simply termed Diabetes, is a syndrome characterized by disordered metabolism and high blood sugar. It is caused due to low levels of insulin hormone or from abnormal resistance to insulin in its target tissues. World Health Organization estimates that India will alone have 79.4 million diabetic patients in 2030. One of its major form Type 2 diabetes, is often associated with obesity, hypertension, elevated cholesterol and metabolic syndrome. Changes in life style, such as consumption of high-calorie diet and lack of exercise, have increased the global prevalence not only of diabetes but also of obesity. Type 2 diabetes is characterized by insulin resistance in target tissue, occurs due to several reasons and one of them being the proinflammacy cytokine, TNF-α. It is also known as the link between diabetes and obesity. High levels of TNF-α interfere with insulin signaling to cause the effect and to further investigate into the situation, gene transcription profiling was examined in control and TNF-α treated HepG2 cells. Results indicated that TNF-α could significantly alter the expression of a significant number of genes that were identified to be related to lipid and fat metabolism on one hand and to immunoglobulin receptor activity and Igf binding thereby on the other thereby indicating global dysregulation of fat metabolism and compromise in immune defense mechanism(s) within the hepatocyte by TNF-α. Pathway analysis revealed “biosynthesis of steroids” to be most effected. All these indicate TNF-α to be significantly altering the transcriptome profiling within HepG2 cells with genes involved in lipid and steroid metabolism being the most favoured and this could explain one of the underlying mechanisms of TNF-α action in the liver.

**Gene expression**

**Diabetes**

Muscular dystrophy

Tumorgenesis

Arthritis

Cardiac hypertrophy

Neuropathological diseases

**TNF-α**

Major physiological and pathological roles of TNF-α

**Genes altered by TNF-α treatment in HepG2 cells.**

A volcano plot of genes altered by TNF-α in HepG2 cells

A. 67 genes up-regulated by TNF-α

B. 73 genes down-regulated by TNF-α

Classification of TNF-α regulated genes into functional groups

**Validation of microarray gene expression data by Real Time PCR**

**Over representation of conserved transcription factor binding sites within putatively co-regulated genes.**

**“Biosynthesis of steroids” identified as the top canonical pathway altered by TNF-α in HepG2 cells**

**Conclusion**

- As many as 140 genes were significantly altered by TNF-α.
- Pathway analysis identified the biosynthesis of steroids and cholesterol to be the most favored.
- Signatures of conserved transcription factor binding sites were identified in genes of similar GO functional term and within the same cluster.
- Over represented genes upregulated by TNF-α consisted of several Gene ontology terms related to lipid and fat metabolism.
- Within the down-regulated category, those involved in varied aspects of the immune response were over-represented in the GO classes of both biological processes and molecular function.

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