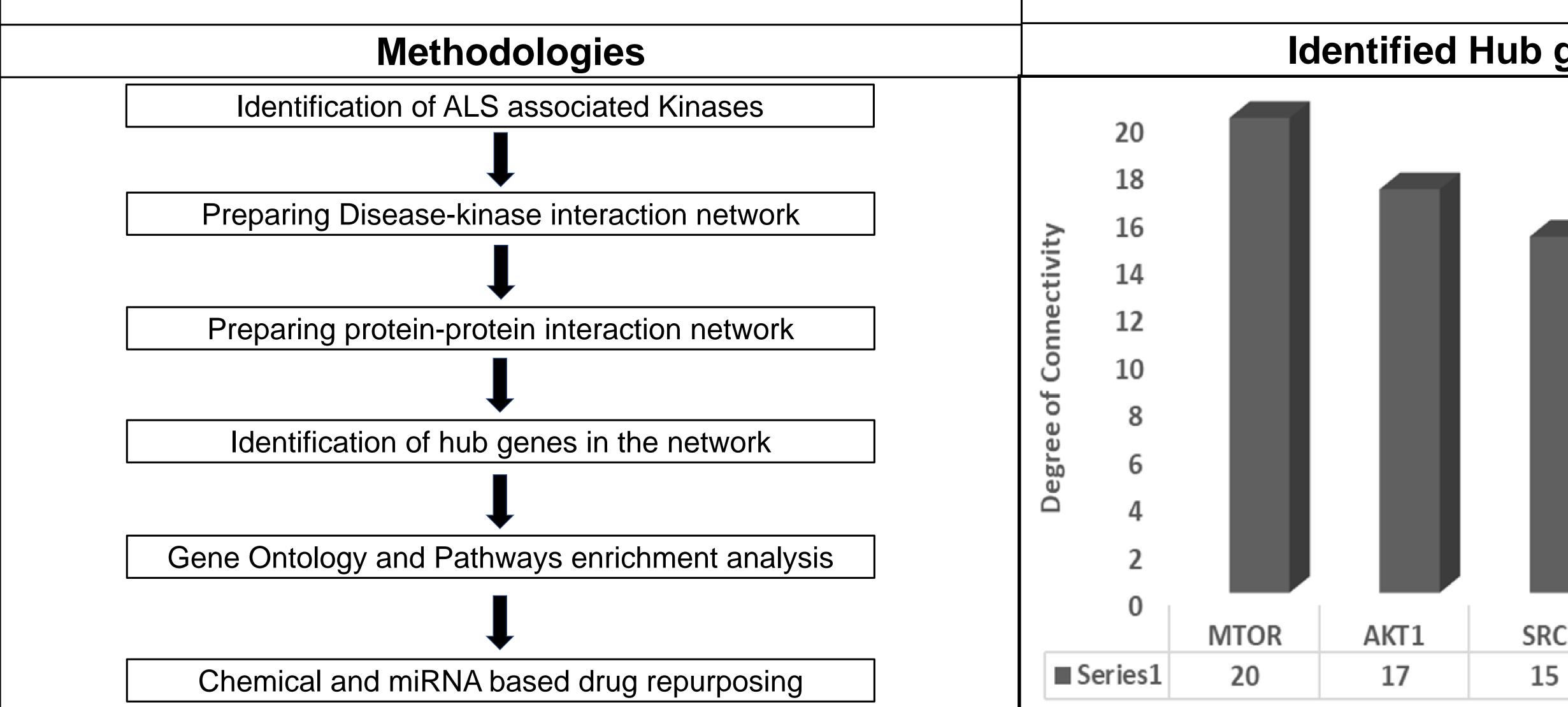


Abstract

Amyotrophic Lateral Sclerosis (ALS) is a rare progressive and chronic motor neuron degenerative disease for which at present no cure is available. In recent years, multiple genes encode kinases and other causative agents for ALS have been identified. Kinases are enzymes that show pleiotropic nature and regulate several signal transduction processes and pathways. Our study showed 32 ALS associated kinases interacting with multiple disorders including cancers and we prepared a kinase-disease interaction network. Further, the hub genes in the disease-causing network were identified by calculating the network topological properties. Drug and miRNA repurposing was also done against the hub genes in the network to identify the potential drug target to disrupt the disease-causing network. Our study expands the current knowledge and understanding of the role of kinases in ALS and cancers indicating the link between both the disease and suggested some drug to repurpose to improve the situation.

