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In-Silico Investigation of *Lablab Purpureus* Phytoconstituents Against Neurodegenerative Disease Using Network Pharmacology

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ABSTRACT

Neurodegenerative diseases are progressive and debilitating disorders defined by neuronal death and inhibition of central nervous system functions. These include Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis. These disorders have common pathological mechanisms consisting of oxidative stress, chronic neuroinflammation, mitochondrial dysfunction, calcium dysregulation, and activation of apoptotic pathways. The multifactorial complexities of these disorders render conventional mono-targeting-type medicines inefficient in tackling such flaws. From this perspective, network pharmacology provides a systems-level understanding of the multiple therapeutic potential targets of natural compounds.

The present study was conceptualized to investigate the neuroprotective potential of Lablab purpureus against 5 major neurodegenerative diseases through an integrated network pharmacology strategy. Bioactive compounds of Lablab purpureus were first screened, and their pharmacokinetic properties, including ADME parameters, were evaluated using the SwissADME database for drug-likeness and oral bioavailability. The potential molecular targets of the selected phytocompounds were predicted using Binding DB and the relevant target prediction platforms. Likewise, disease-associated targets corresponding to Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis were retrieved from the databases, and intersecting targets were identified to ascertain the common therapeutic nodes.

Finally, PPI (Protein-Protein Interaction) analysis was carried out using the STRING database, with a network of interactions being generated using the Cytoscape software package. Finally, thirty such hub genes were estimated based on degree centrality and associated topological parameters. After enrichment analysis, including the GO and KEGG pathways, it was determined that the involved pathways include PI3K-Akt signalling, calcium signalling pathway, and PPAR signalling pathway, including disease-specific neurodegenerative pathways, especially associated with Alzheimer's and Parkinson's diseases. Significantly, these pathways have been intrinsically associated with the regulation of neuroinflammatory cascades, repression of reactive oxygen species (ROS) production, modulation of the apoptotic cascade, and stimulation of neuronal survival. The involvement of these pathways, PI3K-Akt and PPAR, also implies that Lablab purpureus may have a role in neuroprotection through attenuation of ROS production, regulation of neuroinflammatory processes, and apoptotic signalling conducive to neuronal survival. To conclude, the present findings demonstrate that Lablab purpureus holds a multi-component, multi-target therapeutic potential against the major neurodegenerative disorders. The current study opens up opportunities for future experimental investigations, using network pharmacology as a basis for identifying and developing plant-based neuroprotective agents.

Keywords: Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), Amyotrophic Lateral Sclerosis (ALS), and Multiple Sclerosis (MS), *Lablab purpureus,* Kyoto Encyclopedia of Genes and Genomes (KEGG), Gene Ontology (GO)..

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INTRODUCTION

Neurodegenerative diseases are a heterogeneous group of chronic, progressive disorders characterised by the loss of structure or function of neurons, leading to cognitive and motor dysfunction. Disorders growing global health challenge due to increasing life expectancy and the demographic shift toward an ageing population. At the cellular level, mechanisms such as protein folding and aggregation, oxidative stress, mitochondrial dysfunction, and impaired neuronal homeostasis in the pathogenesis of many neurodegenerative conditions, including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS).Parkinson's disease (PD) is primarily a movement disorder caused by the degeneration of dopaminergic neurons in the substantia nigra, causing tremor, rigidity, bradykinesia, and postural instability. Estimates from large-scale neurological burden studies suggest that approximately 770,000 people were living with PD in India in 2019, with prevalence increasing significantly in older age groups. Emerging clinical observations suggest diagnosis in younger cohorts is becoming more common, underscoring the need for localised epidemiologic data.

Huntington's Disease (HD) is a rare, autosomal-dominant neurodegenerative disorder characterised by involuntary movements (chorea), psychiatric symptoms, and cognitive decline. Systematic epidemiologic data from India are limited, but available clinic-based estimates suggest prevalence rates in the range of approximately 3–5 per 100 000 persons, potentially representing tens of thousands of affected individuals nationwide.

Amyotrophic Lateral Sclerosis (ALS) is a rapidly progressive motor neuron disease affecting both upper and lower motor neurons, leading to muscle weakness, atrophy, and eventual respiratory failure. Indian population studies report ALS prevalence at approximately 3–5 per 100 000 population, with higher incidence in middle and older age groups and a slight male predominance.

Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disorder of the central nervous system, clinically distinct from the classical protein-aggregation neurodegenerative diseases. Although less extensively studied in India, registry and cohort data suggest a crude prevalence of approximately 10–20 per 100 000 population, with rising diagnosis rates likely reflecting improved access to diagnostic imaging and case ascertainment.

Collectively, neurodegenerative disorders in India represent a substantial and expanding component of the non-communicable disease burden. According to recent Global Burden of Disease analyses, AD and related dementias, PD, MS, and motor neuron diseases together contribute significantly to disability-adjusted life years in the Indian population, with prevalence and burden projected to rise further with ongoing demographic transitions.Natural products derived from herbal medicines have recently attracted considerable attention as potential therapeutic agents for neurodegenerative disease. Lablab purpureus (L.) Sweet, commonly known as hyacinth bean, is a medicinal plant traditionally used in various systems of medicine and is rich in bioactive phytoconstituents such as flavonoids, phenolic acids, saponins, and alkaloids. Extracts and isolated compounds from Lablab purpureus have been reported to possess a broad spectrum of pharmacological activities, including anti-inflammatory, antioxidant, neuroprotective, and anti-apoptotic effects.

Recent studies suggest that the phytochemicals present in Lablab purpureus may exert beneficial effects in neurodegenerative disorders. Collectively, these multifaceted actions suggest that Lablab purpureus, through its multitargeted pharmacological profile, holds promise as a potential therapeutic agent for the management of neurodegenerative disease and may offer advantages over conventional single-target treatments.

Network pharmacology, an emerging discipline grounded in systems biology, integrates polypharmacology, molecular network analysis, bioinformatics, and computational modelling. Because it is designed to elucidate the complex interactions of multitarget drugs, network pharmacology is particularly well-suited for

investigating the mechanisms underlying Lablab purpureus's anti-AD effects. In the present study, we applied network pharmacology to clarify the detailed mechanisms by which Lablab purpureus may act against AD.

MATERIALS AND METHODS:

PHARMACOKINETIC PROPERTIES AND TOXICITY PREDICTION:

To obtain the active ingredients of Lablab purpureus, an initial screening based on the absorption, distribution, metabolism, and excretion (ADME) properties [oral availability and drug-likeness], was conducted by using SwissADME https://swissadme.ch database.

OB represents the proportion of oral medication absorbed into the circulation, and DL is a filter to exclude the non-drug-like molecules.

These early-stage pharmacokinetic evaluations are of vital importance to reduce the probability of unsuccessful drug discovery.

The names and structure formulas of compounds were verified using the PubChem https://pubchem.ncbi.nlm.nih.gov database, and the concentration of active components in this study was retrieved from literature and IMPPAT: Indian Medicinal Plants, Phytochemistry and Therapeutics database.

PREDICTION OF LABLAB PURPUREUS TARGETS:

The active compounds are retrieved from the IMPPAT IMPPAT | IMPPAT: Indian Medicinal Plants, Phytochemistry And Therapeuticsdatabase and the SMILES are collected and imported into the BindingDB https://www.BindingDB.org database to predict all potential targets of Lablab purpureus.The gene symbols of the potential target were obtained by searching the Uniprot (https://www.uniprot.org) database.

DISEASE TARGETS ACQISITION OF NEURODEGENERATIVE DISEASE:

Using disease names AD, PD, HD, ALS, and MS as keywords, the disease gene was searched and screened by the following electronic databases: GeneCard (GeneCards - Human Genes | Gene Database | Gene Search)database, OMIM database (https://www.omim.org), PharmGKB (ClinPGx)database, DrugBankData (https://go.drugbank.com). Then, through the UniProt (https://www.uniprot.org) database corrected their protein names as official names and defined the species source as human.

SCREENING OF INTERSECTION TARGETS:

To clarify the interaction between disease-related targets and potential targets, we intersected the disease targets and Lablab purpureus targets and drew the Venn diagrams with an online Venn diagram tool (http://bioinfogp). After this, the Panther Classification System performed protein classification of the lablab purpureus-related anti-disease targets (http://www.pantherdb.org).

PROTEIN-PROTEIN-INTERACTION NETWORK ANALYSIS:

We acquired the common targets of the drug and disease by intersection and then constructed a Protein-Protein-Interaction (PPI) network on the STRING database (https://string-db.Org). Set the biological species as "Homo sapiens" and hide the unconnected nodes. In addition, the network topology parameters were visualized and analyzed by cytoscape3.7.2 to identify the core targets.

The Degree value represents the number of nodes connected by a node, so the higher the Degree of a node, the more important it is in the network.If there were too many targets, a PPI core network would be extracted twice with nodes whose Degree, Betweenness centrality (BC), and Closeness centrality (CC) values were all greater than the median.

GO AND KYOTO ENCYCLOPEDIA OF GENES AND GENOMES

(KEGG) ENRICHMENT ANALYSIS:

To illustrate the targets on a systematic level, the Gene Ontology Biological Process (GOBP) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were carried out on the Enrichr platform and KEGG Mapper.The visualisation of **GO** and **KEGG** pathway enrichment analysis for green module genes from the Bioconductor project. The level of significance was set to $P < 0.05$ for all the tests. The top relevant enriched **GO** and **KEGG** terms were visualised using an online tool (http://www.bioinformatics.com.cn/).

INGREDIENT-TARGET-PATHWAY NETWORK ANALYSIS:

To investigate the interaction among the active ingredients, common targets and the key **KEGG** pathway, the Ingredient Target-Pathway (I-T-P) network of Lablab purpureus for AD was constructed and visualised by **CytoScape3.7.2**.

The main active components were judged according to the network topology parameters, which were analysed by the built-in network analyser.

Then, collect the results obtained from Microsoft Excel.

MOLECULAR DOCKING:

Molecular docking analysis was performed through AutoDockTools for exploring the interaction of bioactive compounds from Lablab purpureus and the selected target protein. The three-dimensional structure of the protein was obtained from the protein data bank. The docking simulations were done three times for every drug to ensure the results are consistent and reproducible. Its chemical structure making the selected phytoconstituent of Lablab purpureus was obtained from the PubChem database. Finally, the docking poses and interaction patterns were examined using Molegro Molecular Viewer. Detailed representation on hydrogen bonding and hydrophobic interaction is carried out using Molegro Molecular Viewer.

RESULTS:

THE PHARMACOKINETIC PROPERTIES AND TOXICITY PREDICTION OF LABLAB PURPUREUS

The structural information of Lablab purpureus was obtained from KingDraw (Figure 1), and the relevant ADME information was obtained from **swissADME https://swissadme.ch** database.

This database shows the **SwissADME** predicted pharmacokinetics of the lablab purpureus, including topological polar surface area and Lipinski rule of 5. The results showed that Lablab purpureus complies with the Lipinski rule of 5 and is predicted to have a good drug-likeness.

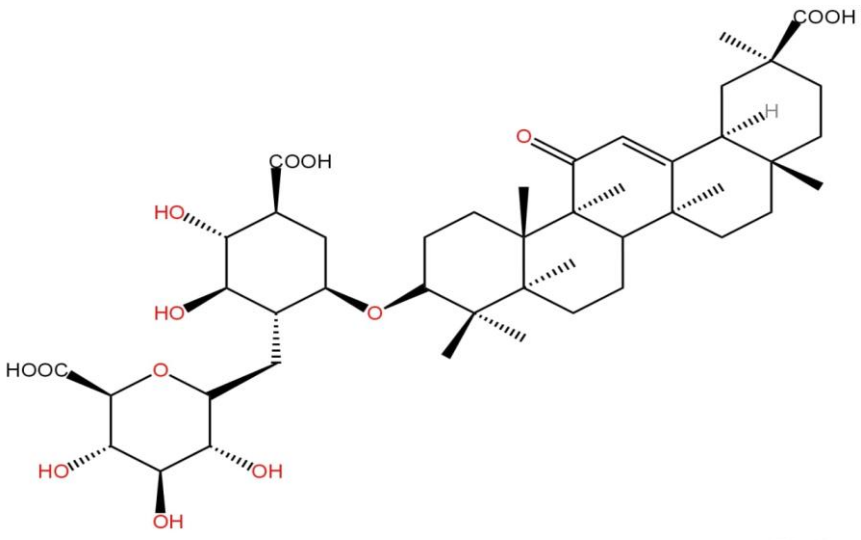


Figure 1: Structure Of Lablab purpureus

SCREENING OF TARGETS OF LABLAB PURPUREUS AGAINST NEURODEGENERATIVE DISEASE:

ALZHEIMER'S DISEASE:

To identify the lablab purpureus-associated targets, 292 targets were collected from **Binding DB** and IMPPAT. In addition, A total of 15,405 disease-related targets was obtained from **Gene Card, Malacards, ClinVar, OMIM**, and **PharmGBK**. Based on the above results, we identified 102 targets of Lablab purpureus against AD by the intersection of 292 Lablab purpureus-associated targets and 15,405 disease-related targets.

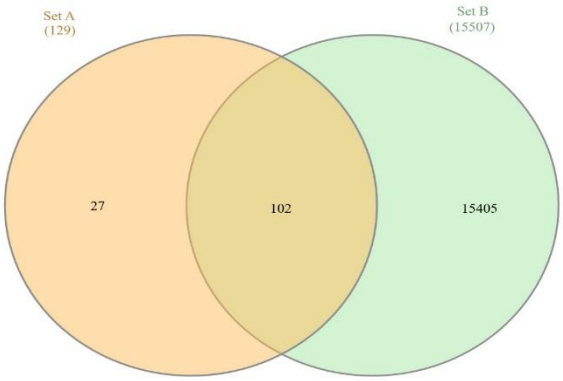


Figure 2: Venn diagram of Alzheimer's disease

PARKINSON DISEASE:

To identify the lablab purpureus-associated targets, 292 targets were collected from **Binding DB** and **IMPPAT.** In addition, A total of 15,974 disease-related targets was obtained from **Gene Card, Malacards, ClinVar, OMIM,** and **PharmGBK**.

Based on the above results, we identified 92 targets of Lablab purpureus against PD by the intersection of 292 Lablab purpureus-associated targets and 15,974 disease-related targets.

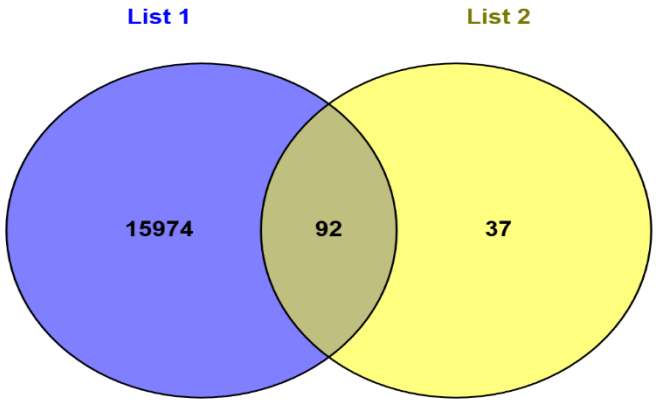


Figure 3: Venn diagram of Parkinson disease

HUNTINGTON DISEASE:

To identify the lablab purpureus-associated targets, 292 targets were collected from **Binding DB** and **IMPPAT**. In addition, A total of 11,762 disease-related targets was obtained from **Gene Card, Malacards, ClinVar, OMIM, and PharmGKB**. Based on the above results, we identified 77 targets of Lablab purpureus against HD by the intersection of 292 Lablab purpureus-associated targets and 11,762 disease-related targets.

