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ORIGINAL ARTICLE **OPEN ACCESS**

In Silico Studies of PPARγ gene related to Diabetes Mellitus and Inflammation

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ABSTRACT
Bioinformatics is the improvement of healthcare information of data and knowledge. It uses computational tools and techniques to analyse vast amount of biological data or databases. The diseases such as metabolic disorder, genetic disorder, inborn disorder, rheumatoid arthritis and other inflammatory conditions can be analysed at remediable stage using these bioinformatics and computational methods. These methods or tools which can used to process at genomics and proteomics levels can compare with healthcare data. And also identify the genetic interaction studies and gene variant and also phylogenetic tree analysis. Diabetes is an endrocrinological condition that affects millions of people and can cause myriad health complications. Numerous bioinformatics tools are being used in diabetes research and related inflammation.
Keywords: *Diabetes, Inflammation, Genomics, Proteomics, Phylogenetic.*

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INTRODUCTION

Bioinformatics is the centralised field that can explains the procedure and software tools for demonstrating biological information. Bioinformatics came to read to result and give direction to the vast amount of data through molecular biology techniques. Bioinformatics is the combination of different fields like, software engineering, computer science, and statistics etc. The field of bioinformatics can guise the examination of molecular data quants clinical and diagnostic data for personalised medicine of healthcare. Bioinformatics is used to identify the candidate gene to analyse at genetic basics level, cellular and molecular levels of different populations. The large or vast amount of data from bioinformatics or computational biology and health informatics domains link with analyses and deliver near future of preventive, personalized healthcare cards. [1,2] In basic biology it helps in increase the display of DNA, RNA and 3D protein structures and some additional bio-molecular interactions which can be accelerated advance of gene therapy, genome editing and drug discovery.[3,4]

Type 2 Diabetes Mellitus (Diabetes Mellitus) originates from insulin resistance and impaired β-cell function and create a major health problem throughout the world. Liver is involved in glucose metabolism, including gluconeogenesis, glycogenosis and insulin extraction. Variation of glucose metabolism in liver contributes development of Type 2 diabetes (Diabetes Mellitus). Diabetes often leads to cardiovascular complications which effect shows on patient quality of life. Type 2 Diabetes is mainly caused by genetic factors and environmental influence. To prevent and reduce the complications of Diabetes Mellitus important to analyse the pathophysiological mechanism at genetic level. [5-8] At present with wide use and development of high-throughput sequencing, bioinformatics analysis is a big advantage to understand the Diabetes Mellitus at genetic basis. A research acknowledgement that the methylation of key genes participate in diabetic nephropathy. Studies of mRNA expression profiles at peripheral Diabetes Mellitus from Database so these profiles which will result that which genes will express and which genes will not express in profiles. And also see the regulation of up regulation and down regulation process based on cut off of p-value. And also see study gene interaction levels i.e how other genes are interacting with major causing gene. [9-12]

The peroxisome proliferator activated receptorγ (*PPARG*) gene is a member of the nuclear hormone receptor superfamily that regulates the transcription of several genes involved in glucose metabolism, adipocyte differentiation, lipid oxidation, angiogenesis and inflammation. Most of the mutation analysis has focused on the coding region of the *PPARG* gene. In different independent studies, the association of the *PPARG* gene with type 2 Diabetes Mellitus has been consistently reported. In the present study, we screened the coding regions of the *PPARG* gene, and examined the association of the *PPARG* gene with type 2 Diabetes Mellitus in the population of West Bengal, India. [13-20]

MATERIAL AND METHODS

The aim of the computational tools is to provide the information about phylogenetic examinations and physiochemical properties of proteins.

A. Gene Identification and Sequence Analyses: The apprehension of biomolecules such as nucleic acid and proteins can be achieved by investigations. Sequence analysis is the subject to analyse DNA, RNA, and Protein sequence to understand structure, function and evolutionary studies.

BLAST (Basic Local Alignment Search Tool): It is homology and similarity search tool. BLAST is the biological database containing amino acids of protein sequences and nucleotides of DNA sequences. BLAST find out patches of sequence similarity rather than best alignment and also produce un-gapped alignments. BLAST is based on explicit statistical theory.

B. Prediction of Protein Structure: Protein structure can be identified or constructed using three dimension structures can be predicted. It is difficult to determine the secondary, tertiary or quaternary structure of proteins so we use X-ray crystallographic studies and bioinformatics tools. Using multiple sequence alignment (MSA) also predict protein structure.

C. Phylogenetic Analysis: It refers to ancestral relationship in a set of species or taxa. The study to work out the ancestral relationship among various species or taxa is called phylogenetic analysis or phylogenetic. It demonstrates to which extent various species or taxa are related to each other and whether one of these species or taxa could be the possible ancestor for rest of species.

Phylogenetic Analysis helps us to understand the similarity among species or individuals, Dissimilarity between species, close relative of species, possible ancestor of a group.

D. Gene Interactions: It occur when two alleles affecting different genes combine within an organism to yield phenotype not simply explained by adding together the phenotype associated with each of two alleles.

E. Comparative Genomics: It is an exciting field of biological research in which researchers use variety or various tools, including computer-based analysis to compare complete genome sequence of different species.

Comparison of gene numbers, gene locations and biological functions of gene, in the genome of different organisms, one object being identify groups of genes that play unique biological role in the organism.

F. Gene variants: It is used to describe the variation in the DNA sequence in each of our genomes.

G. Functional Genomics: Branch of genomics that determine biological functions of genes and their products. Functional genomics (transcriptomics and proteomics) is a global, systematic and comprehensive approach for identification and description of the process and pathways involved in the normal and abnormal state of genes.

It is largely experiment based with a focus on gene functions at the whole genome level using high throughput approaches. High throughput analysis of all expressed genes is also termed as transcriptome analysis.

H. IGSR: The International Genome Sample Resource: It is providing ongoing support for the 1000 Genomes project data. It is ran between 2008 and 2015. It is creating a large public archive of human variation and genotype data. The overview of 1000 Genome project data was the find most genetic variants with frequencies of atleast 1% in the population studied.

The Advantage of this project is development of sequencing technology which can sharply the cost of sequencing. It can provide comprehensive resource of human genetic variation. Data from 1000 genome project was quickly made available to the worldwide scientific community through freely accessible public databases.

I. Gene Mania: find other genes that are related to a set of input genes using a large set of functional association data. Association data include protein and genetic interactions, pathways, co- expression, co-localization and protein domain similarity. You can use Gene Mania to find new members of a pathway or complex find additional genes you may have missed in your screen or find new genes with a specific function such, as protein kinase etc.

J. String: is a database of known and predicted protein-protein interactions. These associations include direct (physical) and indirect (functional) associations. They stem from computational prediction from knowledge transfer between organisms, and from interactions and from other primary databases.

Software of Bioinformatics

Tool and software	Methods and Applications
RAPTORX	Is a software and web server of protein structure and prediction
MEGA	Is designed for comparative analysis of homologous sequences
Network analyst	Web application that enables complex meta-analysis and visualization
String	Is a database of known and predicted protein-protein interactions
Gene Mania	Which can generate hypotheses about gene function and list of genes for functional assays

RESULTS AND DISCUSSION

BLAST Analysis of PPARγ gene

Peroxisome Proliferator-activated receptor is the sub family of nuclear receptors. PPARs form heterodimers which regulate transcription of various genes. Three subtypes of PPARs are known: PPAR-alpha, PPAR-delta, and PPARγ. The protein encoded by this gene is PPARγ and is a regulator of adipocyte differentiation. PPARγ has been implicated in the pathology of numerous diseases such as Obesity, diabetes and cancer. Diseases associated with PPARG include Diabetes, Lipodystrophy, Familial partial, and Rheumatoid Arthritis etc. Sequence alignment and BLAST analysis of DNA and protein sequence of PPARγ gene transcript variant shows 100% similarity and no gaps in alignment (Figure 1-4).

