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CONSTRUCTION AND ANALYSIS OF MYOPATHY AND PARKINSON DISEASE PROTEIN NETWORK

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ABSTRACT

Neurological Disorders are diseases of the central and peripheral nervous system. The disorders Parkinson's disease and myopathy are the traumatic disorders of the nervous system. The myopathies are neuromuscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber and Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells. Biological network is a network that applies to the biological system. These networks are widely used in many branches of biology as convenient representation of patterns of interaction between appropriate biological elements.Proteins-protein interaction (PPIs) in a cell form protein interaction networks (PINs) where proteins are nodes and their interaction are edges. In the present work we will investigate the network properties of proteins in disease protein-protein interaction network framework and identify common proteins between myopathy and Parkinson diseases.

Key Words: Framework, Interaction, Network, Edges, Neuromuscular

INTRODUCTION

Neurological Disorders are diseases of the central and peripheral nervous system.In other words, the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system, neuromuscular junction, and muscles are responsible for neurological disorders. These disorders include epilepsy, Alzheimer disease, myopathy and other dementias, cerebrovascular diseases including stroke, migraine and other headache disorders, multiple sclerosis, Parkinson's disease, neuro-infections, brain tumours, traumatic disorders of the nervous system such as brain trauma, and neurological disorders as a result of malnutrition.**[11]** Hundreds of millions of people worldwide are affected by neurological disorders. Approximately 6.2 million people die because of stroke each year; over 80% of deaths take place in low- and middle-income countries. More than 50 million people have epilepsy worldwide. It is estimated that there are globally 35.6 million people with dementia with 7.7 million new cases every year - Alzheimer's disease is the most common cause of dementia and may contribute to 60–70% of cases.**[13]**

The Parkinson's disease and myophaty on the traumatic disorders of the nervous system. The Myopathies are neuromuscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber. Other symptoms of myopathy can include muscle cramps, stiffness, and spasm. Myopathies can be inherited (such as the muscular dystrophies) or acquired (such as common muscle cramps). Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which are the result of the loss of dopamine-producing brain cells. The four primary symptoms of PD are tremor, or trembling in hands, arms, legs, jaw, and face; rigidity, or stiffness of the limbs and trunk; bradykinesia, or slowness of movement; and postural instability, or impaired balance and coordination. As these symptoms become more pronounced, patients may have difficulty in walking, talking, or completing other simple tasks. PD usually affects people over the age of 60. **[12]**

Biological network is a network that applies to the biological system. These networks are widely used in many branches of

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biology as convenient representation of patterns of interaction between appropriate biological elements. **[14]**Proteins-protein interaction (PPIs) in a cell form protein interaction networks (PINs) where proteins are nodes and their interaction are edges. The present study is designed to investigate the network properties of proteins in diseases, identification of common protein and their structural properties and protein-protein interaction network framework between myopathy and Parkinson diseases.

DISCUSSION

We have collected 5 miRNAs for Parkinson Disease and 31 miRNAs for Myopathy by using literature mining such as PubMed, miR2disease database. (Table-1)

Using miRNA target database mirWalk, miRecords**,** miReg and miRTarBase. We have identified 298 targets for parkinson Disease and 1602 targets for myopathy disease. We made an interaction network using target proteins of miRs with the help of Visant. We have found the Degree of Distribution (Fig. 1, 2, 3) and Clustering- Coefficient Distribution of target proteins. (Fig 4, 5, 6)

There are 131 proteins which are common between two diseases. It seems that these proteins are hotshots in these diseases, so required much more attention. We have plot a degree distribution of disease protein and the results indicate that most of the proteins are having 4 degrees. This is an interesting finding. It means that networks are obeying power law and they are scale-free in nature. The power laws are often interpreted as signatures of hierarchy and robustness**.**