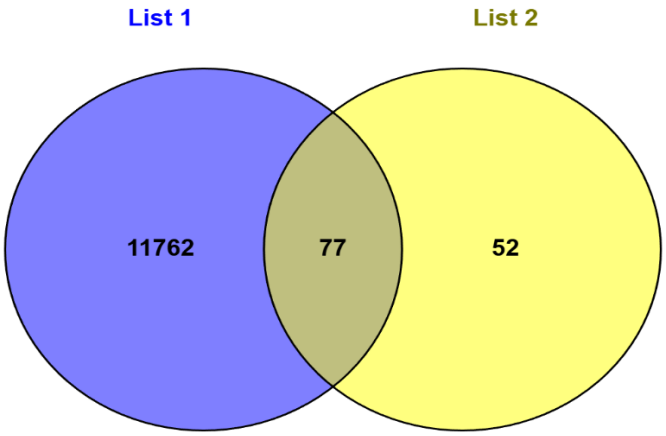


Figure 4: Venn diagram of Huntington disease

AMYOTROPHIC LATERAL SCLEROSIS:

To identify the lablab purpureus-associated targets, 292 targets were collected from **Binding DB** and **IMPPAT**. In addition, A total of 27676 disease-related targets were obtained from **Gene Card, Mala cards, ClinVar, OMIM,** and **PharmGKB**. Based on the above results, we identified 102 targets of Lablab purpureus against ALS by the intersection of 292 Lablab purpureus-associated targets and 27676 disease-related targets.

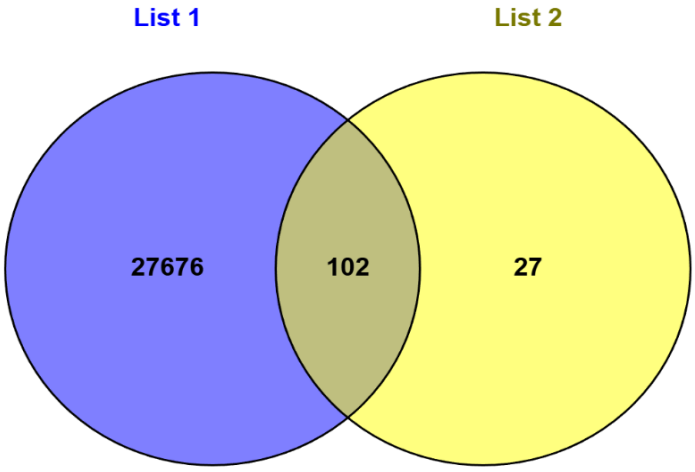


Figure 5: Venn diagram of amyotrophic lateral sclerosis disease

MULTIPLE SCLEROSIS:

To identify the lablab purpureus-associated targets, 292 targets were collected from **Binding DB** and **IMPPAT**. In addition, A total of 22769 disease-related targets were obtained from **Gene Card, Mala cards, ClinVar, OMIM,** and **PharmGKB**. Based on the above results, we identified 98targets of Lablab purpureus against MS by the intersection of 292 Lablab purpureus-associated targets and 22769 disease-related targets

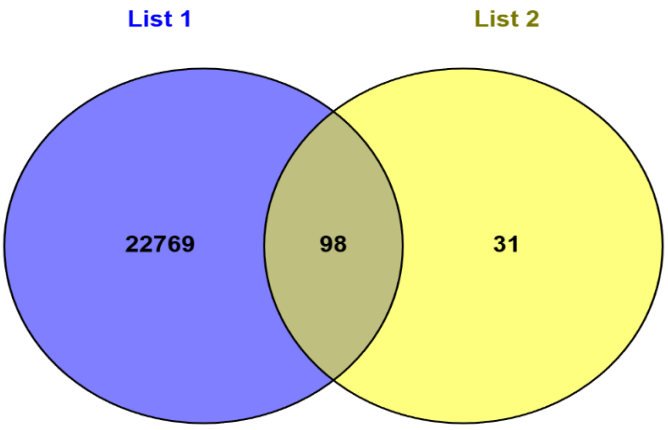


Figure 6: Venn diagram of Multiple sclerosis disease.

CONSTRUCTION AND ANALYSIS OF PPI NETWORK OF LABLAB PURPUREUS:

PPI NETWORK OF ALZHEIMER DISEASE:

The PPI network was constructed using the **cytoscape3.7.2** based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyser, and the top10 targets were selected as core targets. The top 10 targets were; CYP1A1, CYP1A2, HMGCR, PPARD, ABCG2, RXRA, MAOA, ESR2, IGF1R, FGF2. Taken together, the above results imply this core targets may play a Critical Role in AD treatment.

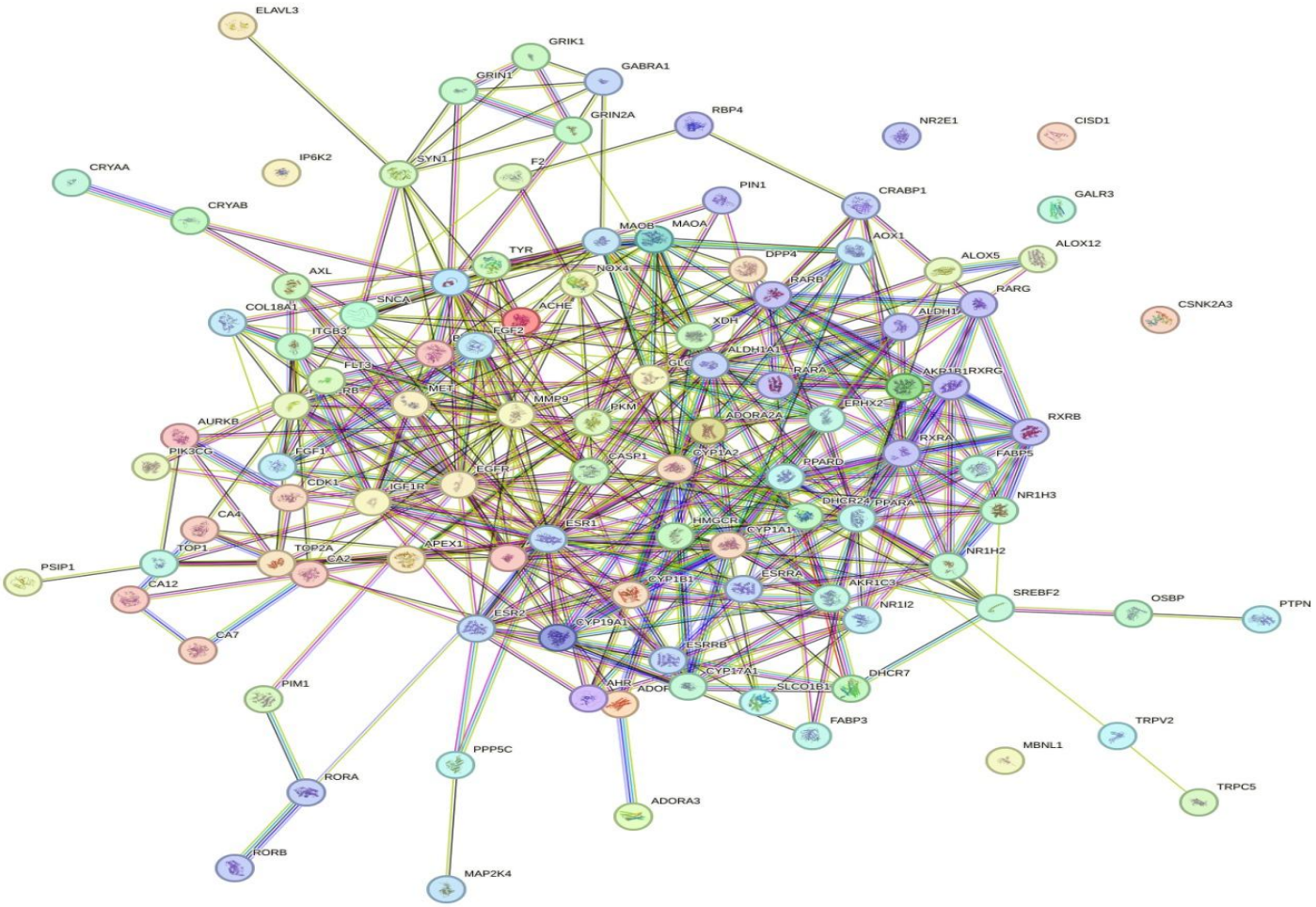


Figure 7: STRING of Alzheimer's disease

PPI NETWORK OF PARKINSON DISEASE:

The PPI network was constructed using the **cytoscape3.7.2** based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyser, and the top10 targets were selected as core targets. The top 10 targets were CYP1A1, CYP1A2, ALDH1A1, HMGCR, PPARD, ABCG2, ESR2, IGF1R, MET, FGF2.Taken together, the above results imply this core targets may play a Critical Role in PD treatment.

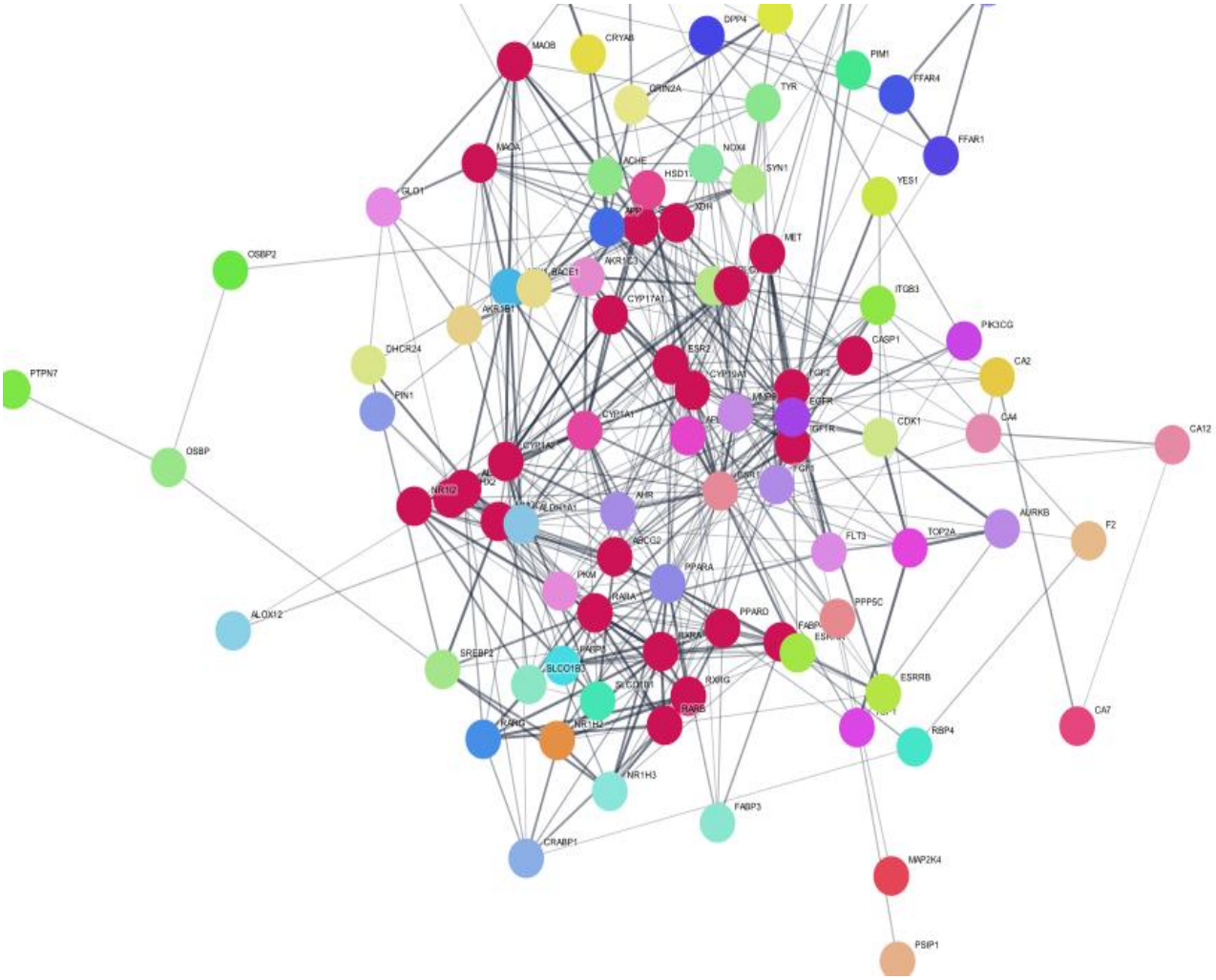


Figure 8: STRING of Parkinson disease

PPI NETWORK OF HUNTINGTON DISEASE:

The PPI network was constructed using the **cytoscape3.7.2** based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyser, and the top10 targets were selected as core targets. The top 10 targets were PPARA, MAOA, PPARD, ALDH1A1, FGF2, HMGC2, SNCA, ABCG2, MAOB, and CYP1A2. Taken together, the above results imply this core targets may play a Critical Role in HD treatment.

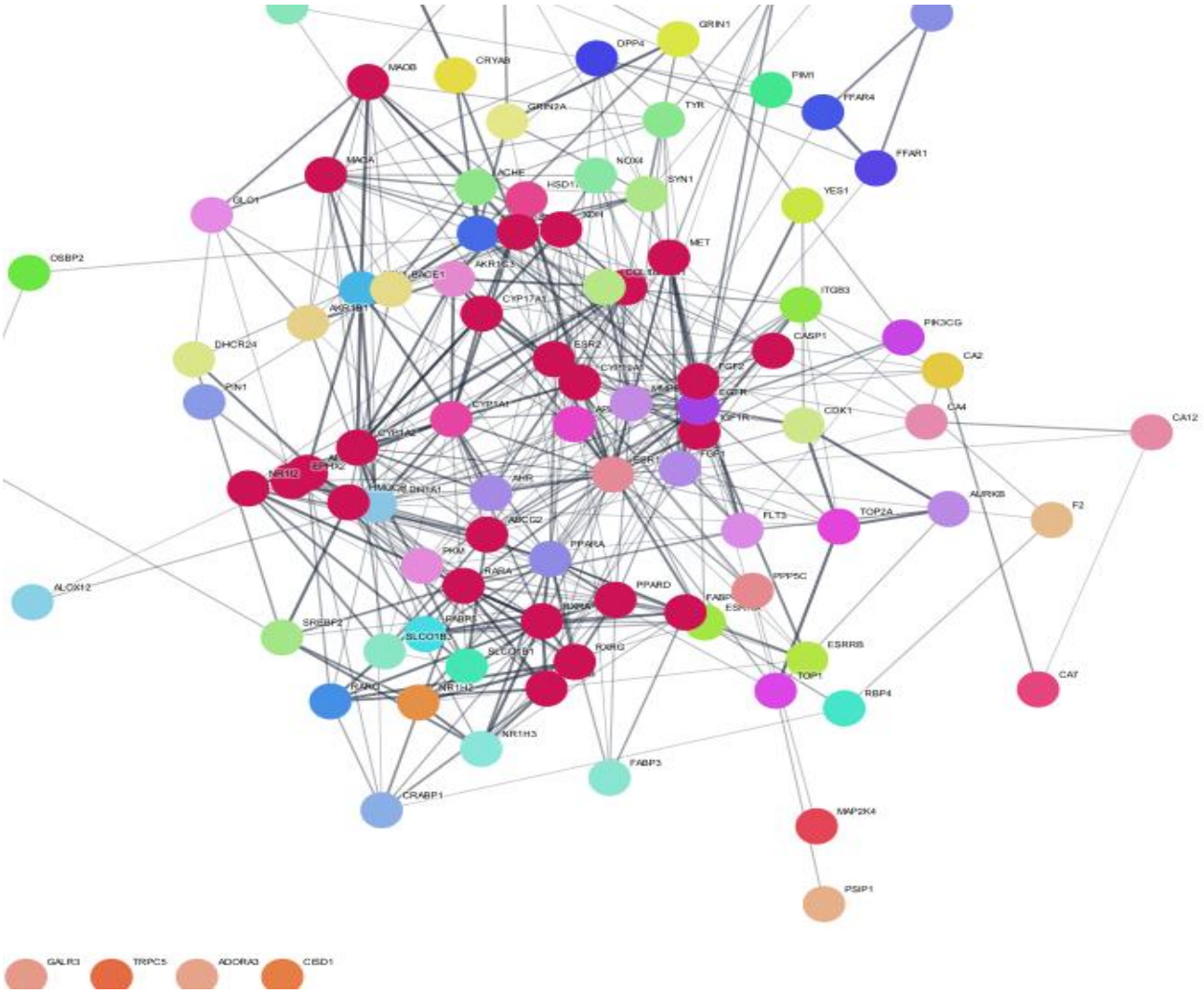


Figure10: STRING of Amyotrophic lateral sclerosis disease

PPI NETWORK OF MULTIPLE SCLEROSIS DISEASE:

The PPI network was constructed using the cytoscape3.7.2 based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyzer, and the top10 targets were selected as core targets. The top 10 targets were NR1H78, CYP1A2, NR1H65, NR1H54, ESR2, NR1H40, RXRA, FGF2, MET. Taken together, the above results imply these core targets may play a Critical Role in MS treatment.

