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Association analysis of Type 2 Diabetes Proteins Interaction Network

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Preamble

Diabetes is a **chronic disease** that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.

- Diabetes is classified into **Type 1** and **Type 2**

  - Type 1 diabetes (previously known as insulin-dependent, childhood-onset) is characterized by **deficient insulin production** and requires daily administration of insulin.

  - Type 2 diabetes (formerly called non-insulin-dependent or adult-onset) results from the body’s ineffective use of insulin.
Preamble

- Type 2 diabetes comprises 90% of people with diabetes around the world.

- 85 to 95 percent of the total number of diabetes cases in developed countries and an even higher percentage in developing countries.

- 347 million people worldwide have diabetes.
The drug discovery process is labor intensive and expensive in case of *In vitro* and *In vivo*.

For eradicating such hurdles and paving the way for the drugs of future, *insilico* methods have been envisaged.

In this regard, study the relation between type 2 diabetes proteins using the advanced concepts of data mining and bioinformatics.

Identifying the target proteins for a disease like Diabetes, their interactions and associations would lead to find the novel drug for this disease.
The Methodology for Type 2 Diabetes proteins interaction network

- In the present study, Association analysis of Type 2 Diabetes proteins interaction network was implemented in modular manner.

- It was divided into four modules. The procedure is as follows.

Step 1: Collect the Genes/Proteins responsible for T2D from Biological Databases

Step 2: Construct the Phylogenetic tree for T2D proteins

Step 3: Construct the Protein-Protein Interaction network for T2D proteins

Step 4: Identify the association between T2D proteins.
Block diagram of present study

- W.W.W
  - Genes Collections for T2D
    - Protein Sequences Extraction from Genes
      - ClustalW
        - Phylogenetic tree Construction
          - Protein-Protein Interaction Network
            - STRING
              - Gene Cards, NCBI

Association Analysis for T2D
Collection of Diabetes Genes/Proteins

Enter Key word “Diabetes Disease”

Pre-process the data

Prepare the data set

Find frequent patterns (proteins/genes)

Gene cards

Uniport

NCBI

Pubmed

Diabetes Disease Genes/Proteins
Proteins that have been cause to T2D

- Selected 12 genes that have been caused for Type 2 Diabetes through Text mining, Literature survey, and protein interaction networks like STRING and Genecards websites

<table>
<thead>
<tr>
<th>S.No</th>
<th>Ac. No</th>
<th>Gene Name</th>
<th>Protein Name</th>
<th>Sequence length (Amino acids)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P01308</td>
<td>INS</td>
<td>Insulin</td>
<td>110 AA</td>
</tr>
<tr>
<td>2</td>
<td>P22303</td>
<td>AChE</td>
<td>Acetylcholinesterase</td>
<td>614 AA</td>
</tr>
<tr>
<td>3</td>
<td>P06276</td>
<td>BChE</td>
<td>Butyrylcholine esterase</td>
<td>602 AA</td>
</tr>
<tr>
<td>4</td>
<td>P06213</td>
<td>INSR</td>
<td>Insulin receptor</td>
<td>1382 AA</td>
</tr>
<tr>
<td>5</td>
<td>P05067</td>
<td>APP</td>
<td>Amyloid beta A4 protein</td>
<td>770 AA</td>
</tr>
<tr>
<td>6</td>
<td>P02649</td>
<td>APOE</td>
<td>Apolipoprotein E</td>
<td>317 AA</td>
</tr>
<tr>
<td>7</td>
<td>P28329</td>
<td>CHAT</td>
<td>Choline O-acetyltransferase</td>
<td>748 AA</td>
</tr>
<tr>
<td>8</td>
<td>P14735</td>
<td>IDE</td>
<td>Insulin-degrading enzyme</td>
<td>1019 AA</td>
</tr>
<tr>
<td>9</td>
<td>P01275</td>
<td>GCG</td>
<td>Glucagon</td>
<td>180 AA</td>
</tr>
<tr>
<td>10</td>
<td>P41159</td>
<td>LEP</td>
<td>Leptin</td>
<td>167 AA</td>
</tr>
<tr>
<td>11</td>
<td>P27169</td>
<td>PON1</td>
<td>Serum paraoxonase/arylesterase 1</td>
<td>355 AA</td>
</tr>
<tr>
<td>12</td>
<td>P05019</td>
<td>IGF1</td>
<td>Insulin-like growth factor I</td>
<td>195 AA</td>
</tr>
</tbody>
</table>
From the Phlogenetic analysis it is observed that
1. LEP and CHAT play significant role in T2D because both proteins have highest scores 0.45884 and 0.45406 respectively.
2. AChE, BChE, and Insulin proteins have close distance and similar sequence
3. APP & APOE, IDE & GCG, and INSR & PON1 have similar protein sequence
4. Finally twelve proteins have to be divided into two classes. One class has AChE, BChE and Insulin proteins and another class has remaining nine proteins.
Protein-Protein Interaction Network

- Protein-protein interaction refers to the association of protein molecules.

- Protein-Protein interaction information is essential for a systems level understanding of cellular behavior and is needed to place the molecular function of individual proteins into their cellular context.

- These networks provide a global view of the interactions between various proteins that are essential for the accomplishment of most protein functions.

- Finally, this information helpful to find the drug for disease through target proteins and ligand.
From the above BChE Interaction network diagram, it is observed that

- BChE interact with INS and GCG
From the AChE Interaction network diagram, it is observed that

- AChE interact with APP and CHAT
From the INS Interaction network diagram, observed that

- INS interact with IDE and INSR
From the LEP Interaction network diagram, observed that

- LEP interact with GCG and INS
From the CHAT Interaction network diagram, observed that

- CHAT interact with AChE
From the APP Interaction network diagram, observed that

- APP interact with APOE
Observations from Protein-Protein Interaction Networks

From the above all Protein-Protein Interaction network diagrams, it is observed that

1. BChE interact with INS and GCG
2. AChE interact with APP and CHAT
3. INS interact with IDE and INSR
4. LEP interact with GCG and INS
5. CHAT interact with AChE
6. APP interact with APOE
Conclusion

- In the present work we tried to outline the association analysis that could be performed to arrive at the relationship and association between T2D proteins.

- It is observed that BChE, Insulin, Chat and LEp are plays key role in T2D diabetes through phylogenetic and proteon protein interaction networks.

- BChE functionality in humans is not clear.

- In future, studies of this nature may pay way for in silico protein-protein interaction experiments that be extended to develop for new therapeutic interventions.
Conclusion

- We will going to develop novel method, which extracts the highly ranked target proteins and most important pathways when given disease genes as input.

- The construction protein-protein interaction by using another novel new method call dynamic programming approach.

- Finally prune the network and identify the target protein/proteins for specified disease.


References (2)


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