ABCC1, ACTB, ACTG1, AKT1, ALDH1A1, APC, ARC, ARCN1, ARPP-21, ASAHL, ATP11C, BCL2, BCL2L11, BMP2, ,CBS, CBX5, CCND1, CDKN1B, CDKN1C, CEBPA, CNN3, CTGF, CXCL12, DGCR8, DICER1, DMPK, E2F1, E2F3, EGF, EGFR, EPHB2, ERBB2, ERG, ETS2, EXOSC1, FASLG, FASN, FBLIM1, FGFR1, FLT3, GALNT1, GAPDH, GRB2, HCN2, HDAC4, HELLS, HIST1, H2BB, HLA-G, HMGB1, HMOX1, HOXA9, HOXD10, HSPA1B, HSPB6, IARS, IDH1, IGF1, IGF1R, IGF2R, IL6, IMPACT, IRS1, ITGB1, ITLN1, JAG1, KLF4, KRT7, LIN28, LRRFIP1, LRRK2, MBL2, MCL1, MEF2A, MET, MLC1, MOCOS, MSI2, MYC, MYOD1, NFKB1, NFYC, NKX2-3, NOTCH1, NPM1, NXN, PAK1, PAX3, PAX6, PAX7, PDE3A ,PIK3CA, PIWIL1, POLA2, POLR2A, POMC, PROC, PTBP1, PTBP2, PTEN,P TGS2, RAB34, RAC1, RDH10, RELB, RHOA, RHOD, RNASEN, RPE, RPL27, RUNX2, SLC11A1, SLC2A4, SLC7A1, SMAD2, SMAD5, SNCA, SOX2, SOX4, SRF, TFB1M, TGFB1, TGFBI, TGFBR2, TIAL1, TIMP2, TLR4, TLR9, TPPP, VEGFA, WT1

By doing functional annotation we found that all proteins which are common in these two diseases are reported in these following neurological pathways. (Table-2)

CONCLUSION

This study illustrates the analysis of Myopathy and Parkinson diseases. For this we have designed the protein-protein interaction analysis because each and every protein which involves in this study has their own role and importance and help to understand how Proteins are distributed in this network.

We have identified about 131 common proteins which are hotshots for these two diseases and required much more attention to find out the drug target so that farther study can be designed to obtain the inhibitors of these targets.

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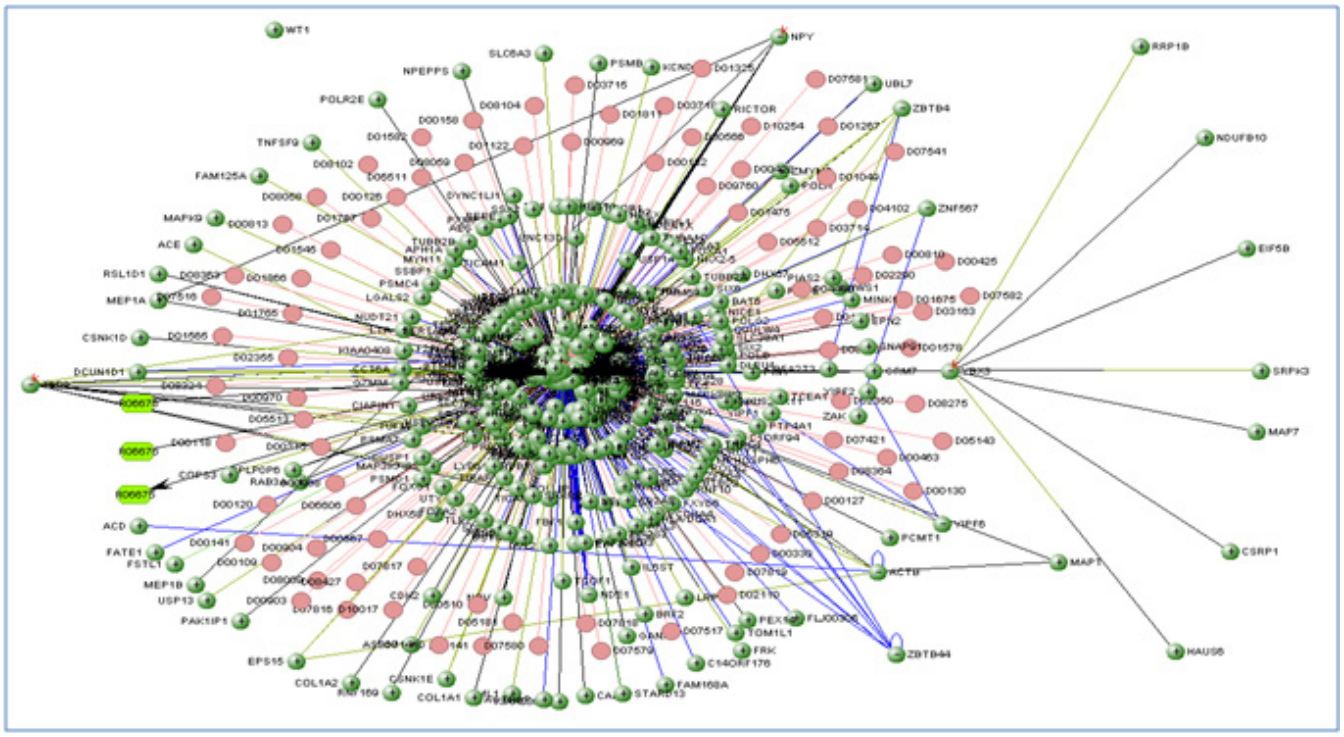