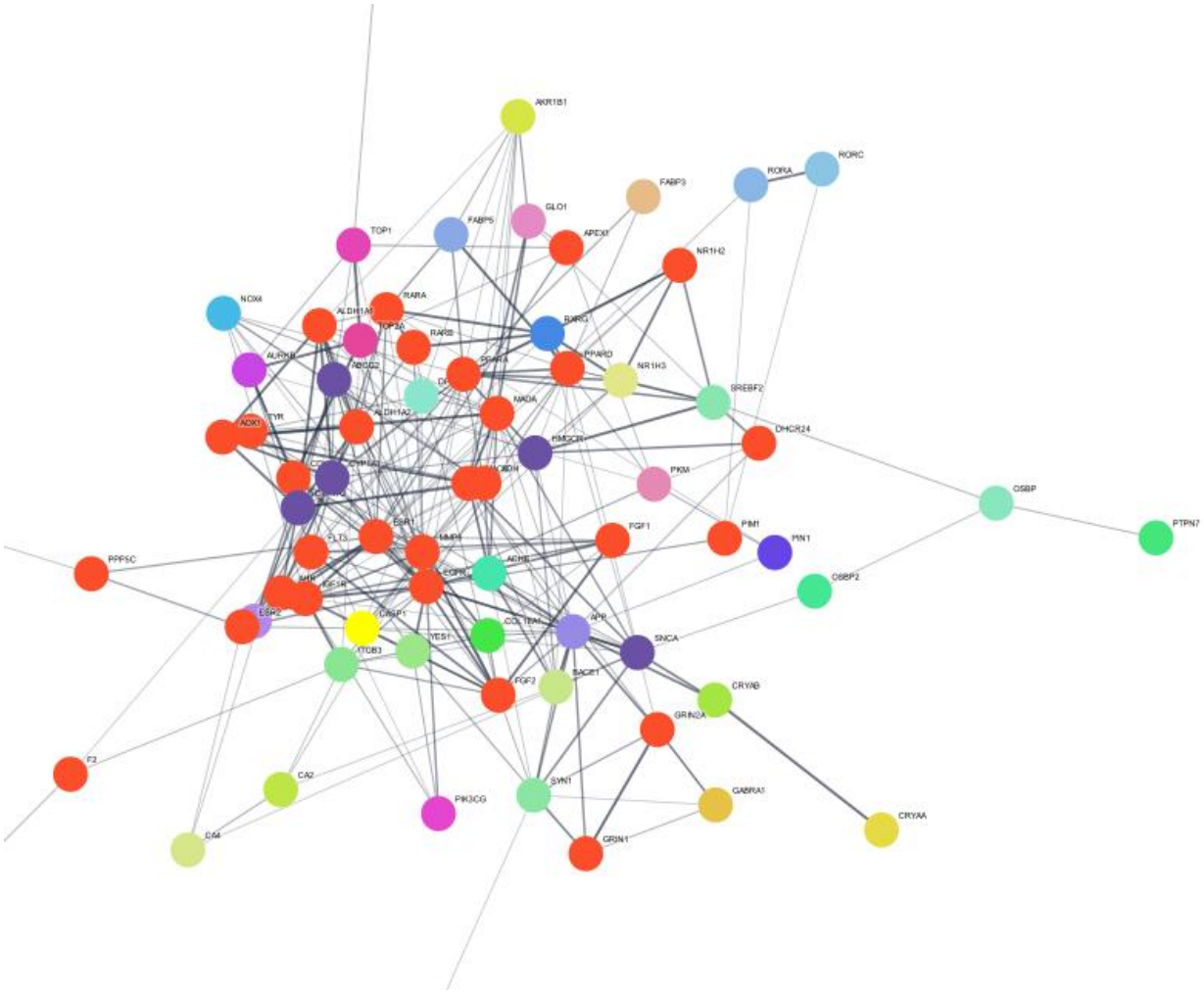


Figure 9: STRING of Huntington disease

PPI NETWORK OF AMYOTROPHIC LATERAL SCLEROSIS DISEASE:

The PPI network was constructed using the **cytoscape3.7.2** based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyser, and the top10 targets were selected as core targets. The top 10 targets were CYP1A2, HMCGR, PPARD, ABCG2, RXRA, ESR2, MAOA, FGF2, MET, IGF1R Taken together, the above results imply this core targets may play a Critical Role in ALS treatment.

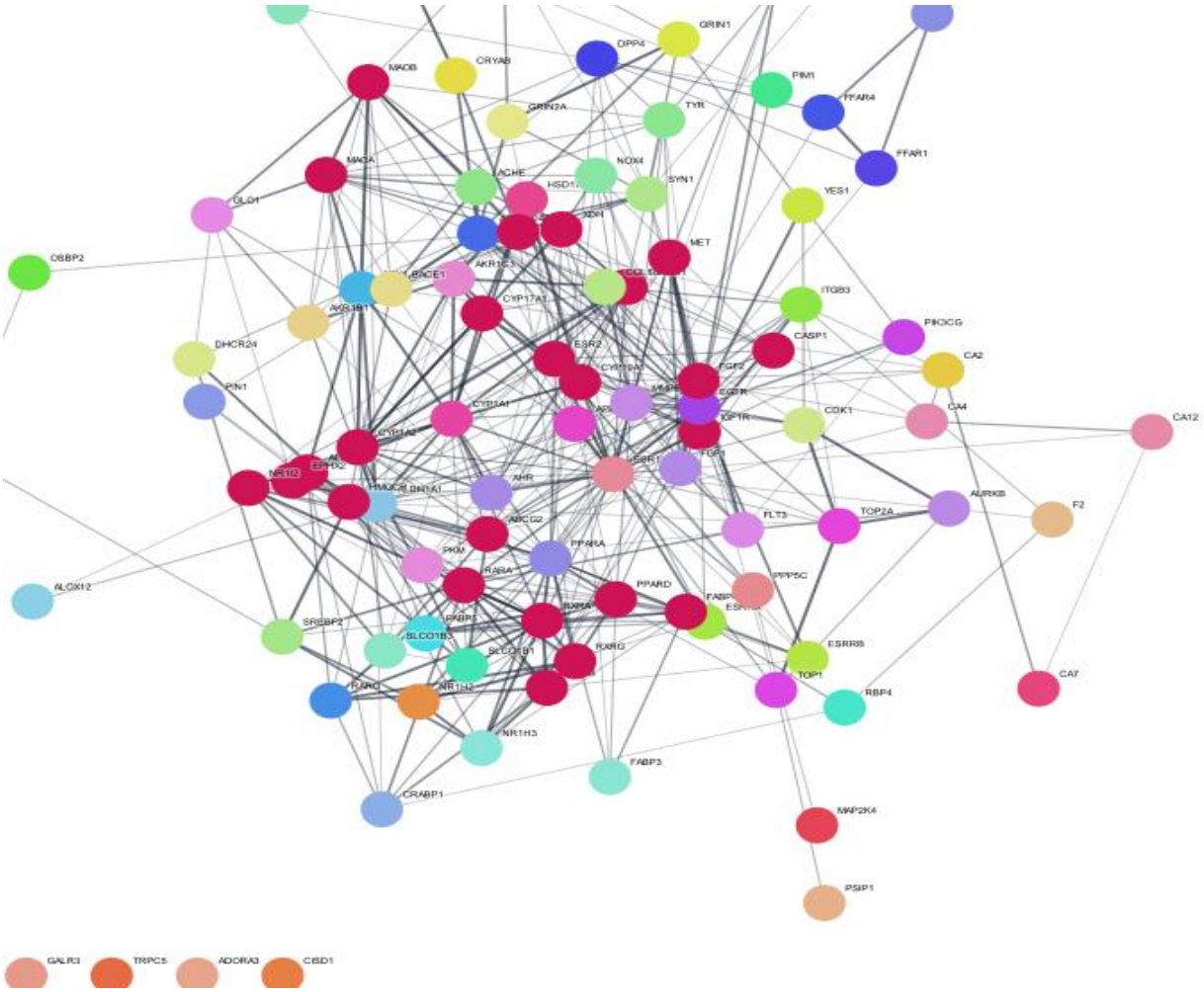


Figure10: STRING of Amyotrophic lateral sclerosis disease

PPI NETWORK OF MULTIPLE SCLEROSIS DISEASE:

The PPI network was constructed using the **cytoscape3.7.2** based on the obtained PPI relationships. In this PPI network, the degree was calculated by the Network Analyzer, and the top10 targets were selected as core targets. The top 10 targets were NR1H78, CYP1A2, NR1H65, NR1H54, ESR2, NR1H40, RXRA, FGF2, MET. Taken together, the above results imply these core targets may play a Critical Role in MS treatment.

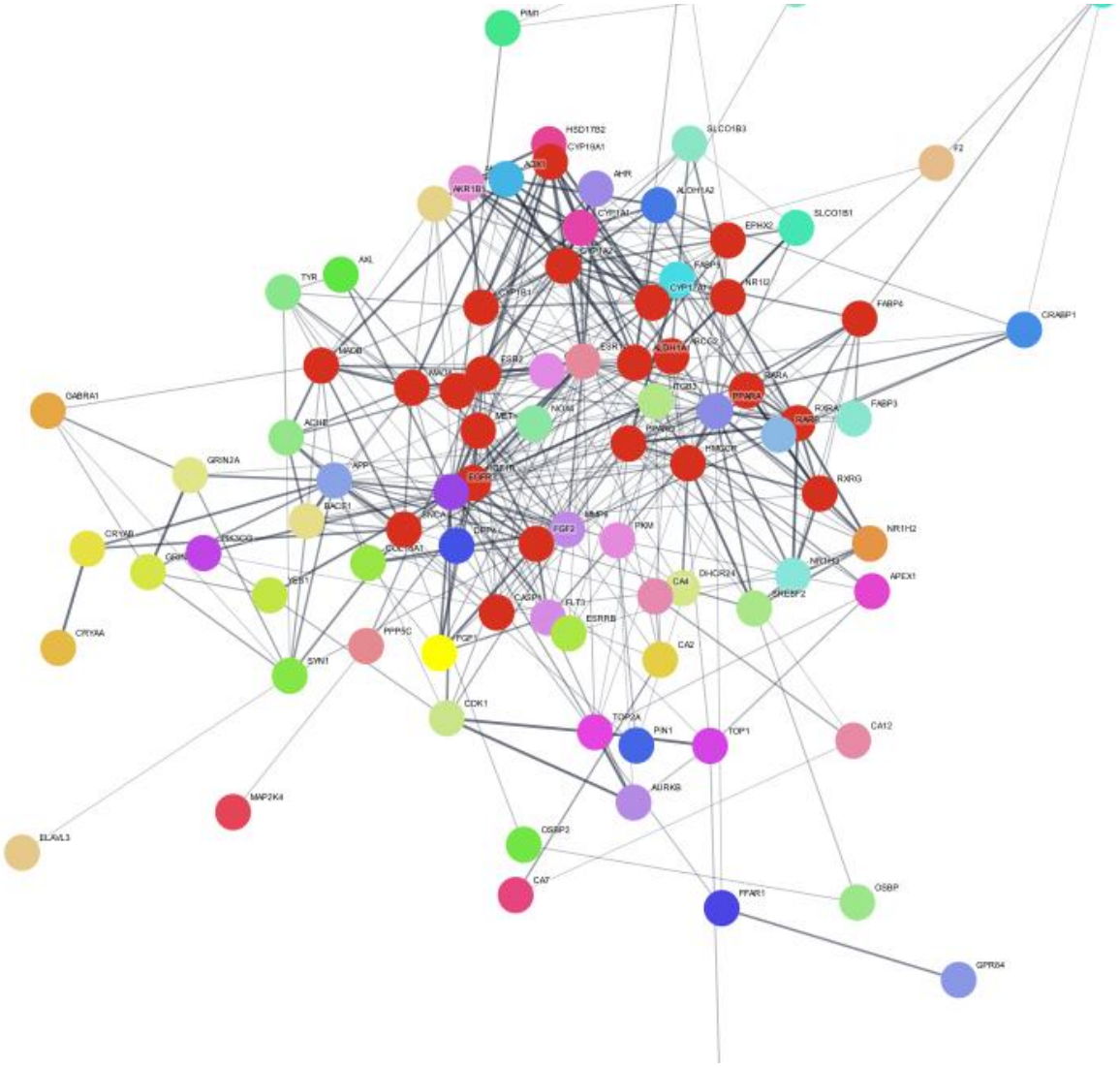


Figure11: STRING of Multiple sclerosis disease

PANTHER CLASSIFICATION SYSTEM:

IN ALZHEIMER DISEASE:

Moreover, these 30 genes were classified into distinct classes using the Panther Classification System. The top 7 protein classes were transmembrane signal receptor (3%,17.6%,15.8%), intercellular signal molecule (1,5%.3,5%.9%), transporter (1,5%.3%,5.9%), gene-specific transcriptional regulator (9%,47.4%,52.9%), cell adhesion molecules (1,5.3,5.9), membrane traffic protein (2%,10.5%,11.8%). Among the protein-modifying enzymes and metabolite interconversion enzymes, ITGB3 is a cell adhesion molecule; RARA, ESR2, PPARD, RARB, NR1H2, RXRB, RXRG, NR1I2, RXRA are gene-specific transcriptional regulator; FGF2 are intercellular signal molecule; SYN1, SNCA are membrane traffic protein; XDH, ALDH1A2, ACHE, CYP1A2, MAOA, CYP1A1, HMGCR, MAOB, CYP19A1, CYP1B1, EPHX2 are metabolite interconversion enzyme; PDGFRB, MET, IGFIR are transmembrane signal receptor; ACHE, ABCG2 are transporter.