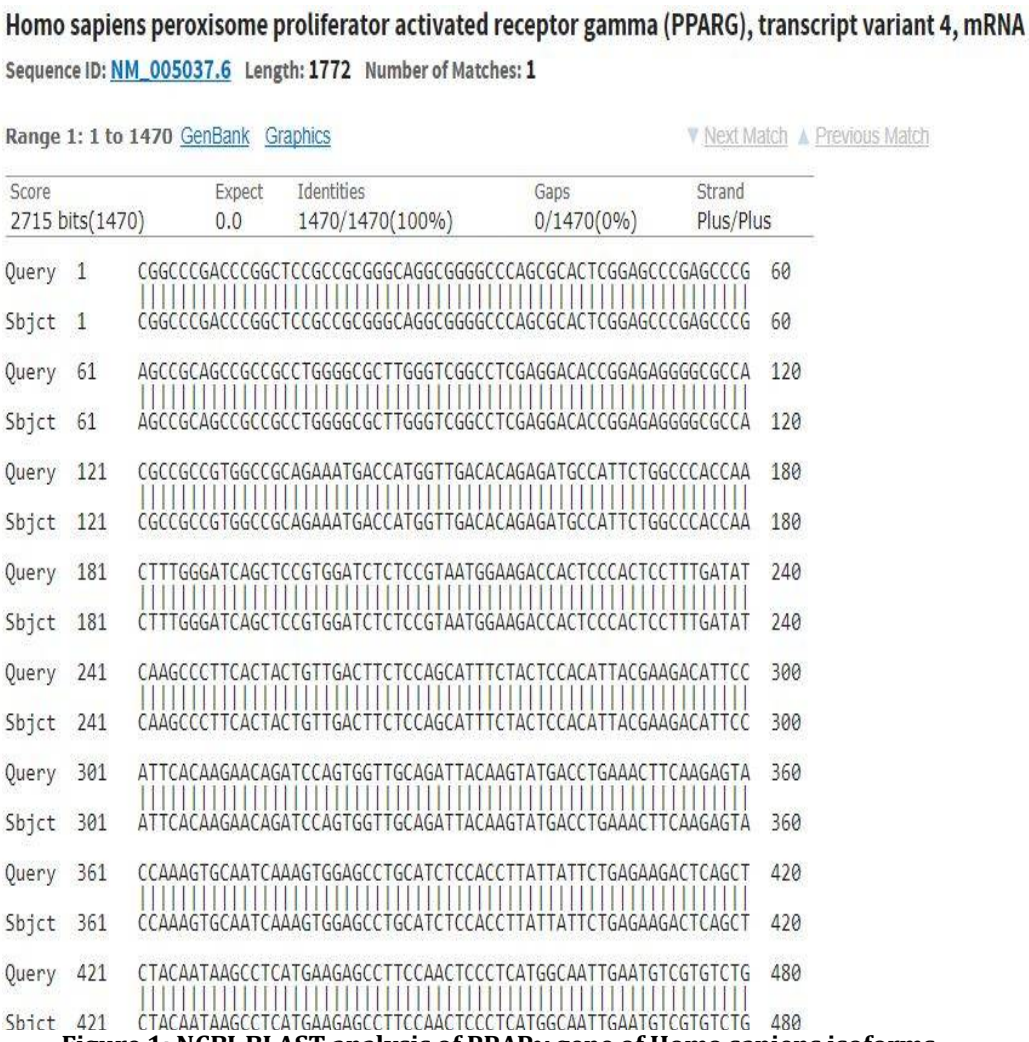


Figure 1: NCBI-BLAST analysis of PPARγ gene of Homo sapiens isoforms

Figure 2: BLAST analysis of the PPARγ gene collected from the public genome databases. Multiple sequence alignment showing complete coverage of 111 blast hits on 100 subject sequence.

peroxisome proliferator-activated receptor gamma isoform 2 [Homo sapiens]

Sequence ID: NP_056953.2 **Length:** 505 **Number of Matches:** 1

See 6 more title(s)

Range 1: 1 to 505 GenPept Graphics ▼ Next Match ▲ Previous Match

Score	Expect	Method	Identities	Positives	Gaps
1049 bits(2713)	0.0	Compositional matrix adjust.	505/505(100%)	505/505(100%)	0/505(0%)

```
Query  1    MGETLGDSPIDPESDSFTDTLSANISQEMTMVDTEMPFWPTNFGISSVDLSVMEDHSHSF  60
            MGETLGDSPIDPESDSFTDTLSANISQEMTMVDTEMPFWPTNFGISSVDLSVMEDHSHSF
Sbjct  1    MGETLGDSPIDPESDSFTDTLSANISQEMTMVDTEMPFWPTNFGISSVDLSVMEDHSHSF  60

Query  61   DIKPFTTVDFSSISTPHYEDIPFTRTDPVVADYKYDLKLQEYQSAIKVEPASPPYYSEKT  120
            DIKPFTTVDFSSISTPHYEDIPFTRTDPVVADYKYDLKLQEYQSAIKVEPASPPYYSEKT
Sbjct  61   DIKPFTTVDFSSISTPHYEDIPFTRTDPVVADYKYDLKLQEYQSAIKVEPASPPYYSEKT  120

Query  121  QLYNKPHEEPSNSLMAIECRVCGDKASGFHYGVHACEGCKGFFRRTIRLKLIYDRCDLNC  180
            QLYNKPHEEPSNSLMAIECRVCGDKASGFHYGVHACEGCKGFFRRTIRLKLIYDRCDLNC
Sbjct  121  QLYNKPHEEPSNSLMAIECRVCGDKASGFHYGVHACEGCKGFFRRTIRLKLIYDRCDLNC  180

Query  181  RIHKKSRNKCQYCRFQKCLAVGMSHNAIRFGRMPQAEKEKLLAEISSDIDQLNPESADLR  240
            RIHKKSRNKCQYCRFQKCLAVGMSHNAIRFGRMPQAEKEKLLAEISSDIDQLNPESADLR
Sbjct  181  RIHKKSRNKCQYCRFQKCLAVGMSHNAIRFGRMPQAEKEKLLAEISSDIDQLNPESADLR  240

Query  241  ALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFKHITPLQE  300
            ALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFKHITPLQE
Sbjct  241  ALAKHLYDSYIKSFPLTKAKARAILTGKTTDKSPFVIYDMNSLMMGEDKIKFKHITPLQE  300

Query  301  QSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLAS  360
            QSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLAS
Sbjct  301  QSKEVAIRIFQGCQFRSVEAVQEITEYAKSIPGFVNLDLNDQVTLLKYGVHEIIYTMLAS  360

Query  361  LMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVII  420
            LMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVII
Sbjct  361  LMNKDGVLISEGQGFMTREFLKSLRKPFGDFMEPKFEFAVKFNALELDDSDLAIFIAVII  420
```

Figure 3: NCBI-BLAST analysis of protein sequence of PPARγ gene isoforms 2.