Figure 1: Parkinson Disease specific TFs/miRs interaction Network.

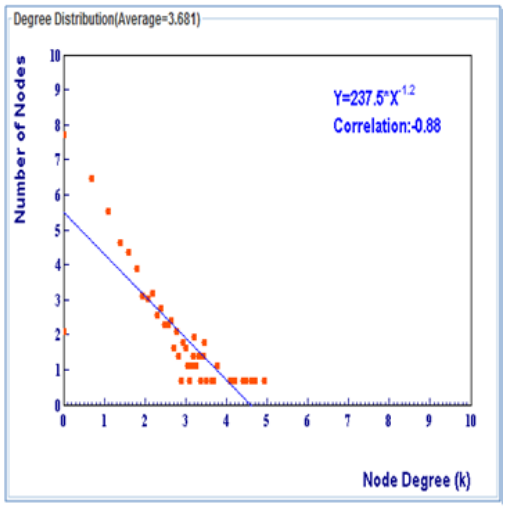

Figure 2: Parkinson Disease specific TFs/miRs interaction Network degree Distribution

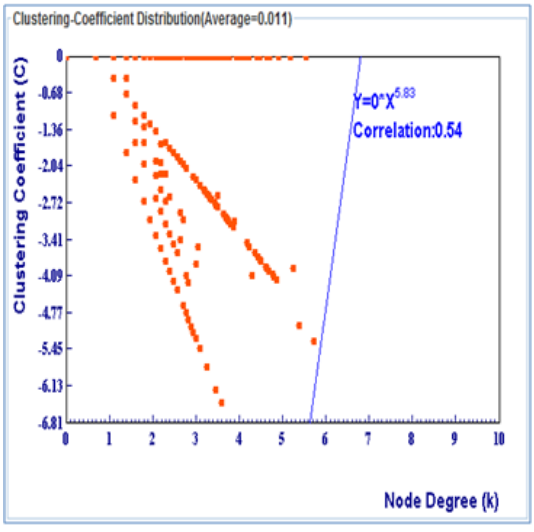

Figure 3: Parkinson Disease specific TFs/miRsinteraction Network Clustering- Coefficient Distribution