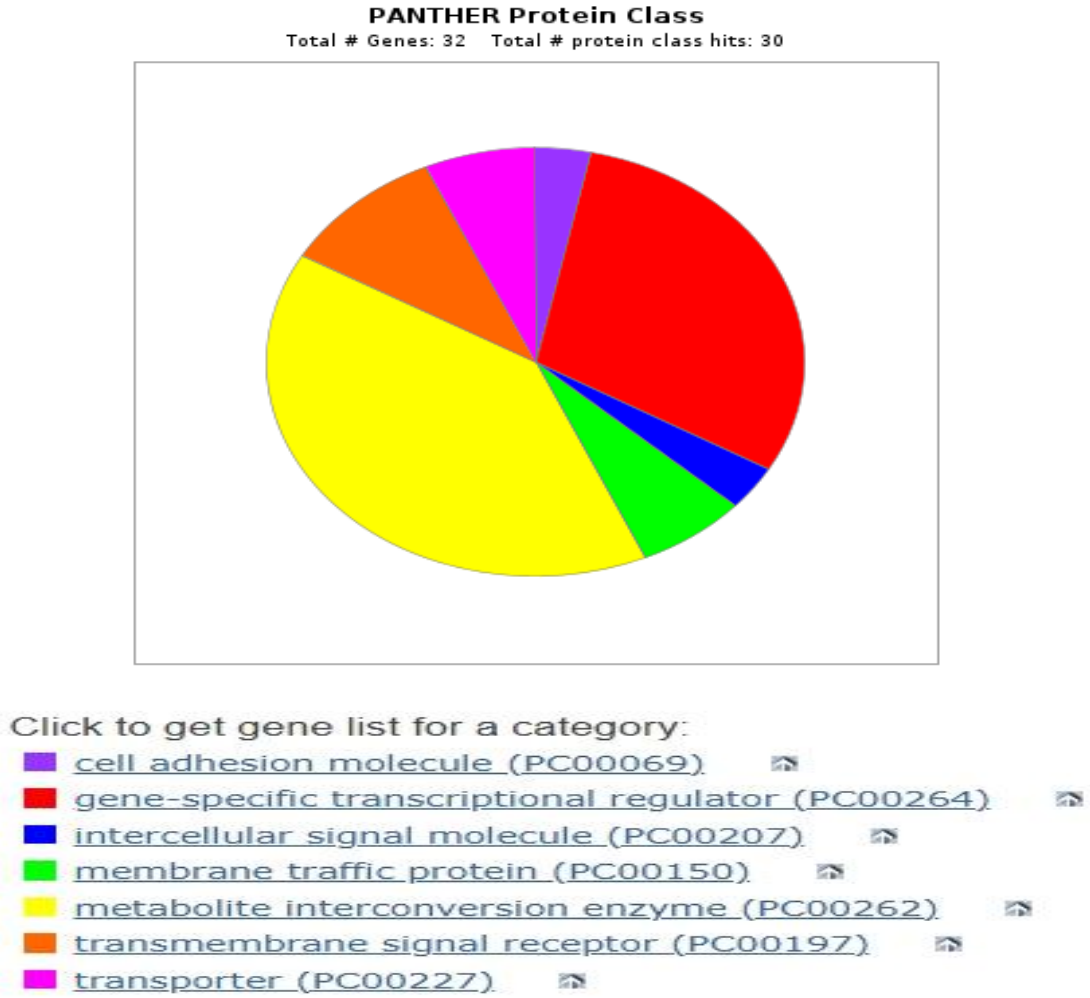


Figure12: protein classes of 30 hub genes of Alzheimer disease

IN PARKINSON DISEASE:

Moreover, these 21 genes were classified into distinct classes using the Panther Classification System. The top 6 protein classes were gene-specific transcriptional regulator (5%;22.7%;23.8%) intercellular signal molecule (1%;4.5%;4.8%) membrane traffic protein (1%;4.5%;4.8%) metabolite interconversion enzyme (11%;50.0%;52.4%) transmembrane signal receptor (2%;9.1%;9.5%) transporter (1%;4.5%:4.8%). Among the protein-modifying enzymes and metabolite interconversion enzymes, RARA, ESR2, PPARD, NR1I2, RXRA are gene-specific transcriptional regulators; FGF2 are intercellular signal molecules; SNCA are membrane traffic proteins; XDH, CYP1A2, ALDH1A1, MAOA, CYP1A1, HMCGR, MAOB, CYP19A1, CYP1B1, FPHX2 are metabolite interconversion enzymes; MET, IGF1R are transmembrane signal receptor; ABCG2 are transporters.

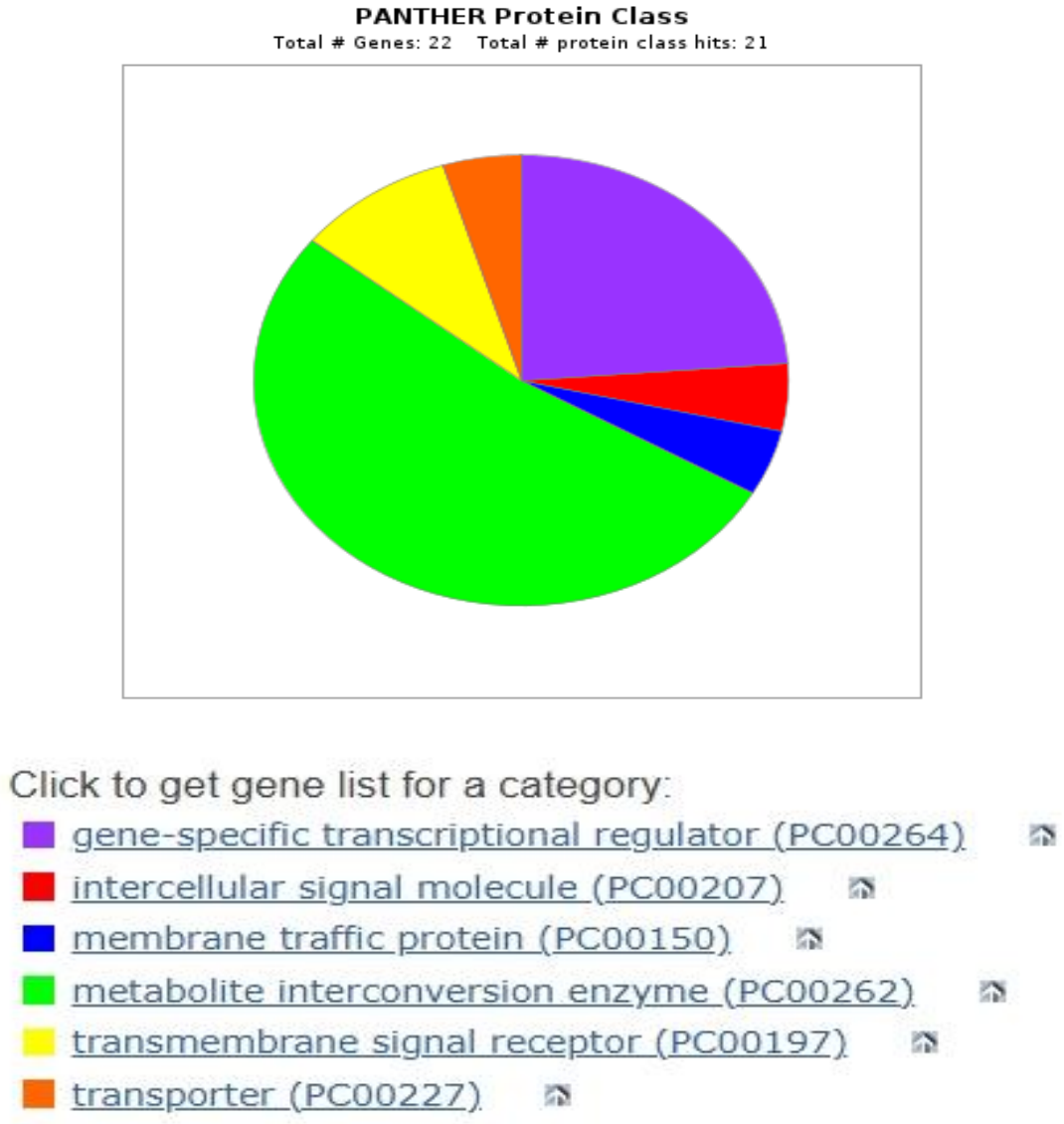


Figure 13: protein classes of 21 hub genes of Parkinson disease

IN HUNTINGTON DISEASE:

Moreover, these 17 genes were classified into distinct classes using the Panther Classification System. The top 6 protein classes were gene-specific transcriptional regulator (4%;23.5%;25.0%) intercellular signal molecule (1%;5.9%;6.3%) membrane traffic protein (1%;5.9%;6.3%) metabolite interconversion enzyme (8%;47.1%;50.0%) transmembrane signal receptor (1%;5.9%;6.3%) transporter (1%;5.9%:6.3%). Among the protein-modifying enzymes and metabolite interconversion enzymes, RARA, ESR2, PPARD, and MAOB are gene-specific transcriptional regulators; FGF2 are intercellular signal molecules; SNCA are membrane traffic proteins; XDH, CYP1A2, ALDH1A1, MAOA, CYP1A1, HMCGR, and MAOB are metabolite interconversion enzymes; IGF1R are transmembrane signal receptors; ABCG2 are transporters.

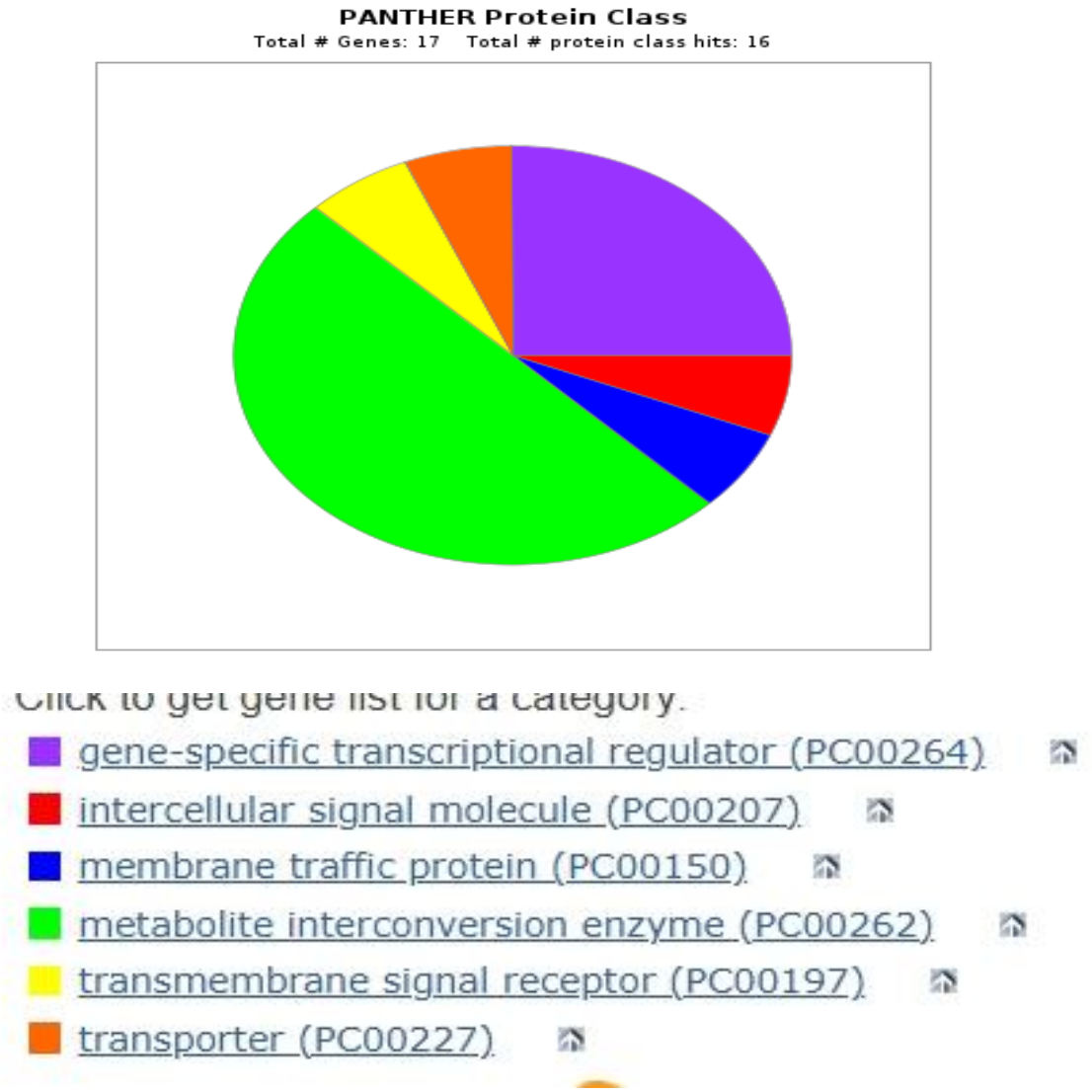


Figure14: protein classes of 17 hub genes of Huntington disease

IN AMYOTROPHIC LATERAL SCLEROSIS:

Moreover, these 25 genes were classified into distinct classes using the Panther Classification System. The top 6 protein classes were gene-specific transcriptional regulator (7%;28.0%;30.4%) intercellular signal molecule (1%;4.0%;4.3%) membrane traffic protein (1%;4.0%;4.3%) metabolite interconversion enzyme (10%;40.0%;43.5%) transmembrane signal receptor (10%;40.0%;43.5%) transporter (1%;5.9%:6.3%). Among the protein-modifying enzymes and metabolite interconversion enzymes, RARA, ESR2, PPARD, RARB, RXRG, RXRA, NR1I2 are gene-specific transcriptional regulators; FGF2 are intercellular signal molecule; SNCA are membrane traffic proteins; XDH, CYP1A2, ALDH1A1, MAOA, CYP19A1, HMCGR, MAOB, CYP1B19, EPHX2 are metabolite interconversion enzyme; FABP4 are transmembrane signal receptor; ABCG2 are transporters.

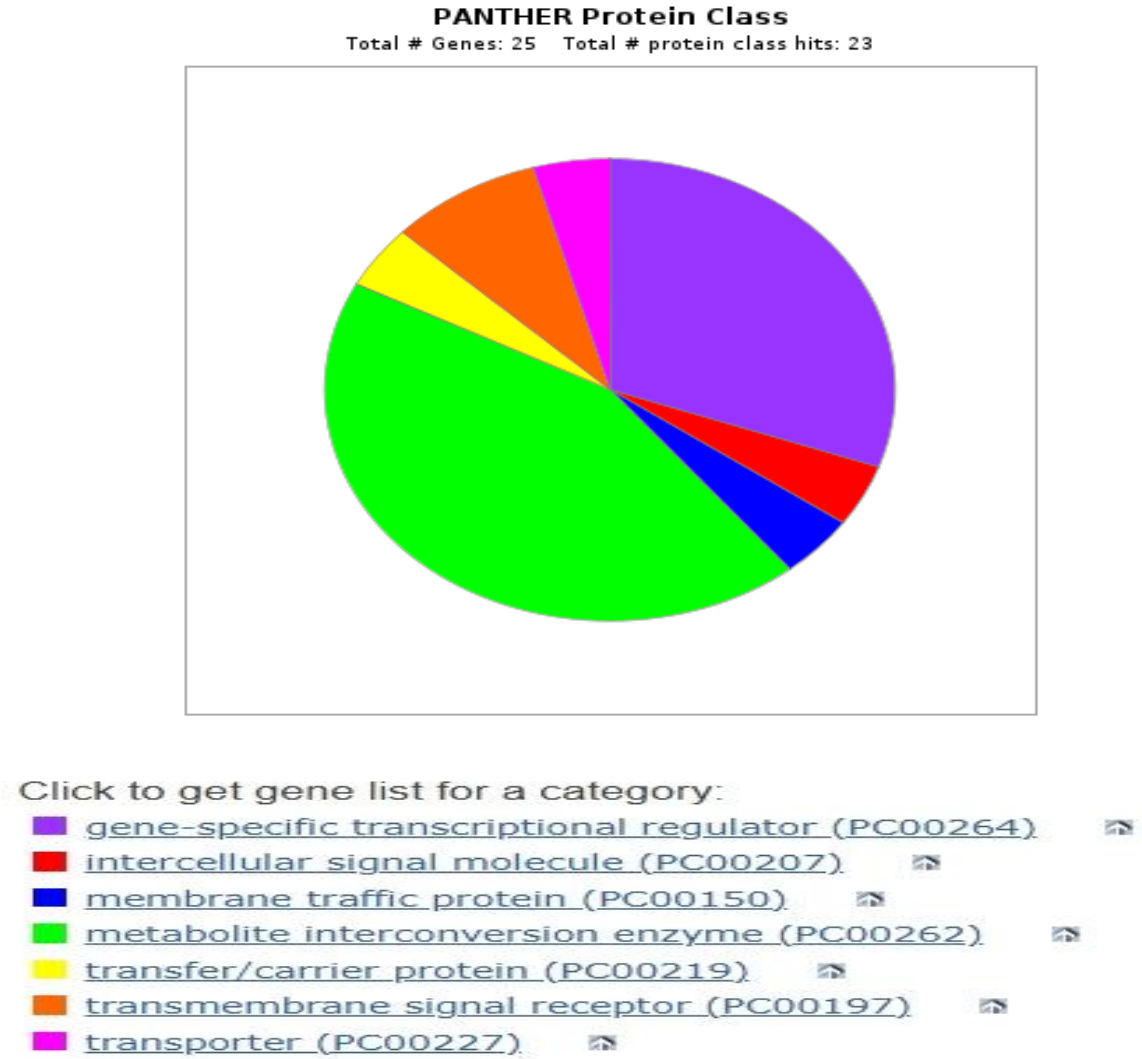


Figure 15: protein classes of 25 hub genes of Amyotrophic lateral sclerosis disease