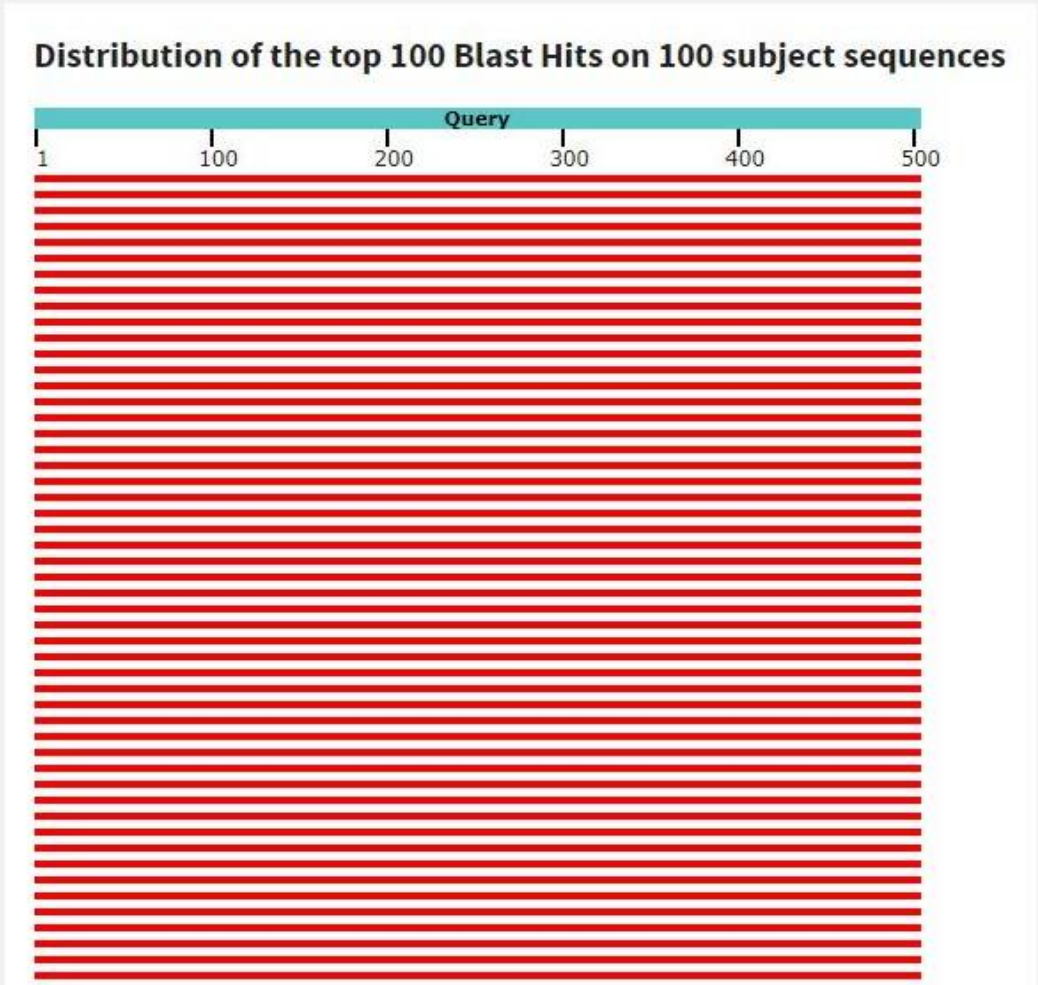
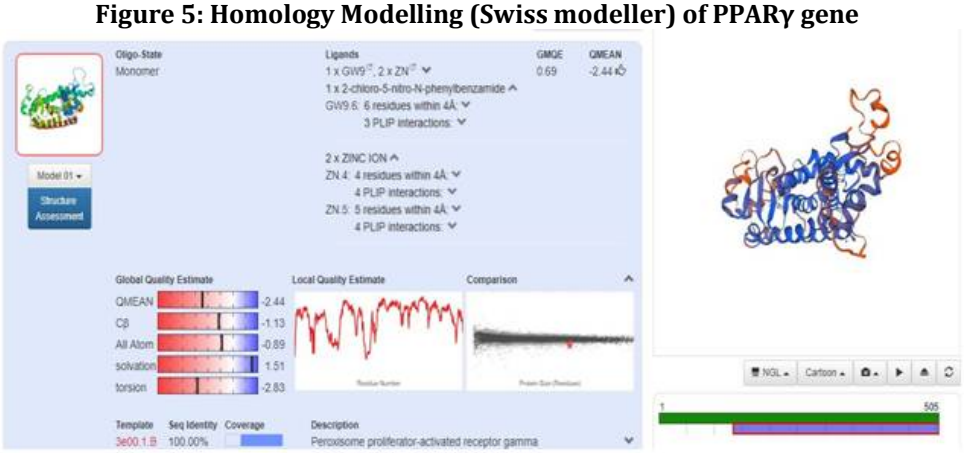


Figure 4: BLAST analysis of protein sequence of PPARγ gene collected from the public genome databases. Multiple sequence alignment showing complete coverage of 100 blast hits on 100 subject sequence.

Homology Modelling (Swiss modeller) of PPARγ (Protein)

Homology modelling is an important technique in structural biology which narrowing the gap between known protein sequences and experimentally determined structures. Peroxisome proliferator-activated receptorγ (PPARγ) is a type II nuclear receptor present in adipose tissue, colon and macrophages. It reduces the hyperglycemia associated type II diabetes-related cardiovascular system risk in human beings. Moreover, fatty acid storage and glucose metabolism are regulated by PPARγ activation in human body. Molecular docking studies have been conducted to characterize the 3-D structure of PPARγ and ligand binding efficiency. Result suggested 100 % sequence identity of PPARγ gene (Figure 5).

Figure 5: Homology Modelling (Swiss modeller) of PPARγ gene



Phylogenetic studies of PPARγ gene using Maximum Likelihood Method

Phylogenetic studies of transcript variant 4, 5 and 7 of PPARγ gene was conducted using Maximum Likelihood Method. Length of branches which represents the genetic distance in a horizontal manner. So the gene IDs like NM 001354667.2 (transcript variant 7) and NM 001330615.2 (transcript variant 5) and NM 005037.6 (transcript variant 4) are closely related species. Length of horizontal lines is called branches. So these branches is divided nodes. Among all 3 species, last 2 species are sister taxa. Nodes represent two species are called clade. Here 0.5 refers the nucleotide present in the alignment (Figure 6 and 7).

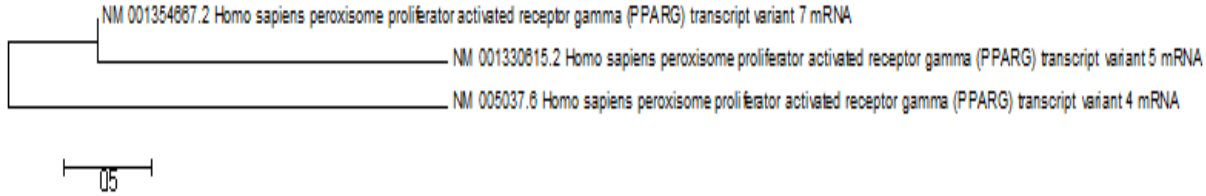


Figure 6: Phylogenetic tree of PPARγ gene (DNA sequence) showing relationship between transcript variant 4, 5 and 7.