Introduction

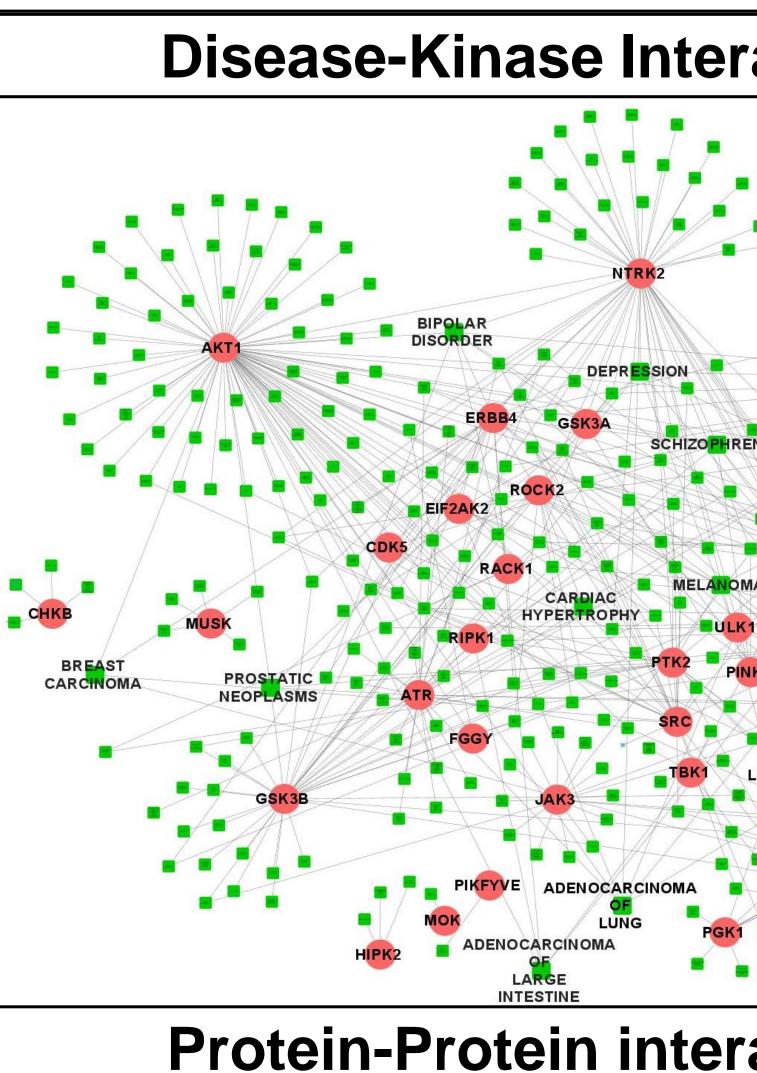
Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease, characterized by the progressive degeneration of upper and lower motor neurons in the brain, in the brainstem, and in the spinal region. It is a heterogeneous disease where several pathophysiological processes have been demonstrated to induce neuronal death, including oxidative stress, mitochondria impairment, growth factor deficiency, neuro-inflammation, defective axonal transport, RNA metabolism, aberrant stimulation of kinase activity, impaired brain energy metabolism, autophagy, and stress-induced cell death. Recent studies also reported several other causative genes that encodes for kinases and involved in ALS and other neurodegenerative diseases. Kinases are enzymes that function as transferases to catalyze almost every signal transduction process and pathway by adding a phosphate group (PO₄³⁻) to hydroxyl groups of substrates such as amino acids, nucleic acids, as well as lipids. The phosphorylation of protein via kinases stimulates the majority of the cell life processes, while the abnormal phosphorylation leads to the consequences of diseases, such as human cancer initiation and progression.

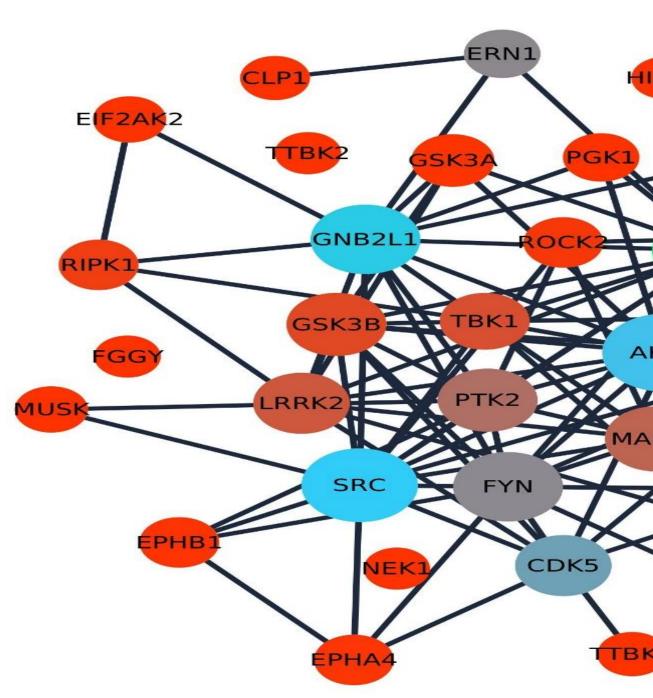


Network-Based Approach for Targeting Human Kinases commonly associated with Amyotrophic Lateral **Sclerosis and Cancer** Fatima Khatoon*, Vijay Kumar