IN MULTIPLE SCLEROSIS:

Moreover, these 25 genes were classified into distinct classes using the Panther Classification System. The top 6 protein classes were gene-specific transcriptional regulator (7%;28.0%;30.4%) intercellular signal molecule (1%;4.0%;4.3%) membrane traffic protein (1%;4.0%;4.3%) metabolite interconversion enzyme (10%;40.0%;43.5%) transmembrane signal receptor (10%;40.0%;43.5%) transporter (1%;5.9%:6.3%). Among the protein-modifying enzymes and metabolite interconversion enzymes, RARA, ESR2, PPARD, RARB, RXRG, RXRA, NR1I2 are gene-specific transcriptional regulators; FGF2 are intercellular signal molecules; SNCA are membrane traffic proteins; XDH, CYP1A2, ALDH1A1, MAOA, CYP19A1, HMCGR, MAOB, CYP1B19, EPHX2 are metabolite interconversion enzymes; FABP4 are transmembrane signal receptor; ABCG2 are transporters.

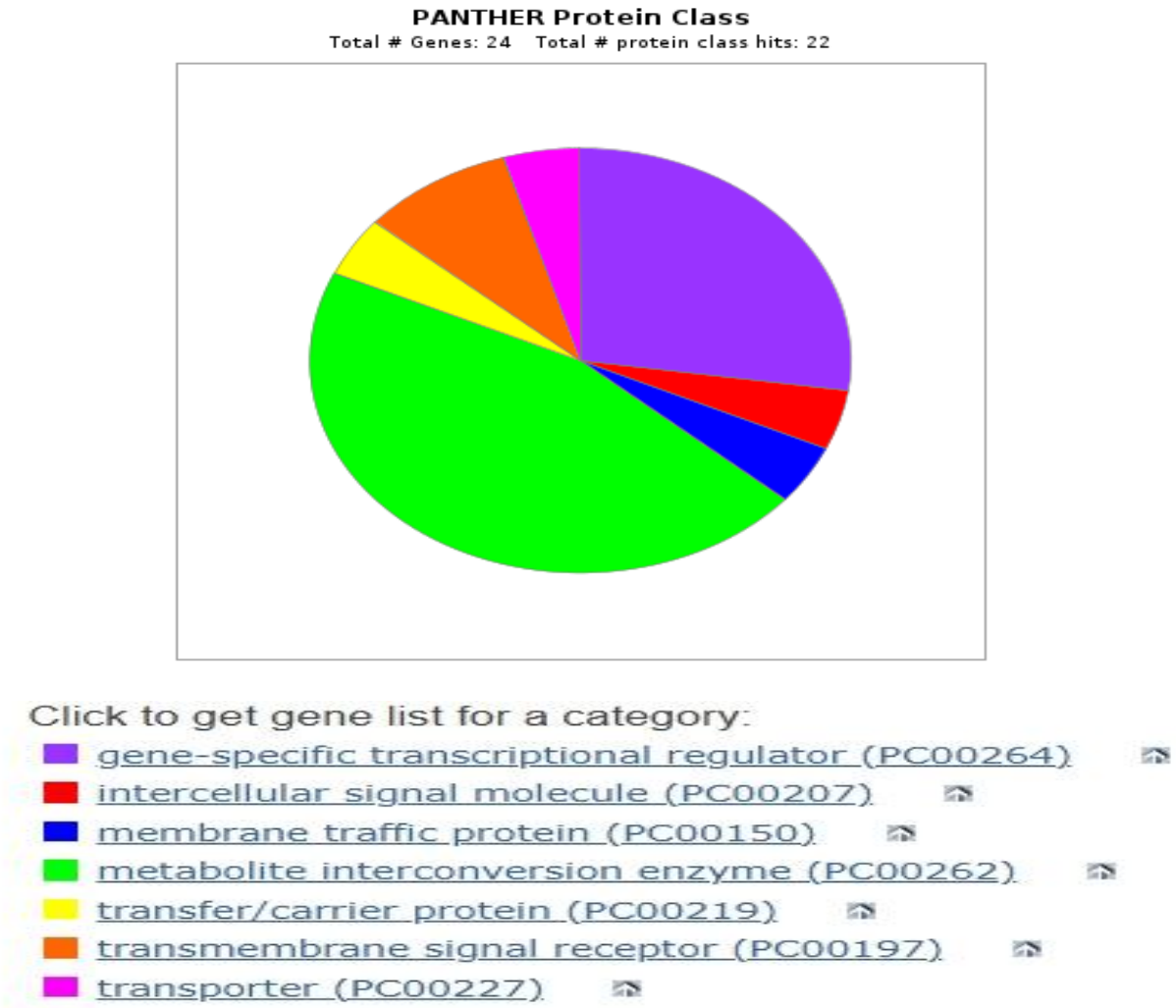


Figure 16: protein classes of 25 hub genes of Multiple sclerosis disease

THE GO BIOLOGICAL PROCESS ENRICHMENT ANALYSIS:

GO enrichment analysis mainly involves 3 aspects: cell composition, molecular function (MF), and biological process (BP). GO enrichment entries of the BP show the top 25. Within the BP categories fatty acid metabolic process (GO:0006631), Positive regulation of fatty acid metabolic process (GO:0045923), Regulation of fatty acid metabolic process (GO:0019217), cholesterol storage/ regulation of cholesterol storage (GO:0010885), negative regulation of lipid storage (GO:0010888), PPAR signalling pathway (GO:0035357), reactive oxygen species (ROS) biosynthetic process (GO:1903406) were dominant terms. This result illustrates that Lablab purpureus against Alzheimer's, Parkinson's, Huntington's, Amyotrophic lateral sclerosis, and Multiple sclerosis involved a variety of targets and was involved in several BPs.

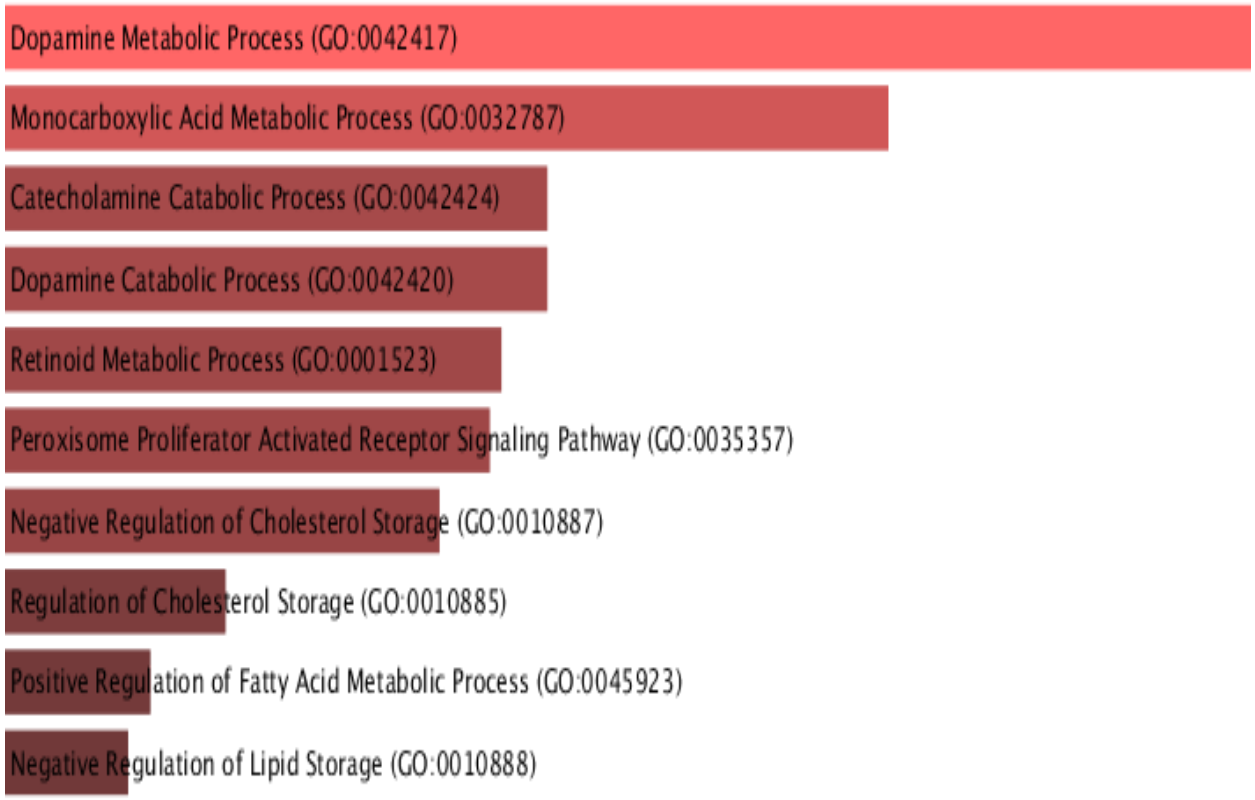


Figure17: Top Ten GO biological process of neurodegenerative disease

TABLE NO:

Index	Name	P-value	Adjusted p-value
1	Dopamine Metabolic Process (GO:0042417)	3.28E-07	0.000108
2	Monocarboxylic Acid Metabolic Process (GO:0032787)	2.005E-06	0.0003298
3	Catecholamine Catabolic Process (GO:0042424)	0.000011	0.0008039
4	Dopamine Catabolic Process (GO:0042420)	0.000011	0.0008039
5	Retinoid Metabolic Process (GO:0001523)	-	0.0008039
6	Peroxisome Proliferator Activated Receptor Signalling Pathway (GO:0035357)	-	0.0008039
7	Negative Regulation of Cholesterol Storage (GO:0010887)	-	0.0008856
8	Regulation of Cholesterol Storage (GO:0010885)	-	0.002254
9	Positive Regulation of Fatty Acid Metabolic Process (GO:0045923)	-	0.002665

10	Negative Regulation of Lipid Storage (GO:0010888)	-	0.002665
11	Positive Regulation of Small Molecule Metabolic Process (GO:0062013)	-	0.002665
12	Regulation of Fatty Acid Metabolic Process (GO:0019217)	-	0.002714
13	Fatty Acid Metabolic Process (GO:0006631)	0.0001153	0.002918
14	Retinol Metabolic Process (GO:0042572)	0.0001316	0.002999
15	Negative Regulation of Transcription by RNA Polymerase II (GO:0000122)	0.0001433	0.002999
16	Long-Chain Fatty Acid Biosynthetic Process (GO:0042759)	0.0001559	0.002999
17	Negative Regulation of miRNA Transcription (GO:1902894)	0.0001559	0.002999
18	Regulation of Reactive Oxygen Species Biosynthetic Process (GO:1903426)	0.0001823	0.002999
19	Positive Regulation of Lipid Metabolic Process (GO:0045834)	0.0001823	0.002999
20	Negative Regulation of miRNA Metabolic Process (GO:2000629)	0.0001823	0.002999
21	Estrogen Metabolic Process (GO:0008210)	0.0002411	0.003777
22	Nuclear Receptor-Mediated Signalling Pathway (GO:0141193)	0.000257	0.003844
23	Intracellular Receptor Signalling Pathway (GO:0030522)	0.0003079	0.004405
24	Negative Regulation of Secretion by Cell (GO:1903531)	0.0004233	0.005803
25	Lipid Catabolic Process (GO:0016042)	0.0004443	0.005847

TABLE NO: 1 shows the GO biological process of neurodegenerative disease

KEGG PATHWAY ANALYSIS TO EXPLORE THE POTENTIAL MECHANISMS OF LABLAB PURPUREUS IN TREATING NEURODEGENERATIVE DISEASE:

After KEGG analysis, 93 KEGG pathways were predicted, and the top 20 enriched KEGG pathways were collected according to the mechanism. The majority of the selected sub-pathways we discuss belong to 5 KEGG pathways: Parkinson disease pathway / Dopaminergic synapse (hsa05012 / hsa04728), Alzheimer disease pathway (hsa05010), Calcium signalling pathway (hsa04020), MAPK signalling pathway (hsa04010), PI3K–Akt signalling pathway (hsa04151).