Figure 7: Phylogenetic tree of PPARγ gene (protein sequence) showing relationship between transcript variant 4, 5 and 7.

Phylogenetic studies of PPARγ gene using Neighbouring (NJ) Method

NJ method is the neighbour joining method is the contract cluster analysis. NJ tracks nodes as tree 0.5 are the nucleotides per site in the alignment. Here in this diagram represents (transcript variant 4, 5, and 7 are closely related. The branch length of the taxonomical units are applied to respective units of the tree. As a result the star tree became irregular and showed some relationship between the taxonomical units (Figure 8 and 9).

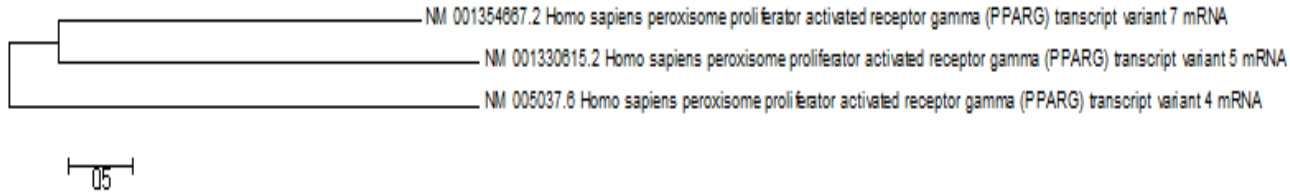


Figure 8: Phylogenetic tree of PPARγ gene (DNA sequence) using Neighbouring (NJ) Method showing relationship between transcript variant 4, 5 and 7.

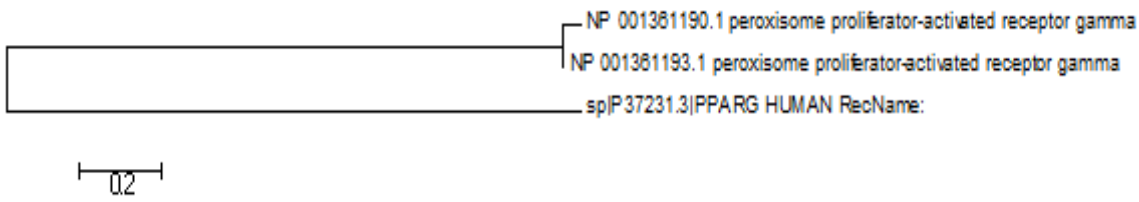


Figure 9: Phylogenetic tree of PPARγ gene (Protein sequence) using Neighbouring (NJ) Method showing relationship between transcript variant 4, 5 and 7.

0.2 is the nucleotide per site of alignment.

Phylogenetic studies of PPARγ gene using Minimum Evolution Method Minimum evolution method is the process in which assumption of tree with sum of the smallest branch length. Phylogenetic study indicate that all species are closely related species. So the gene IDs like NM 001354667.2 (transcript variant 7) and NM 001330615.2 (transcript variant 5) are closely related species in which 0.5 is the nucleotide site per alignment (Figure 10).

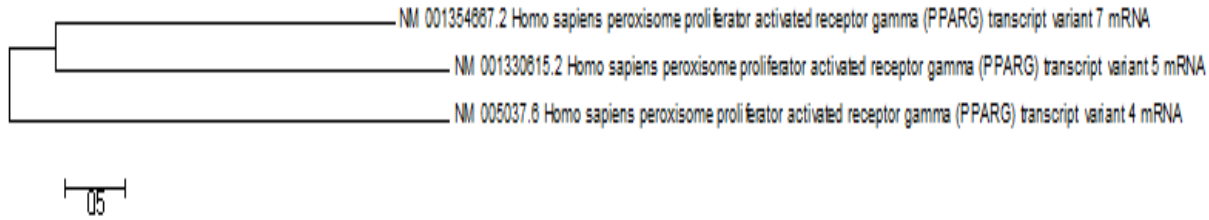


Figure 10: Phylogenetic tree of PPARγ gene (DNA sequence) using Minimum Evolution Method showing relationship between transcript variant 4, 5 and 7.

Minimum evolution method is the process in which assumption of tree within sum of the smallest branch length. From above diagram all species are closely are related to each other. We need to estimate the mutation rate but overall length of time since divergence and below once it indicates 0.2 nucleotide per site of alignment (Figure 11).

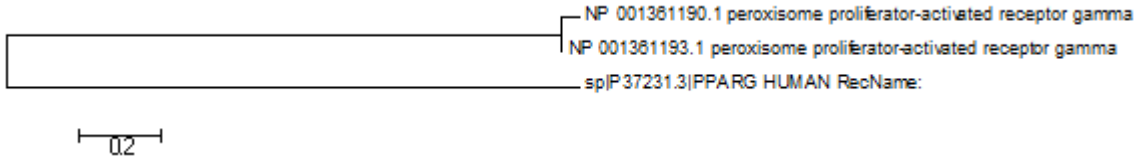


Figure 11: Phylogenetic tree of PPARγ gene (Protein sequence) using Minimum Evolution Method showing relationship between transcript variant 4, 5 and 7.

Phylogenetic studies of PPARγ gene using UPGMA Method

UPGMA is the unweighted pair group method with arithmetic mean it is simplified method to construct the phylogenetic tree. This method is suitable for large data sets considering lineages with relatively constant rates of evolution. Phylogenetic tree shows the close relation between NM 005037.6 (transcript variant 4), NM 001330615.2 (transcript variant 5) and NM 001354667.2 (transcript variant 7). In this diagram all residues are closely related to each other. A distance is the difference in one residue between the orders of residues in the sequences (Figure 12 and 13).

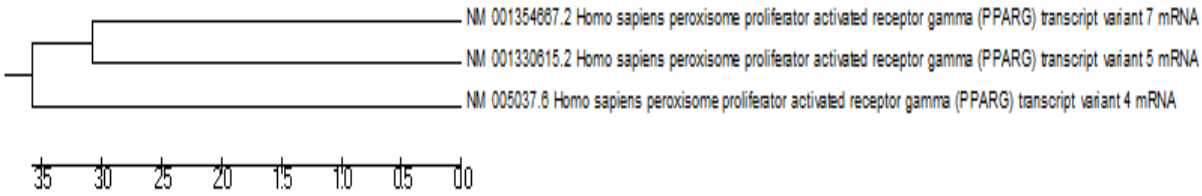


Figure 12: Phylogenetic tree of PPARγ gene (DNA sequence) using UPGMA Method showing relationship between transcript variant 4, 5 and 7.

Figure 13: Phylogenetic tree of PPARγ gene (Protein sequence) using UPGMA Method showing relationship between transcript variant 4, 5 and 7.

Gene Mania analysis of PPARγ gene

Prediction analysis

GeneMANIA (http://www.genemania.org) is a flexible, user-friendly web interface for generating hypotheses about gene function, analysing gene lists and prioritizing genes for functional assays. Functional relationships between genes, often protein interactions. A major source of predicted data is mapping is known functional relationships from another organism via orthology. Study showing functional relationship between PPARγ and other related genes of metabolic pathways (Figure 14).