Amity Institute of Neuropsychology and Neurosciences, Amity University, Noida

Results

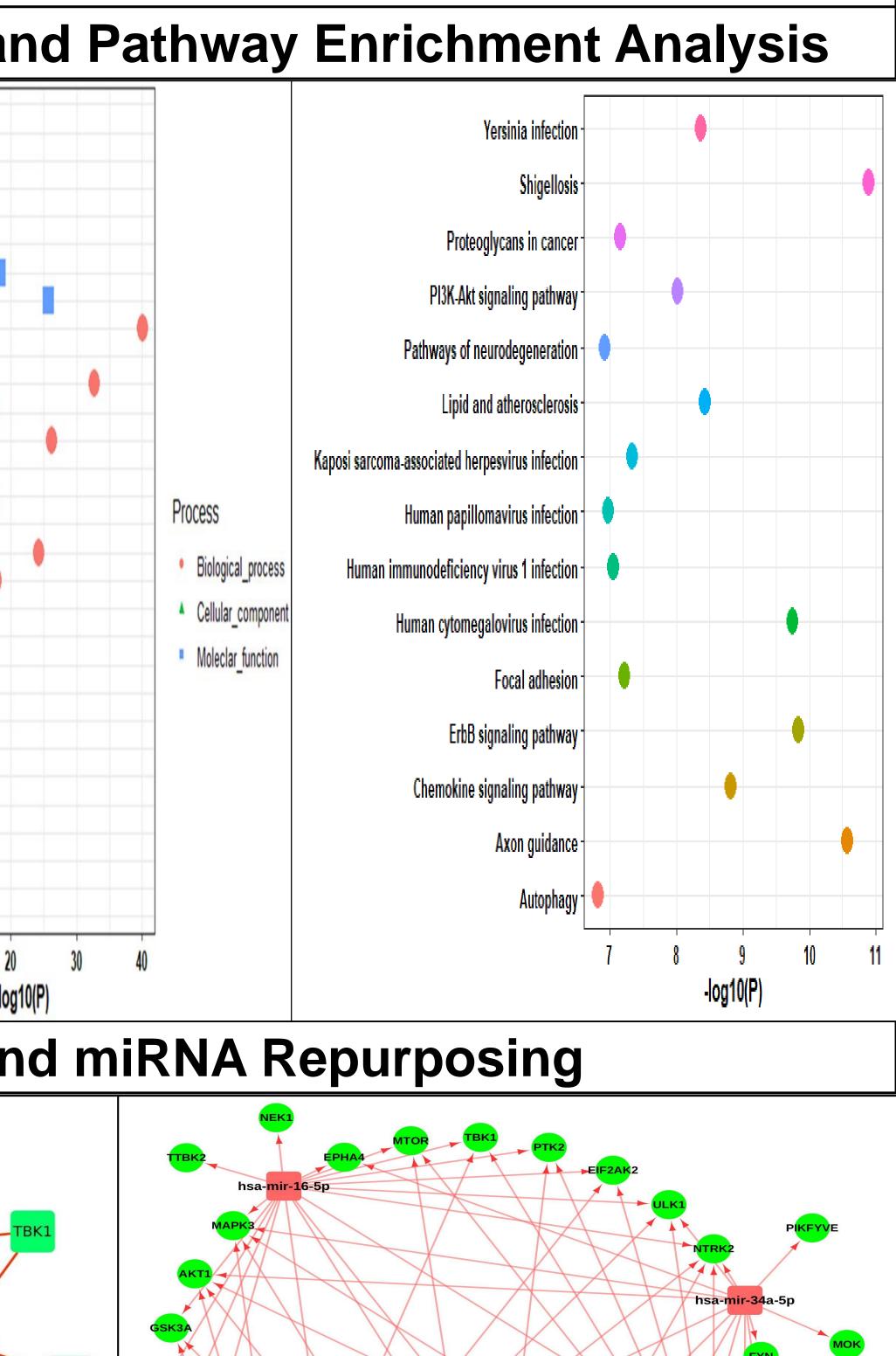


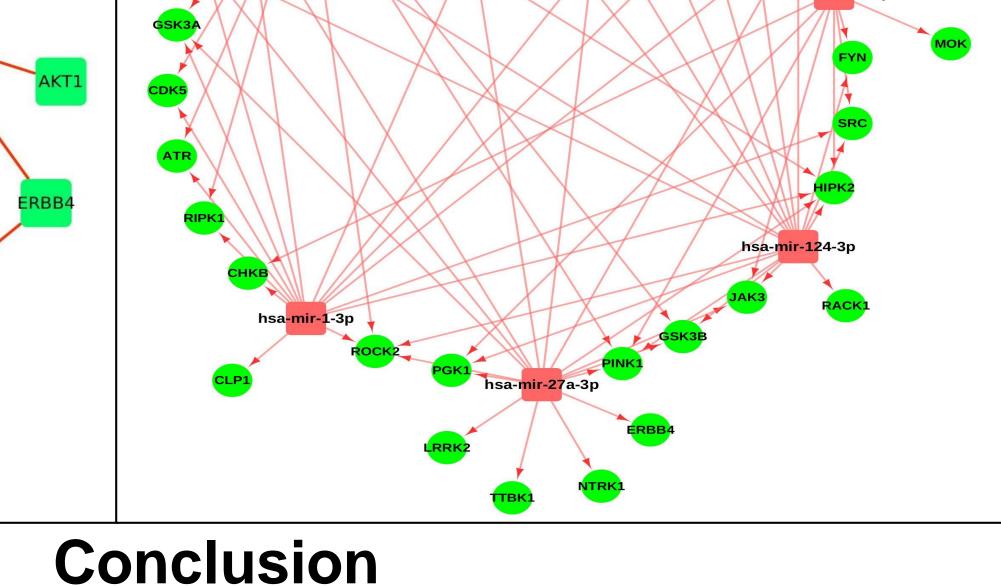


			y , Nora a			
S			Gene	Ontol	ogy	' ar
ractio	n Netwo	rk	transmembrane receptor protein tyrosi transmembrane receptor prote	ne kinase activity (GO:000471 ein kinase activity (GO:001919	4) -	
			ta	u protein binding (GO:004815 ein kinase activity (GO:005032	6) -	
			SH	2 domain binding (GO:004216	9)	
-			protein tyrosi	n phosphorylation (GO:000193 ne kinase activity (GO:000471	3)-	
_ AN				ne kinase activity (GO:000467 n phosphorylation (GO:000646		
ТТВК2			protein homodin	nerization activity (GO:004280 ophosphorylation (GO:004677	3)	
MALIGNANT	NTRK1		positive regulation o	f phosphorylation (GO:004232	7)-	•
RENIA NEOPLASM OF PROSTATE				phosphorylation (GO:001631 osphatase binding (GO:001990	2)-	
	NEK1		peptidyl-three	e phosphorylation (GO:001810 nine modification (GO:001821	0) -	
			peptidyl-serine peptidyl-se	e phosphorylation (GO:001810 erine modification (GO:001820	5) - 9) -	•
		MAPK3		nucleus (GO:000563 neuron projection (GO:004300		
INK1 EPHA4				membrane raft (GO:004512 kinase activity (GO:001630	1) 🔺	
LRRK2 ERN1				ounded organelle (GO:004323	1) 🔺	-
LRRK2 ERN1	EPHB1		gi endo	ial cell projection (GO:009738 psome membrane (GO:001000	8) - 🔺	
	CLP1			early endosome (GO:000576 dendrite (GO:003042	9) - A 5) - A	