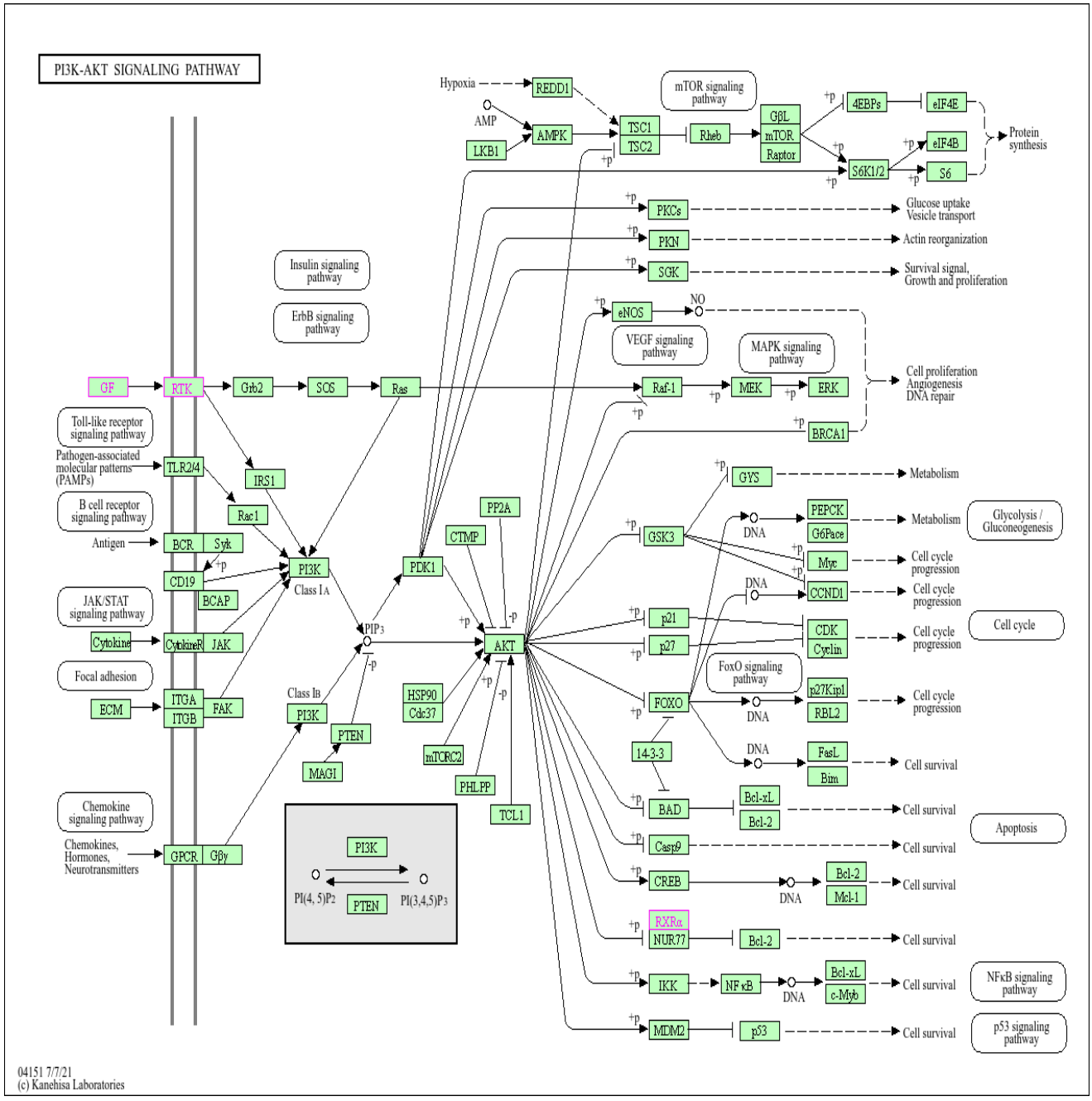


Figure 18: Pathway of PI3K–Akt signalling pathway

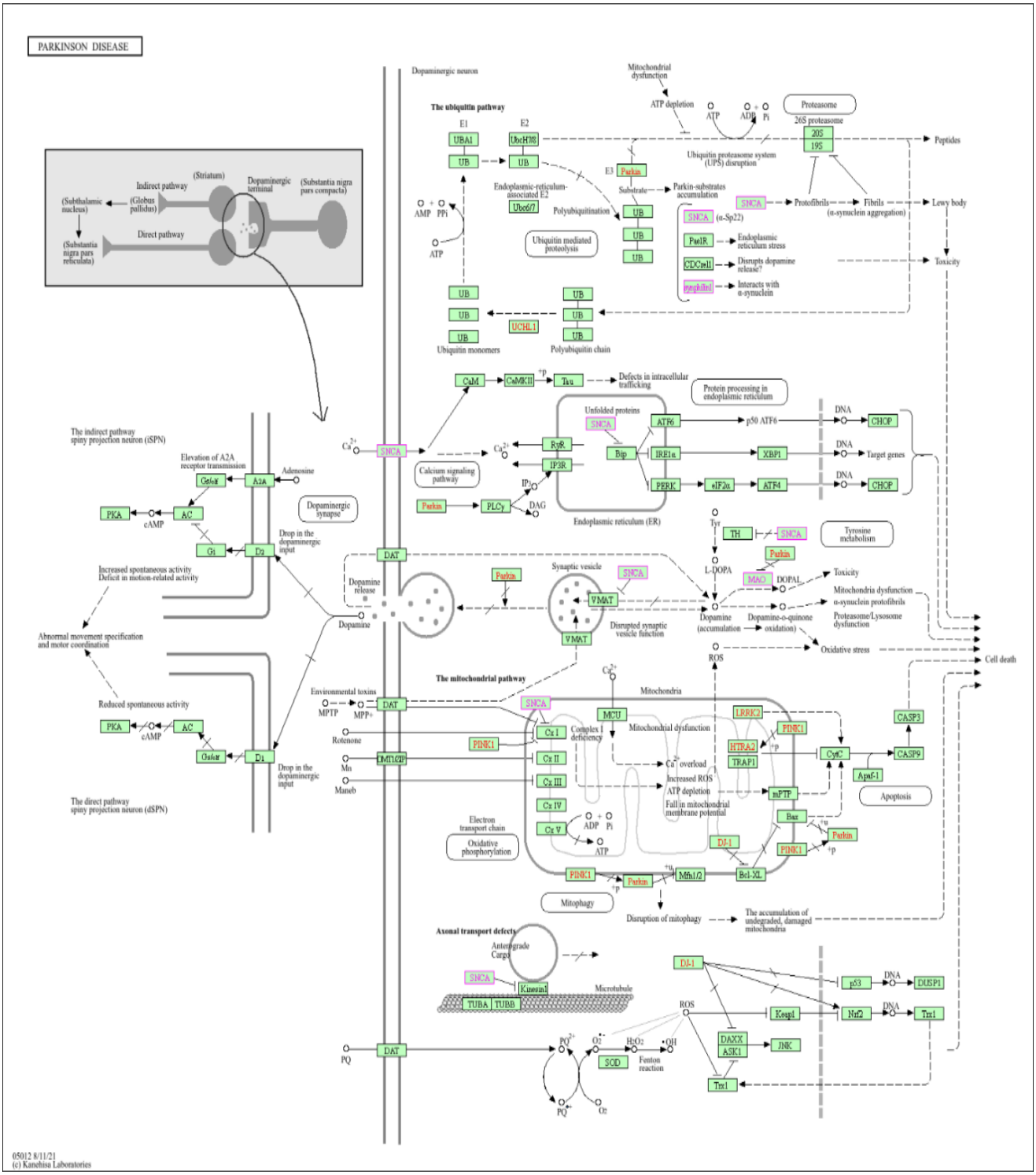


Figure 19: Pathway of Parkinson disease

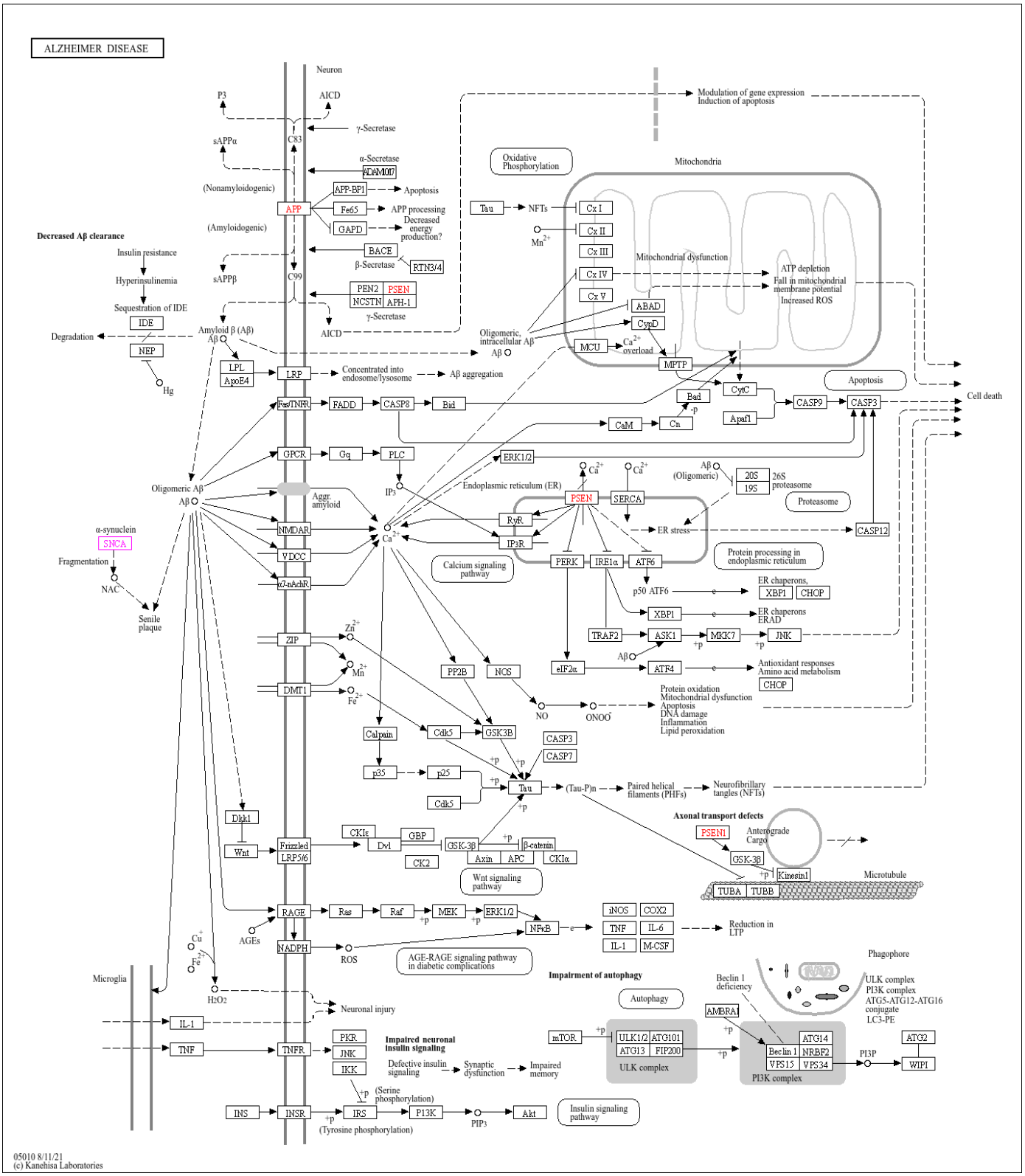


Figure20: Pathway of Alzheimer disease

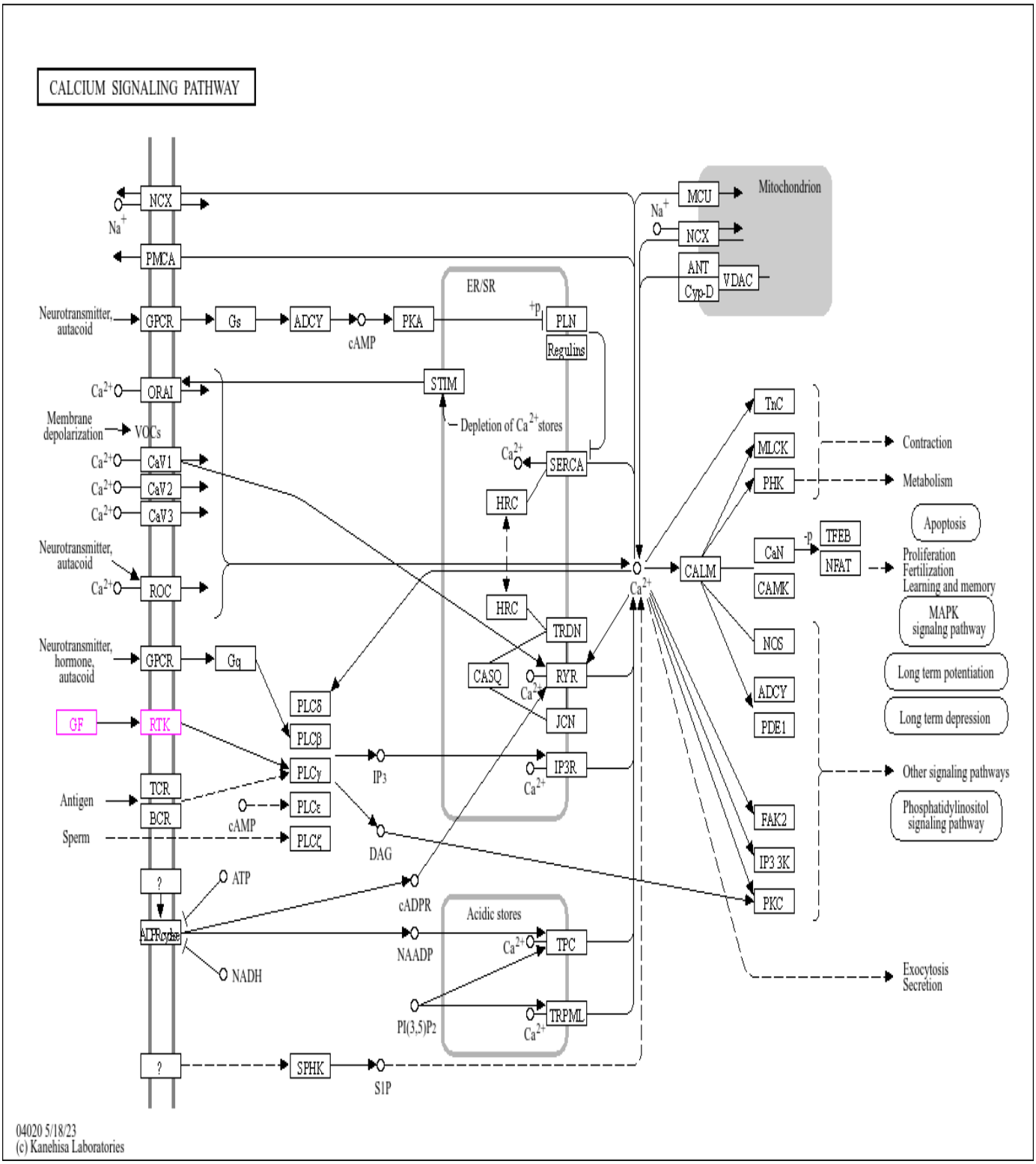


Figure 21: Pathway of Calcium signalling pathway

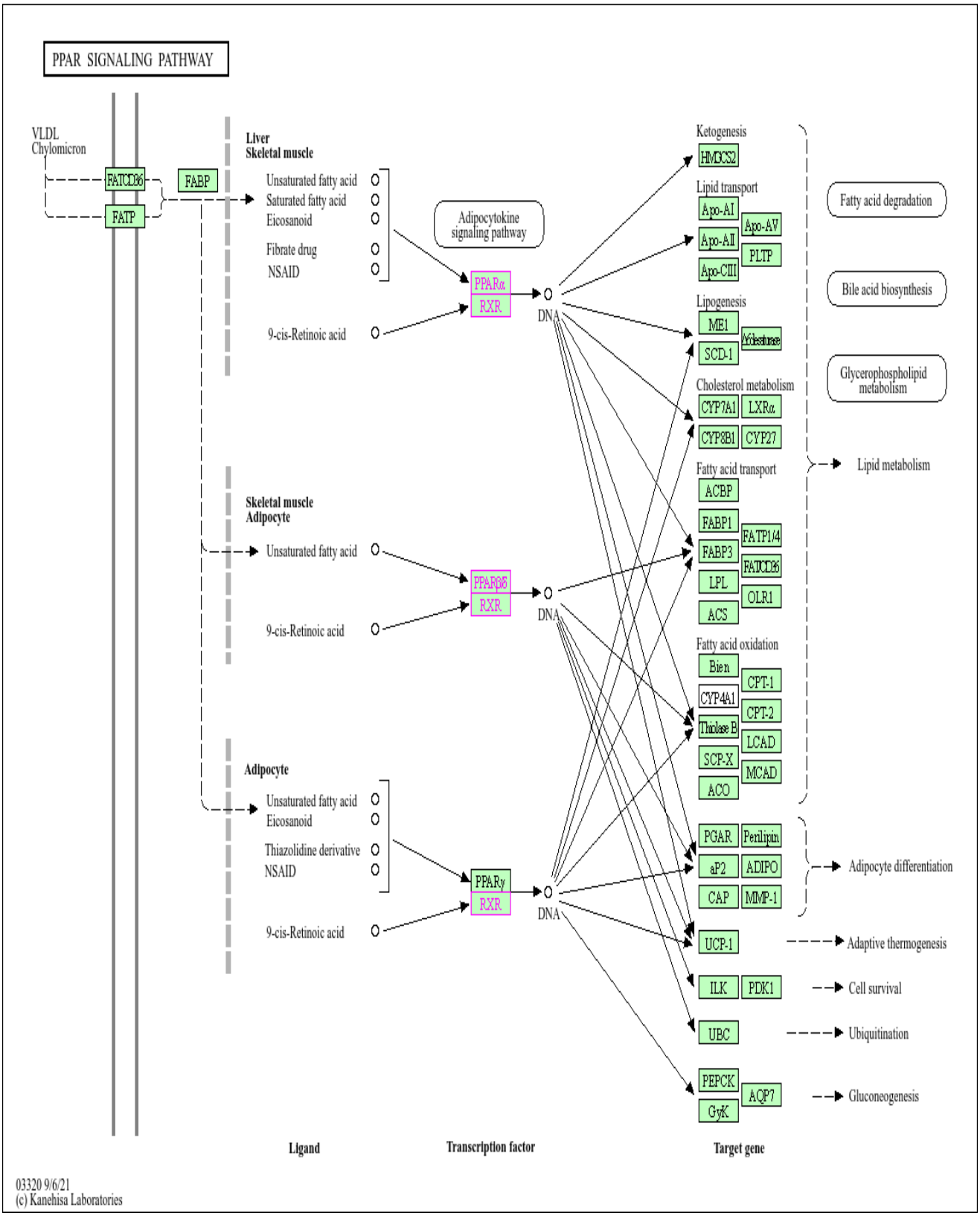


Figure 22: Pathway of PPAR signalling pathway

MOLECULAR DOCKING FOR LABLAB PURPUREUS AGAINST NEURODEGENERATIVE DISEASE IN TAU AND AB PATHOLOGY

To elucidate the binding mode of the lablab purpureus to targets of lablab purpureus against neurodegenerative disease tau and aβ pathology, molecular docking studies were performed. In molecular docking, CYP1B1 has low binding energy of -6.99 against the PPARA of disease gene, and other binding energy are XDH against PPARA is -6.37, XDH against MAOB is-6.76, CYP1B1 against MAOB is -6.44, ABCG2 against MAOB is -6.24 and ABCG2 against MAOB is -6.65.