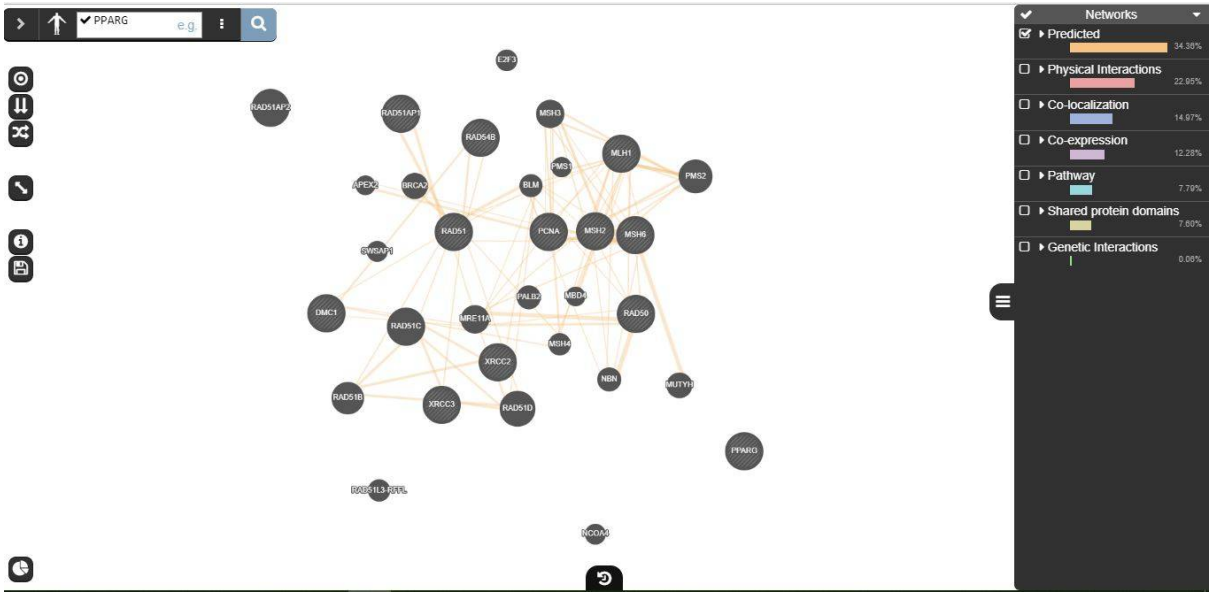


Figure 14: Prediction analysis for PPARγ gene showing functional relationship between PPARγ and other related genes of metabolic pathways.

2. Physical Interaction and Co-localization

Two gene products are linked if they were found to interact in protein-protein interaction. These data has been collected from primary studies from protein interaction data base. Result indicates the physical interaction and co-localization of PPARγ and other related proteins (Figure 15 and 16).

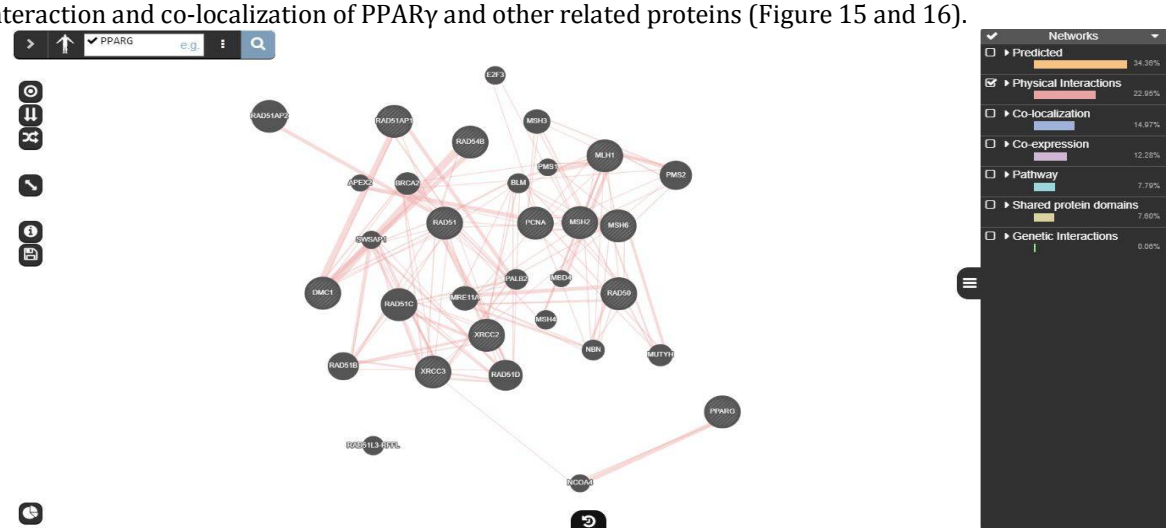


Figure 15: Protein-protein interaction (PPI) network for PPARγ genes

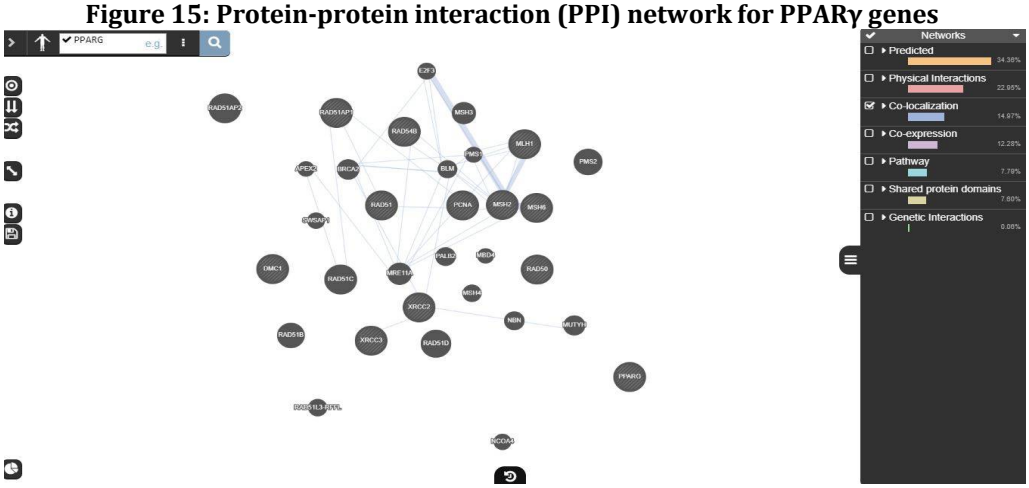


Figure 16: Co-localization study of PPARγ genes.

Co-expression and Pathway analysis: Two genes are linked if their expression levels are similar across conditions in a gene expression study. Most of the data retrieved from Gene Expression Omnibus (GEO). We collect data i.e. associated with publications of research papers. Two genes are linked they participated in same reaction within pathway (Figure 17-19).