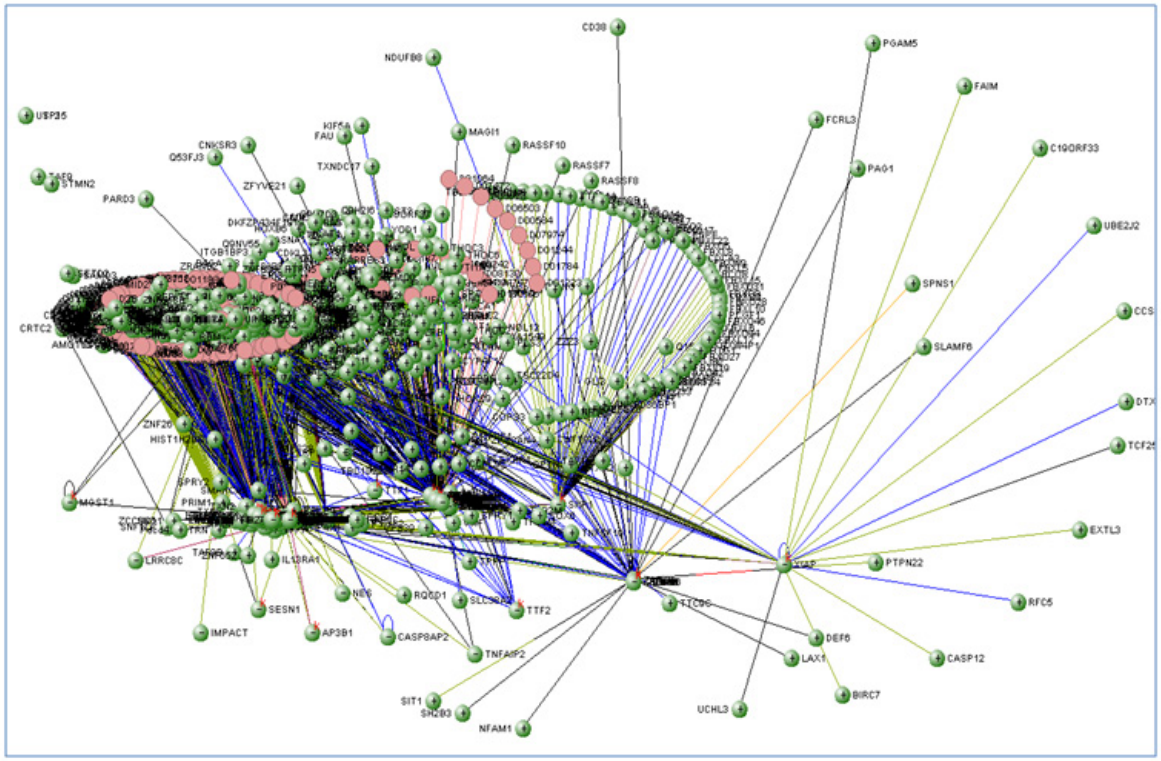

Figure 4: Myopathy Disease specific TFs/miRs interaction Network.

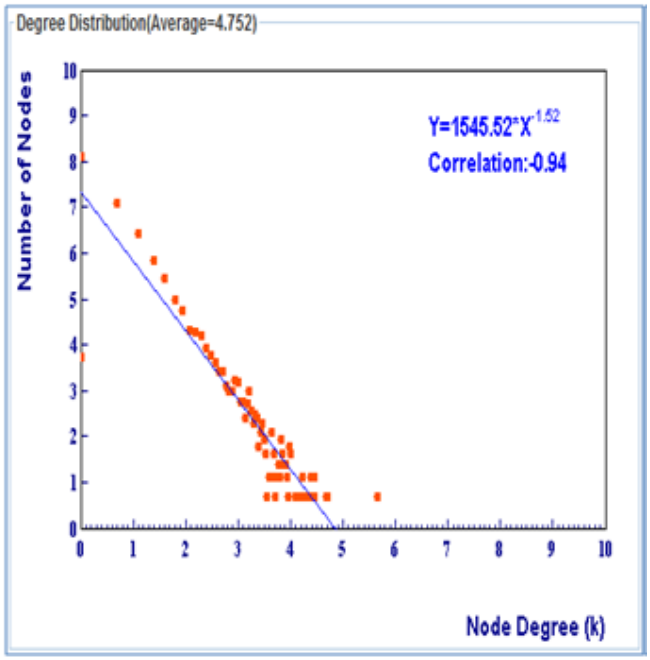

Figure 5: Myopathy Disease specific TFs/miRs interaction Network degree Distribution.