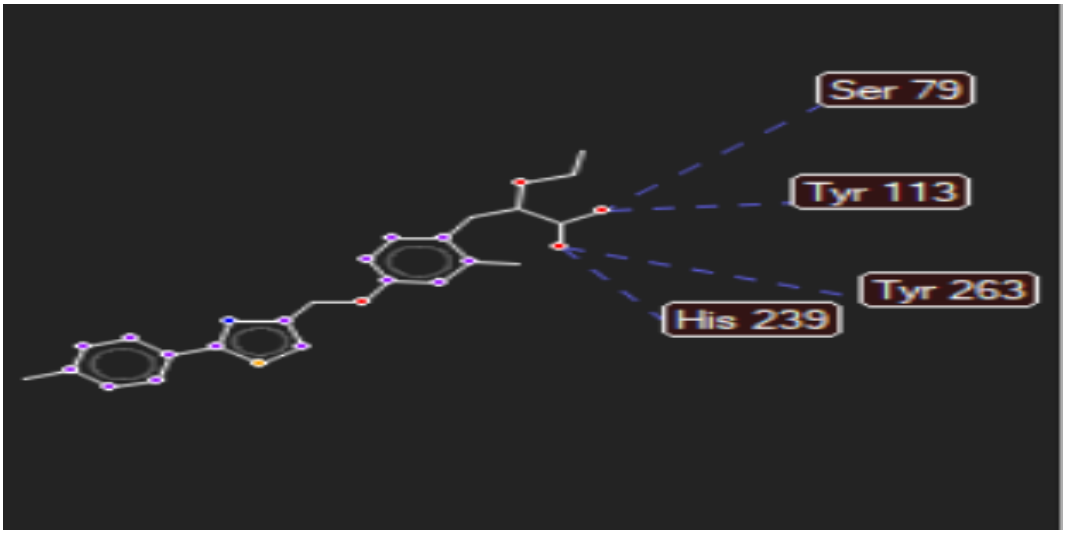


Figure 23: 2D interaction of CYP1B1 against with PPARA

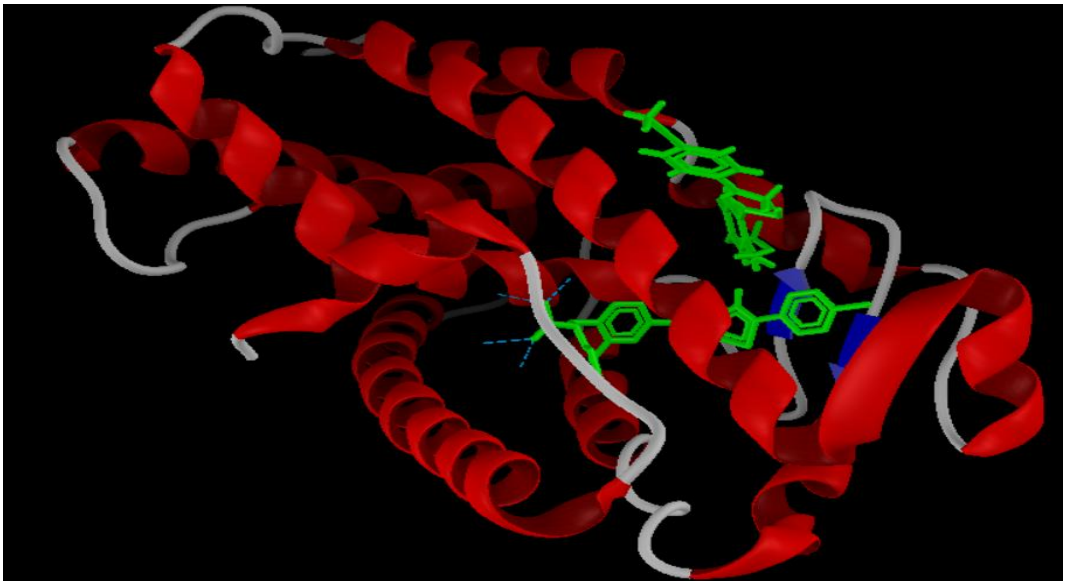


Figure 24: 3D representation with energy mapping of CYP1B1 against with PPARA

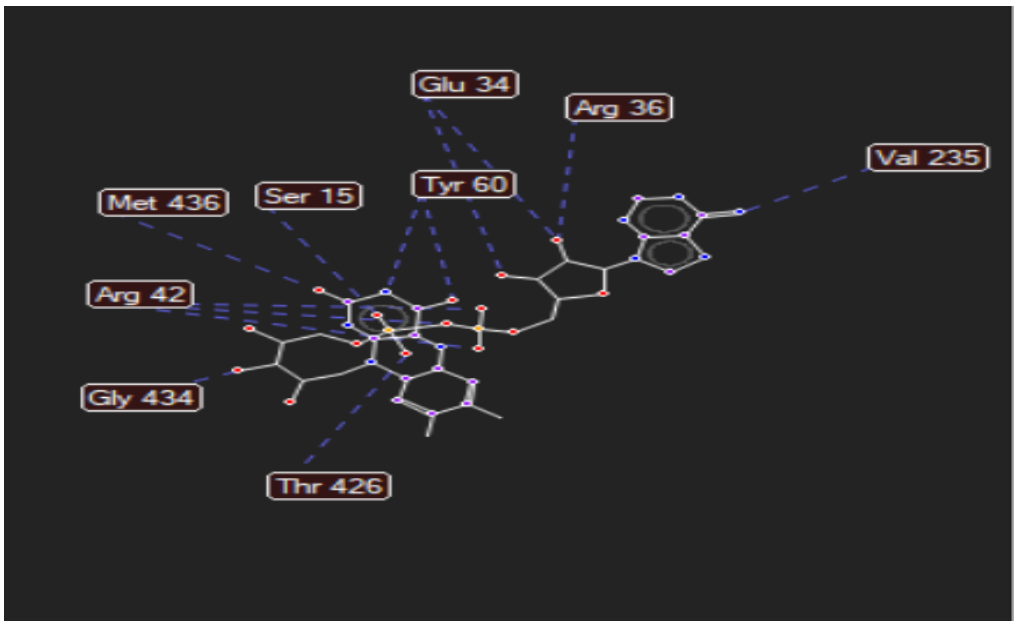


Figure 25: 2D interaction of XDH against with MAOB

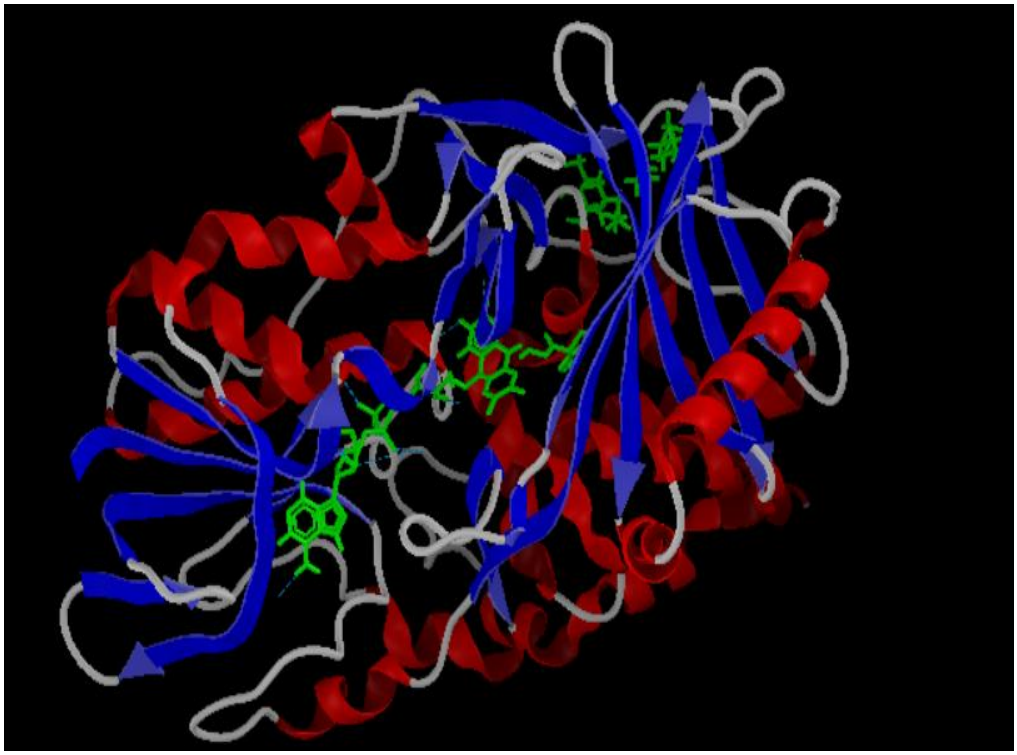


Figure 26: 3D representation with energy mapping of XDH against with MAOB

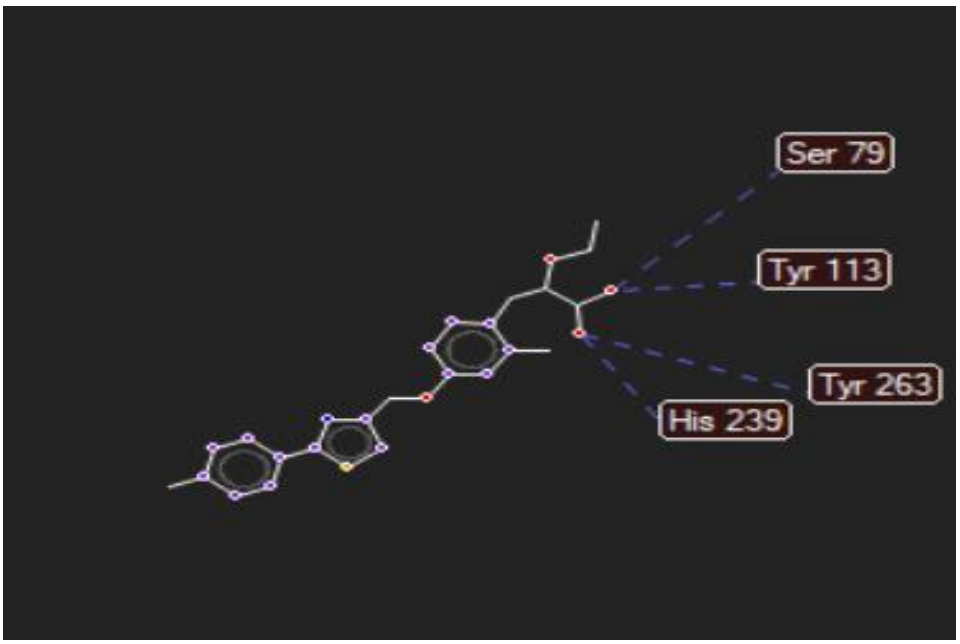


Figure 27: 2D interaction of IGF1R against with PPARA



Figure 28: 3D representation with energy mapping of IGF1R against with PPARA

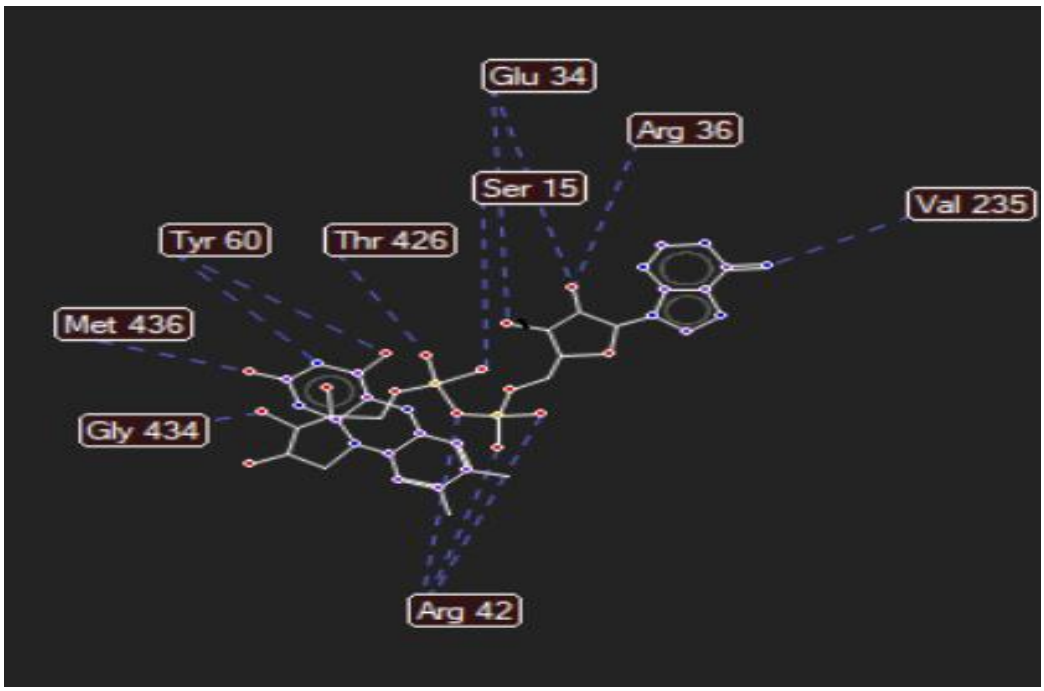


Figure 29: 2D interaction of XDH against with PPARA

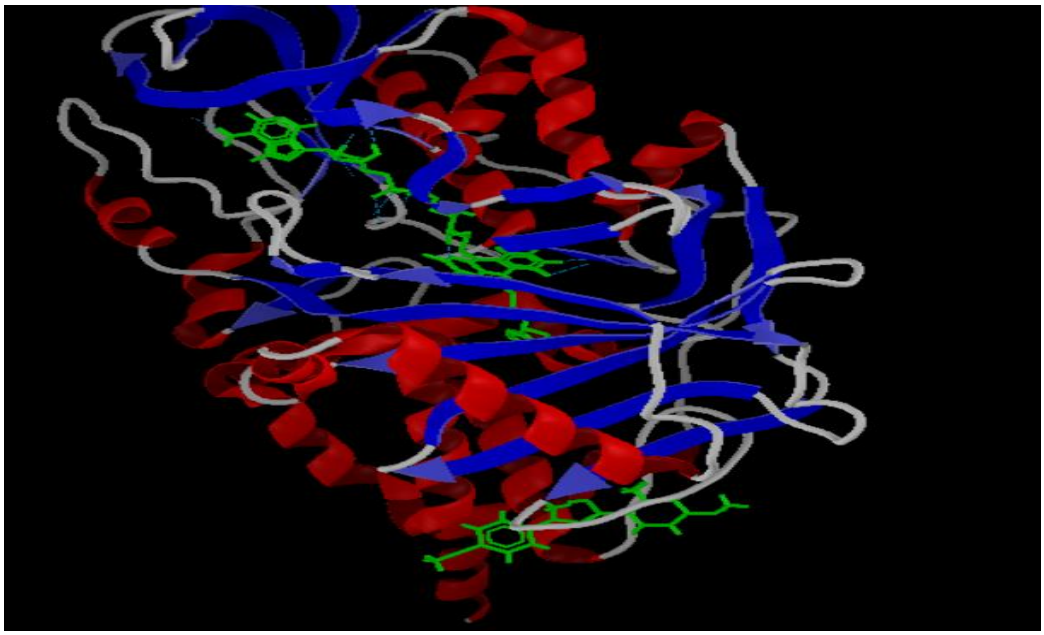


Figure 30: 3D representation with energy mapping of XDH against with PPARA

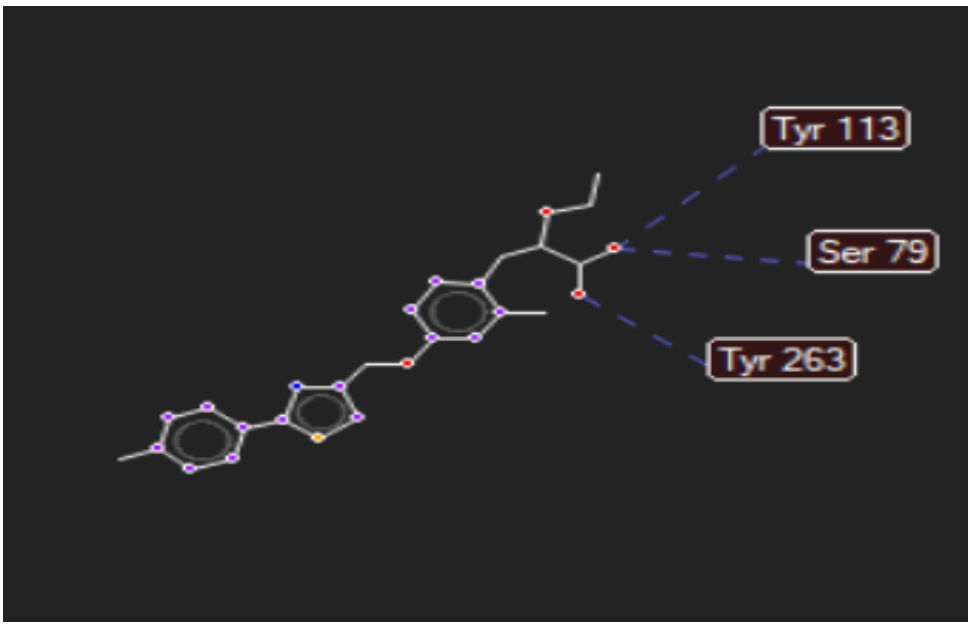


Figure 31: 2D interaction of CYP1B1 against with MAOB

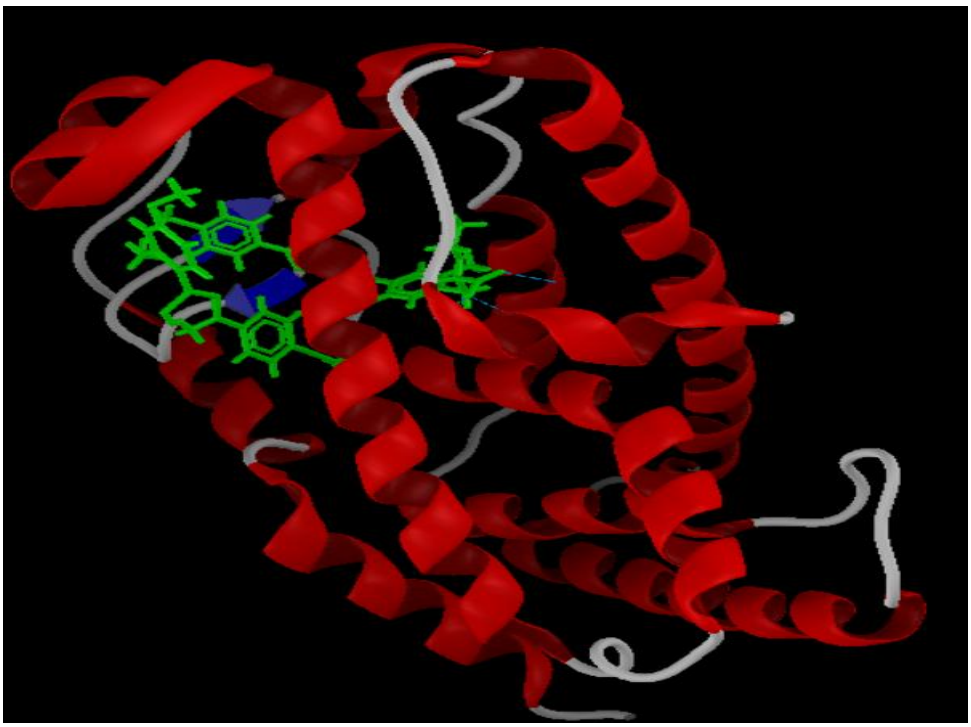


Figure 32: 3D representation with energy mapping of CYP1B1 against with MAOB

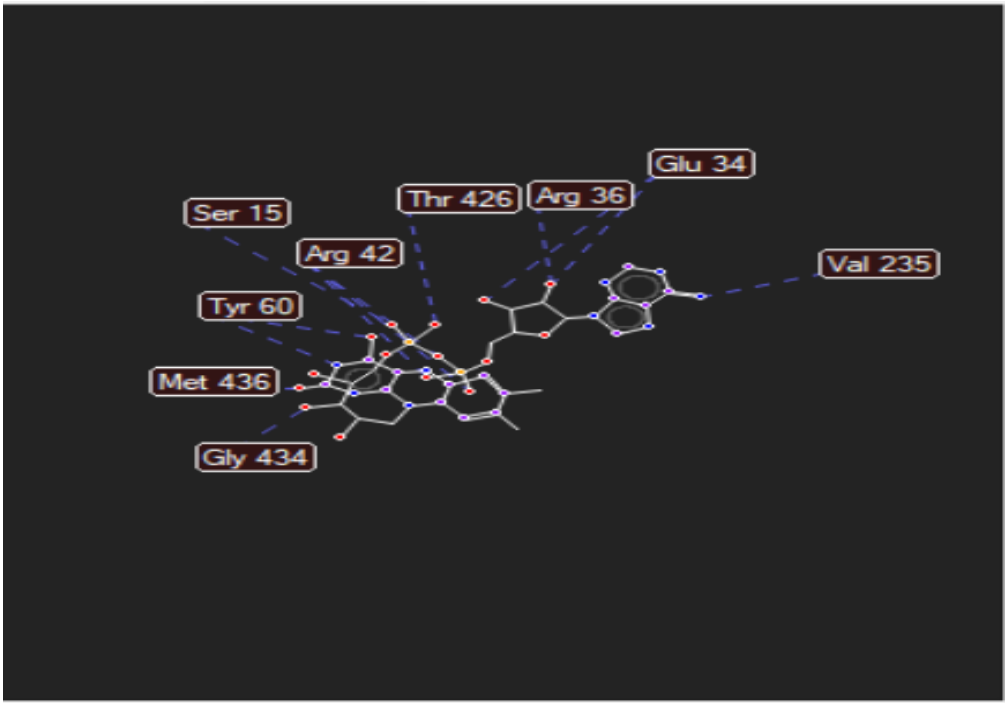


Figure 33: 2D interaction of ABCG2 against with PPARA

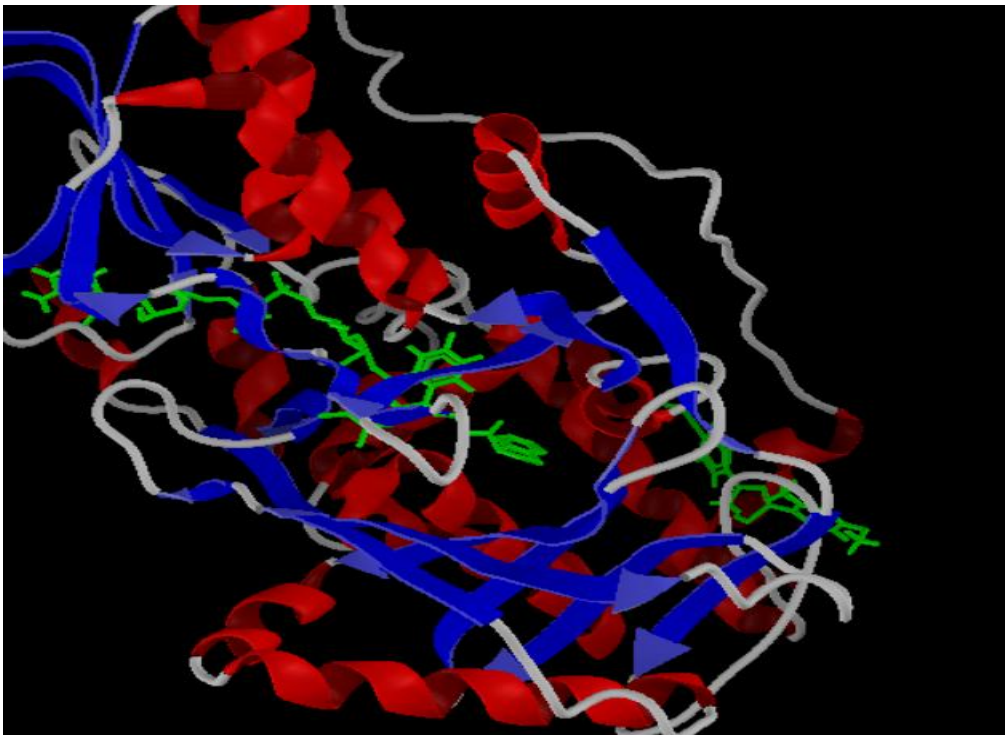


Figure 34: 3D representation with energy mapping of ABCG2 with PPARA

DISCUSSION:

Neurodegenerative diseases remain among the most difficult challenges in modern biomedical research because of their complex origins, progressive course, and the absence of curative treatments. Rather than arising from a single gene mutation or an isolated signalling defect, these disorders develop through the disruption of highly interconnected molecular networks involving numerous genes, proteins, and

biological pathways. In this context, the present study employed a network pharmacology approach to investigate the molecular mechanisms underlying major neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis. By adopting a systems-level perspective, this strategy provides a more comprehensive understanding of disease progression and overcomes the limitations of traditional single-target approaches.

Gene Ontology enrichment analysis revealed that the identified targets were significantly associated with key biological processes such as neuroinflammation, regulation of apoptotic signalling, response to oxidative stress, immune system activity, synaptic organization, and neuronal signalling. Among these, neuroinflammation emerged as a prominent feature, consistent with its well-established role in neurodegenerative diseases. Activation of microglia and astrocytes, along with the release of pro-inflammatory cytokines, contributes to chronic inflammation, which can disrupt neuronal homeostasis and accelerate neuronal damage. The strong enrichment of immune-related processes further highlights the importance of immune dysregulation in disease progression, particularly in disorders such as Alzheimer's disease and multiple sclerosis.

Oxidative stress and mitochondrial dysfunction were also prominently involved in the identified molecular mechanisms. Neurons are especially susceptible to oxidative damage due to their high metabolic demands and limited capacity for regeneration. Excessive production of reactive oxygen species can impair mitochondrial function, damage cellular components, and ultimately trigger apoptotic pathways. The enrichment of apoptosis-related processes suggests that programmed cell death plays a crucial role in neuronal loss across different neurodegenerative conditions. These observations are in agreement with previous studies that have demonstrated a close interplay between oxidative stress, mitochondrial dysfunction, and neuronal apoptosis in neurodegeneration.