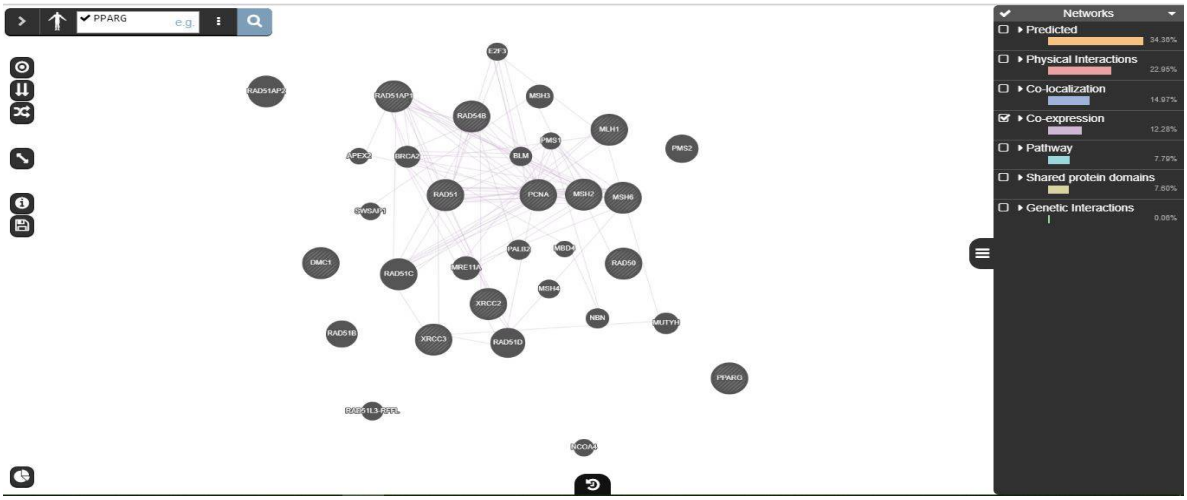


Figure 17: Co-expression study of PPARγ genes.

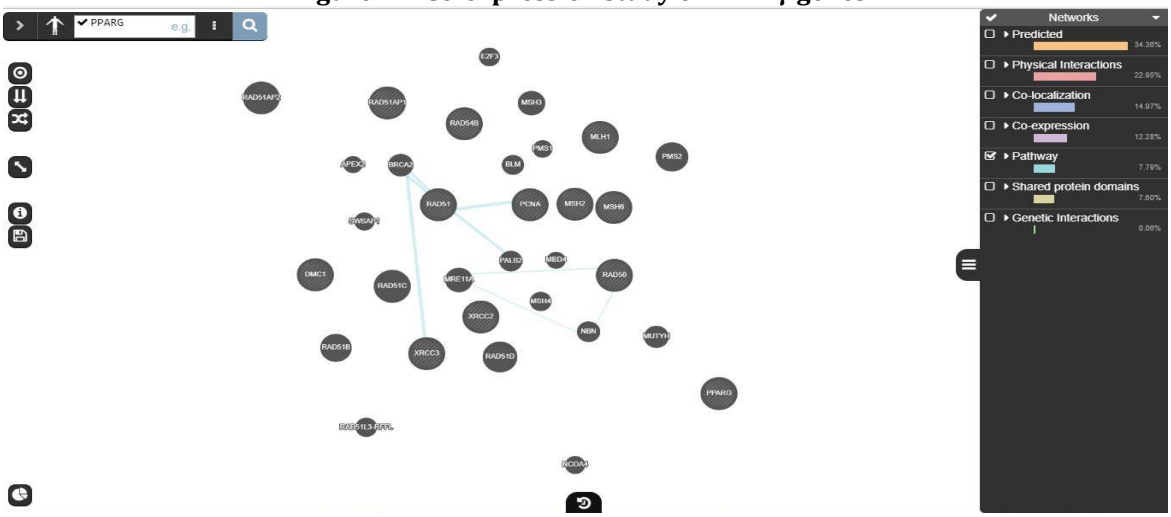


Figure 18: Pathway analysis of PPARγ gene showing association of genes in the same pathway.

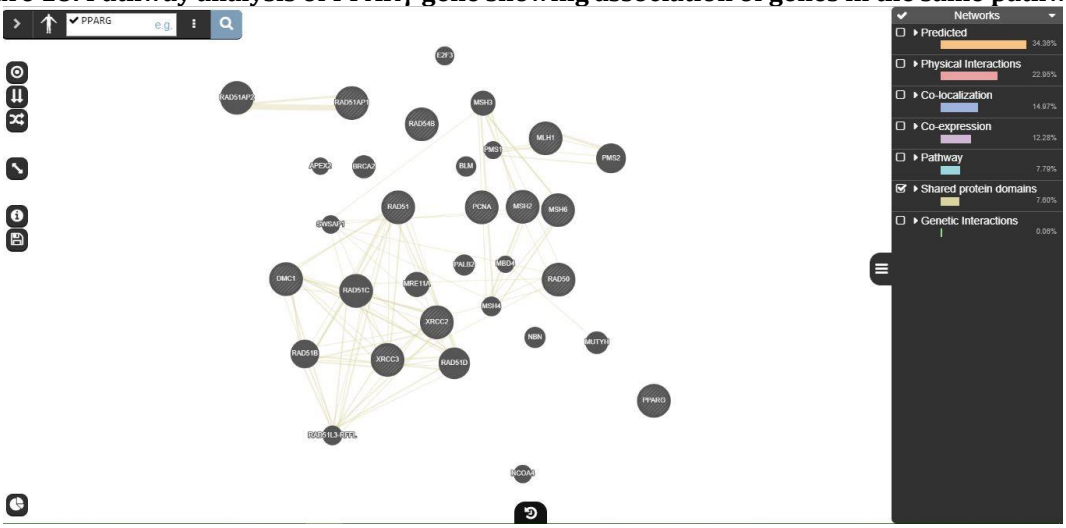


Figure 19. Share domain analysis of PPARγ gene. Two proteins are linked if they have same protein domain.

Gene Interactions

Two genes are functionally associated if the effects of disturb of one gene found to be modified by disturb of other gene or second gene (Figure 20).

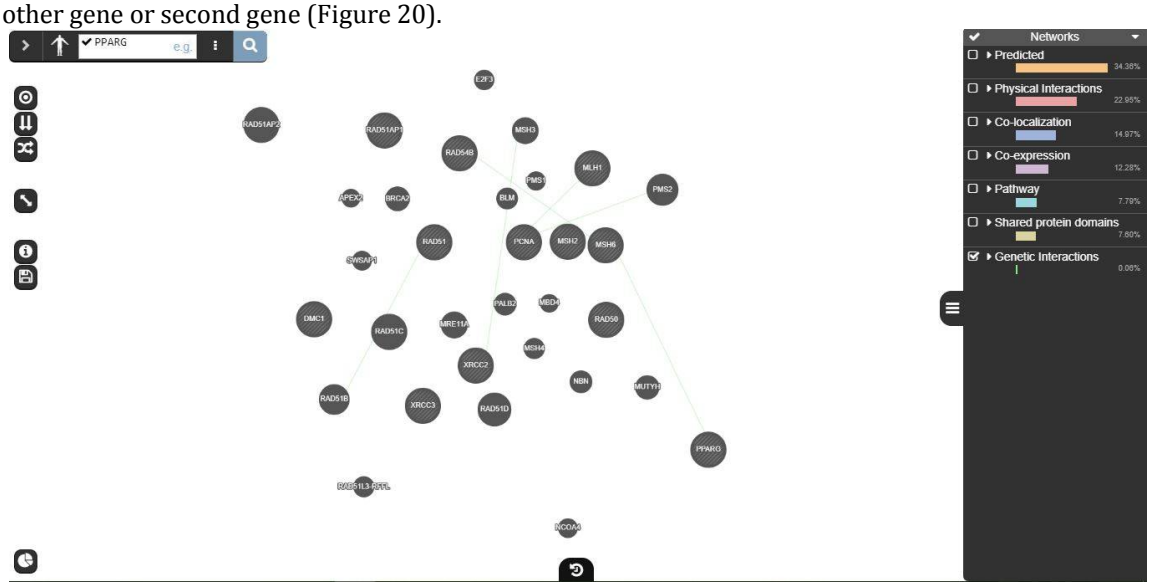


Figure 20. Gene interaction analysis of PPARγ gene.