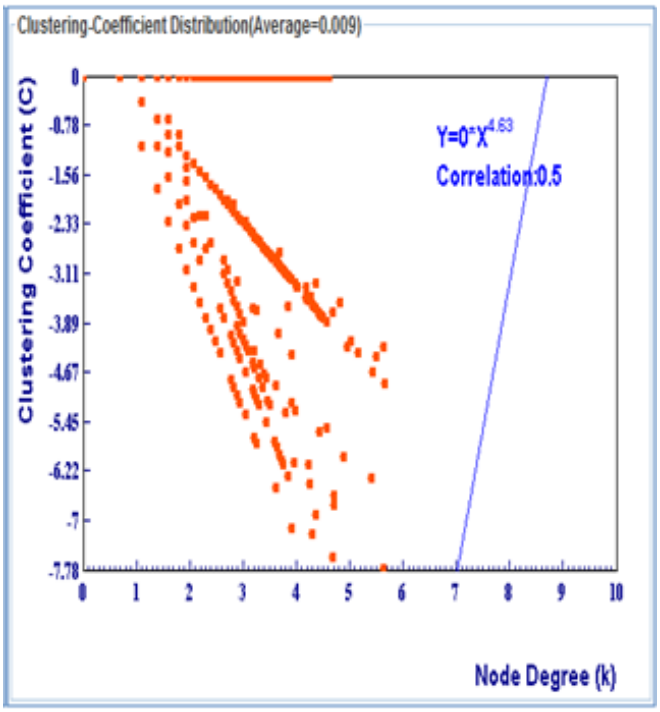

Figure 6: Myopathy Disease specific TFs/miRs interaction Network Clustering- Coefficient Distribution

Table 1: miRNAs Myopathy and Parkinson diseases

S.No	Disease Name	miRNAs
1	Parkinson Disease	hsa-miR-433,hsa-miR-133b,hsa-miR-7,hsa-miR-64,hsa-miR-65
2	Myopathy	hsa-miR-132,hsa-miR-21,hsa-miR-210,hsa-miR-214,hsa-miR-409-3p,hsa-miR-432,hsa-miR-487b,hsa-miR-495,hsa-miR-99b,hsa-miR-130a,hsa-miR-199a,hsa-miR-199a*,hsa-miR-155,hsa-miR-222,hsa-miR-223,hsa-miR-299-5p,hsa-miR-30a-3p,hsa-miR-30c,hsa-miR-335,hsa-miR-34a,hsa-miR-362,hsa-miR-368,hsa-miR-376a,hsa-miR-379,hsa-miR-221,hsa-miR-154,hsa-miR-146b,hsa-miR-148a,hsa-miR-381,hsa-miR-382

Table 2: Pathway study of 131common proteins

S. No.	Pathway Name	Gene Name
1	ErbB signaling pathway	CDKN1B ,EGF, EGFR, GRB2, PAK1, PIK3CA, AKT1, ERBB2, MYC
2	MAPK signaling pathway	FASLG, EGF, EGFR, FGFR1, GRB2, HSPA1B, CACNA1C, NFKB1, PAK1, RAC1, SRF, TGFB1, TGFBR2, AKT1, MYC, RELB
3	Regulation of actin cytoskeleton	ACTB, ACTG1, APC, EGF, EGFR, FGFR1, ITGB1, PAK1, PIK3CA, RHOA, RAC1
4	Hypertrophic cardiomyopathy (HCM)	ACTB, ACTG1, CACNA1C, IGF1, ITGB1, IL6, TGFB1
5	TGF-beta signaling pathway	SMAD2, SMAD5, BMP2, RHOA, TGFB1, TGFBR2, MYC
6	Cell cycle	E2F1, E2F3, SMAD2, CCND1, CDKN1B, CDKN1C, TGFB1, MYC
7	Toll-like receptor signaling pathway	IL6, NFKB1,8PIK3CA, RAC1, TLR4, TLR9, AKT1
8	Multiple antiapoptotic pathways from IGF-1R signaling lead to BAD phosphorylation	9GRB2, IRS1, IGF1R, PIK3CA, AKT1
9	Erythrocyte Differentiation Pathway	FLT3, IGF1, IL6, TGFB1
10	Chemokine signaling pathway	CXCL12, GRB2, NFKB1, PAK1, PIK3CA, RHOA, RAC1, AKT1
11	Apoptosis Pathway	BCL2, FASLG, NFKB1, PIK3CA, AKT1
12	Natural killer cell mediated cytotoxicity	FASLG, GRB2, HLA-G, PAK1, PIK3CA, RAC1
13	T cell receptor signaling pathway	AKT1,GRB2,pAK1,NFKB1,PIK3CA,RHOA