Further insights into disease mechanisms were obtained through KEGG pathway enrichment analysis. Key signalling pathways, including PI3K-Akt, MAPK, neurotrophin signalling, and neurodegeneration-related pathways, were significantly enriched. The PI3K-Akt pathway is essential for neuronal survival, metabolic regulation, and inhibition of apoptosis, and its dysregulation can render neurons more vulnerable to toxic insults. Similarly, MAPK signalling plays an important role in cellular stress responses, inflammation, and cell death, with abnormal activation contributing to neuroinflammatory processes and neuronal degeneration.The enrichment of neurotrophin signalling pathways underscores the critical role of growth factors such as brain-derived neurotrophic factor (BDNF) in maintaining neuronal survival, synaptic plasticity, and cognitive function. Reduced neurotrophin signalling has been reported in several neurodegenerative disorders and is closely associated with synaptic dysfunction and cognitive decline. The identification of this pathway further supports its potential as a promising therapeutic target.

Protein–protein interaction network analysis identified several hub genes that occupy central positions within the molecular network. These hub genes are likely to act as key regulators of multiple biological processes and signalling pathways. From a network pharmacology perspective, targeting such hub nodes is particularly advantageous, as their modulation can influence several downstream pathways simultaneously. This multi-target strategy is especially relevant for neurodegenerative diseases, where complex and interconnected molecular mechanisms limit the effectiveness of single-target therapies. In contrast to peripheral targets, modulating hub genes may help restore network balance and cellular homeostasis.An important observation from this study is the presence of shared molecular pathways and hub targets across different neurodegenerative diseases. Although these disorders differ in their clinical manifestations and affected neuronal populations, the overlap in signalling pathways suggests common underlying pathogenic mechanisms. This finding supports the concept that neurodegenerative diseases may exist along a molecular continuum rather than as entirely distinct entities. Network pharmacology therefore provides a

valuable framework for identifying shared disease mechanisms and developing therapeutic strategies that may be effective across multiple neurodegenerative conditions.Overall, the findings of this study are consistent with existing literature highlighting the roles of neuroinflammation, oxidative stress, protein aggregation, and synaptic dysfunction in neurodegeneration. However, the key advantage of the present approach lies in its ability to integrate diverse datasets and uncover complex interactions among genes, proteins, and pathways. This integrative analysis enhances target prioritization and offers a deeper understanding of disease mechanisms compared to conventional reductionist methods.

Despite its strengths, this study has certain limitations. The analysis relies primarily on publicly available databases and computational predictions, which may introduce bias due to incomplete or uneven data annotation. Moreover, the identified associations do not establish direct causality. Experimental validation using in vitro and in vivo models is therefore required to confirm the functional roles of the identified hub genes and pathways. Future studies incorporating multi-omics data, such as transcriptomics, proteomics, metabolomics, and clinical samples, may further validate and expand these findings, improving their translational relevance.In conclusion, this study demonstrates the value of network pharmacology in elucidating the complex molecular mechanisms underlying neurodegenerative diseases. By identifying key biological processes, signalling pathways, and hub genes, it provides important insights into disease pathogenesis and highlights the potential of multi-target therapeutic strategies. These findings support a systems-level understanding of neurodegeneration and may contribute to the development of more effective and comprehensive treatment approaches in the future.

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