Genetic analysis of PPARγ gene

The study indicates the association of variants with PPARγ gene. PPARγ is a protein coding genes and study indicates which variants at genetic and protein levels at different locations. Each variant can be represented with different colours. So in these variant diagram it show how many and what types of variants involved in specific gene (PPARγ). The result indicates that most of the part is covered with intron variant (Blue colour) similar to this each and every legend indicates a specific variant in the gene. And at that particular location which gene is there or any receptors is present in that particular location can be seen in different colour. All these type of variants can be occurred in different categories of each and every level like prosite pattern, prosite profiles and pfam domain.

Prosite is a database in which it consists of protein families, domains and has functional sites with of amino acids pattern and profiles. Prosite is used for identifying the function of the protein and also identify or any new discovery of protein which is different in structure and function.so we can analyse the known protein functions. And Pfam is a database which consists of accurate and exact classification of protein families and it's domains. So from known functional proteins we can have high point of efficacy (probability) to annotate the genomes.

Prints is a set or collection of finger prints. In the above diagram it provides annotation of protein families and it can be analysed by the tools. These finger prints which consists of motifs and MSA (Multiple Sequence Alignment). These motif can defined of 3 Dimensional structure for molecular binding sites. So fingerprints in which present in between of variation of sequences of family, super family and subfamily. STRING network analysis of PPARγ gene is conducted to establish functional relationship between pathway related genes (Figure 21 and 22).

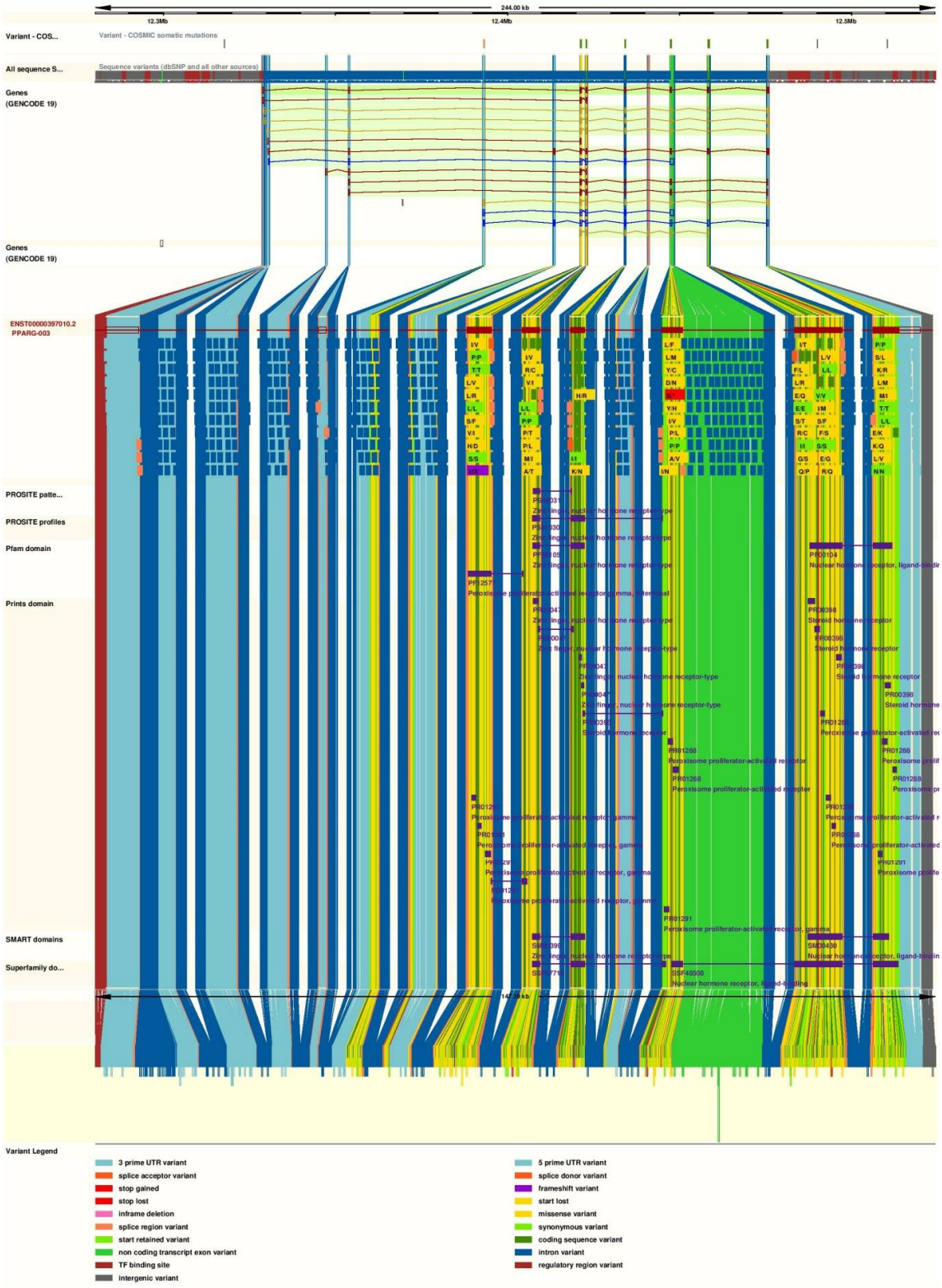


Figure 21. Genetic analysis of PPARγ gene

Edges:

Edges represent protein-protein associations	Known Interactions	Predicted Interactions	Others
associations are meant to be specific and meaningful, i.e. proteins jointly contribute to a shared function; this does not necessarily mean they are physically binding each other.	*from curated databases* *experimentally determined*	*gene neighborhood* *gene fusions* *gene co-occurrence*	*textmining* *co-expression* *protein homology*

Your Input:

		Neighborhood	Gene Fusion	Cooccurence	Coexpression	Experiments	Databases	Textmining	[Homology]	Score
PPARG	*Peroxisome proliferator-activated receptor gamma; Nuclear receptor that binds peroxisome proliferators such as hypolipidemic drugs and fatty acids. Once activated by a ligand, the nuclear receptor binds to DNA specific PPAR response elements (PPRE) and modulates the transcription of its target genes, such as acyl-CoA oxidase. It therefore controls the peroxisomal beta-oxidation pathway of fatty acids. Key regulator of adipocyte differentiation and glucose homeostasis. ARF6 acts as a key regulator of the tissue-specific adipocyte P2 (aP2) enhancer. Acts as a critical regulator of gut ho [...] (505 aa)*									

Predicted Functional Partners:

PPARGC1A	*Peroxisome proliferator-activated receptor gamma coactivator 1-alpha; Transcriptional coactivator for steroid receptors an...*					●	●	●		0.999
NCOA1	*Nuclear receptor coactivator 1; Nuclear receptor coactivator that directly binds nuclear receptors and stimulates the transcr...*					●	●	●		0.998
NCOA2	*Nuclear receptor coactivator 2; Transcriptional coactivator for steroid receptors and nuclear receptors. Coactivator of the st...*					●	●	●		0.998
CREBBP	*CREB-binding protein; Acetylates histones, giving a specific tag for transcriptional activation. Also acetylates non-histone pr...*					●	●	●		0.998
RXRA	*Retinoic acid receptor RXR-alpha; Receptor for retinoic acid. Retinoic acid receptors bind as heterodimers to their target res...*					●	●	●	●	0.997
ADIPOQ	*Adiponectin; Important adipokine involved in the control of fat metabolism and insulin sensitivity, with direct anti-diabetic, a...*						●	●		0.994
FABP4	*Fatty acid-binding protein, adipocyte; Lipid transport protein in adipocytes. Binds both long chain fatty acids and retinoic aci...*						●	●		0.991
LEP	*Leptin; Key player in the regulation of energy balance and body weight control. Once released into the circulation, has centr...*						●	●		0.991
EP300	*Histone acetyltransferase p300; Functions as histone acetyltransferase and regulates transcription via chromatin remodelin...*					●	●	●		0.990
CEBPB	*CCAAT/enhancer-binding protein beta; Important transcription factor regulating the expression of genes involved in immun...*						●	●	●	0.988

Your Current Organism:

Homo sapiens

Biological Process (GO)

GO-term	description	count in gene set	false discovery rate
GO:0019216	regulation of lipid metabolic process	8 of 373	4.69e-09
GO:0045444	fat cell differentiation	6 of 100	7.71e-09
GO:0048511	rhythmic process	7 of 250	1.02e-08
GO:0045934	negative regulation of nucleobase-containing compound m...	10 of 1424	1.73e-08
GO:0031327	negative regulation of cellular biosynthetic process	10 of 1479	1.73e-08

(more ...)

Molecular Function (GO)

GO-term	description	count in gene set	false discovery rate
GO:0051427	hormone receptor binding	9 of 174	3.46e-15
GO:0016922	nuclear receptor binding	7 of 111	5.58e-12
GO:0061629	RNA polymerase II-specific DNA-binding transcription facto...	8 of 257	7.70e-12
GO:0003682	chromatin binding	8 of 501	7.26e-10
GO:0005102	signaling receptor binding	10 of 1513	1.63e-09

(more ...)

Cellular Component (GO)

GO-term	description	count in gene set	false discovery rate
GO:0000790	nuclear chromatin	5 of 333	5.43e-05
GO:0005694	chromosome	6 of 950	0.00016
GO:0005667	transcription factor complex	4 of 326	0.00034
GO:0090575	RNA polymerase II transcription factor complex	3 of 139	0.00064
GO:0032991	protein-containing complex	9 of 4792	0.00088

(more ...)

Reference publications

publication	(year) title	count in gene set	false discovery rate
PMID:26895106	(2016) Pathway of PPAR-gamma coactivators in thermoge...	6 of 8	1.84e-12
PMID:27540349	(2016) Different anti-adipogenic effects of bio-compounds ...	8 of 93	3.21e-12
PMID:26445145	(2015) RNA-Seq Analysis of Abdominal Fat in Genetically F...	9 of 258	2.06e-11
PMID:22118082	(2011) Dietary lipid during the transition period to manipula...	6 of 17	2.06e-11
PMID:29056962	(2017) Chiglitazar Preferentially Regulates Gene Expressio...	6 of 21	3.63e-11

(more ...)

KEGG Pathways

pathway	description	count in gene set	false discovery rate
hsa04919	Thyroid hormone signaling pathway	5 of 115	1.93e-07
hsa04920	Adipocytokine signaling pathway	4 of 69	1.55e-06
hsa03320	PPAR signaling pathway	4 of 72	1.55e-06
hsa04152	AMPK signaling pathway	4 of 120	6.60e-06
hsa05016	Huntington's disease	4 of 193	3.35e-05

(more ...)

Reactome Pathways

pathway	description	count in gene set	false discovery rate
HSA-381340	Transcriptional regulation of white adipocyte differentiation	11 of 83	2.56e-24
HSA-1989781	PPARA activates gene expression	7 of 114	4.67e-12
HSA-3108232	SUMO E3 ligases SUMOylate target proteins	7 of 154	1.94e-11
HSA-1368082	RORA activates gene expression	5 of 18	1.94e-11
HSA-400253	Circadian Clock	6 of 67	1.99e-11

(more ...)

UniProt Keywords

keyword	description	count in gene set	false discovery rate
KW-0090	Biological rhythms	5 of 126	2.50e-07
KW-0010	Activator	6 of 670	1.49e-05
KW-0805	Transcription regulation	8 of 2279	6.12e-05
KW-0550	Obesity	3 of 60	6.12e-05
KW-0219	Diabetes mellitus	3 of 77	7.94e-05

(more ...)

PFAM Protein Domains

domain	description	count in gene set	false discovery rate
PF16665	Unstructured region on nuclear receptor coactivator protein	2 of 3	4.13e-05
PF09030	Creb binding	2 of 2	4.13e-05
PF08832	Steroid receptor coactivator	2 of 3	4.13e-05
PF08815	Nuclear receptor coactivator	2 of 3	4.13e-05
PF08214	Histone acetylation protein	2 of 2	4.13e-05

(more ...)

INTERPRO Protein Domains and Features

domain	description	count in gene set	false discovery rate
IPR009110	Nuclear receptor coactivator, interlocking	4 of 5	3.33e-10
IPR038547	CBP/p300, atypical RING domain superfamily	2 of 2	4.22e-05
IPR037077	Nuclear receptor coactivator, Ncoa-type, interlocking domai...	2 of 3	4.22e-05
IPR037073	Nuclear receptor coactivator, CREB-bp-like, interlocking do...	2 of 2	4.22e-05
IPR036529	Coactivator CBP, KIX domain superfamily	2 of 2	4.22e-05

(more ...)

SMART Protein Domains

domain	description	count in gene set	false discovery rate
SM01250	Histone acetylation protein	2 of 2	2.24e-05
SM01151	This domain, which is usually found tandemly repeated, is f...	2 of 3	2.24e-05
SM00551	TAZ zinc finger, present in p300 and CBP	2 of 2	2.24e-05
SM00291	Zinc-binding domain, present in Dystrophin, CREB-binding p...	2 of 19	0.00019
SM00091	PAS domain	2 of 32	0.00041

(more ...)

Statistical background

For the above enrichment analysis, the following statistical background is assumed: Whole Genome UPDATE

Figure 22: STRING analysis of PPARγ genes. Functional partner predictions were based on available experimental data, databases, text-mining, and homology.

CONCLUSION

Diabetes Mellitus is a chronic metabolic disorder caused by relatively deficiency of insulin. It can destroy the pancreatic cells. Genome-wide association data mining for identifying novel Diabetes Mellitus genes involved in cross talk with insulin signalling system and metabolomics useful for risk factors. Diagnosis of

Diabetes Mellitus is far satisfactory and it has pathways that consists of graphical diagrams and genetic interactions and also the preventive measures for Diabetes Mellitus and also find out the genetic studies i.e. of inheritance from parents and to genome. Using gene sequencing we can identify these type of metabolic disorder and also make the protein drug interactions for this disorder then we may know which drug is suitable for a particular protein. Which will not disturb other proteins. Based on WHO Diabetes is a leading disorder in world. It is place in top 10 diseases list. The present study provide useful information analysis of Diabetes Mellitus and inflammation. In future, more datasets is needed for analysis of bias process.

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