			cellular protein mo	dification process (GO:000646 caveola (GO:000590	4)-	•
				axon (GO:003042		
actio	n networ	'k			10	20 -log1
				D	rug	an
			GSK3B			K3A
ATR	СНКВ		NTRK1	\mathcal{N}	1	F
	PIKFYVE		Р	F-00562271	T	7
MTOR			јакз	44		
	ULK1		РТК2		CENISI	HP IB
un		RK1	HIPK2	TX	\times	\backslash
аркз					$/ \setminus$	
PINK1	ERBB4 MOK		SRC	ROCK2		
				\searrow	//	
JAI	КЗ			VANDE	TANIB	
				EPHA4		MTOR
				EPH	нв1	
b gen	es		In this stud	lv we ha		ISEC
			investigate	•		
			human dis			
			interactom			
			several hu			
			depression			
			hub genes			
			high degre	e of in	terac	ctior
			identified 2	28 kinas	es ir	nclu
			well as va	rious hu	ıman	ca
			developing	a bette	r un	der
			as well as i	in cance	r	
						•
				, the set - 11	Λ	//
SRC	FYN	GNB2L1	F.K sincerely	y thank th	ie Am	nty l
15	13	13				

13

13





ed a network-based system biology approach to sed molecular interplay between ALS and other cancer. We constructed the disease-kinase trates the significant involvement of kinases in including ALS, schizophrenia, bipolar disorder, cancers. Here, from PPI network the resulting 1, GNB2L1, SRC, FYN, and mTOR showing ons between the kinases. Moreover, we also uding hub genes, that are involved in ALS as ancers. We believe that this study will help in rstanding of kinases role in neurodegeneration

Acknowledgment

University, Noida, for providing facilities.