study showed that disease-causing TDP-43 mutations do not primarily affect the interacting capacity. They revealed that TDP-43 interacting proteins, functionally associated with RNA metabolism, forms two clusters composed of the nuclear splicing cluster and the cytoplasmic translation cluster. By importing their dataset into pathway analysis tools, we found that these proteins are most closely associated with "Ribosome" pathway of KEGG, "Protein Synthesis, RNA Post-Transcriptional Modification, Cell Cycle" network of IPA, and "spliceosome assembly" pathway of KeyMolnet, being consistent with a central role of TDP-43 in splicing and translation as reported previously (Freibaum et al., 2010). Based on these results, we concluded that TDP-43 and interacting proteins cooperatively regulate mRNA splicing on spliceosome and translation on ribosome, by dynamically translocating themselves from the nucleus to the cytoplasm. Previous studies indicate that TDP-43 continuously shuttles between the nucleus and the cytoplasm in a transcription-dependent manner (Ayala et al., 2008), supporting this view. Defective karyopherin-mediated nuclear import causes cytoplasmic accumulation of TDP-43 (Nishimura et al., 2010). TDP-43 proteins in the nucleus are concentrated in perichromatin fibrils (PFs), which act as nuclear sites for mRNA transcription and cotranscriptional splicing (Casafont et al., 2009).

The expression of approximately 95% of human multi-exon genes involves alternative splicing that contributes to protein diversity and tissue-specific gene expression (Chen and Manley, 2009). Both constitutive and alternative splicing events are carried on the spliceosome, composed of a battery of small nuclear ribonucleoproteins (snRNPs) and auxiliary proteins that cooperate to recognize the exact splice site and catalyse the precise splicing reaction (Chen and Manley, 2009). The cis-regulatory elements of mRNA precusors are classified into four groups, such as exonic splicing enhancers (ESEs), exonic splicing silencers (ESSs), intronic splicing enhancers (ISEs), and intronic splicing silencers (ISSs). ESEs are recognized by the serine/arginine-rich (SR) protein family members, while ISSs and ESSs are bound by heterogeneous nuclear RNPs (hnRNPs). ISEs are recognized by several proteins, including neuro-oncological ventral antigen 1 (NOVA1), NOVA2, *Caenorhabditis elegans* fox-1 homolog 1 (FOX1), FOX2, hnRNPF, and hnRNPH (Chen and Manley, 2009). Binding of

TDP-43 to pre-mRNAs influences alternative splicing in a position-dependent manner similar to NOVA proteins (Tollervey et al., 2011).

Finally, we for the first time investigated the integrated molecular network of total 4,063 presumptive human TDP-43 target RNAs and 227 TDP-43 interacting proteins by using pathway analysis tools. We found that all of these molecules are most closely associated with "Ribosome" pathway of KEGG, "RNA Post-Transcriptional Modification, Genetic Disorder, Neurological Disease" network of IPA, and "Transcriptional regulation by p53" pathway of KeyMolnet. We identified the set of 106 genes concurrently serving as both TDP-43 target RNAs and interacting proteins (Table 2), which suggest the existence of an autoregulatory loop in the control of gene expression of TDP-43 interacting proteins. The list of 106 genes includes DDX17, DDX3, DHX9, ILF2, and ILF3, all of which were previously identified in HeLa cells as the components of the microRNA processing machinery (Ling et al., 2010). These results support an active role of TDP-43 in microRNA biogenesis (Buratti and Baralle, 2010). Actually, the levels of expression of let-7b are reduced, while those of miR-663 are elevated in TDP-43 knockdown Hep-3B cells (Buratti et al., 2010). The set of 106 genes also includes TDP-43 (TARDBP) itself. Importantly, TDP-43 negatively regulates its own protein expression level by binding to 3' untranslated region (UTR) of TDP-43 mRNA and increasing mRNA degradation (Ayala et al., 2011). Thus, cellular TDP-43 protein levels are tightly regulated autonomously, and overexpression of exogenous TDP-43 induces a dramatic depletion of normal nuclear TDP-43 in transgenic mouse brains *in vivo* (Igaz et al., 2011).

CONCLUSIONS

TDP-43 with RNA-binding and protein-interacting domains in its structure forms a functional complex with multiple target RNAs and interacting proteins *in vivo*. By using KEGG, IPA, and KeyMolnet, the present study characterized the comprehensive molecular network of TDP-43 target RNAs and interacting proteins recently identified. Although the three different tools did not illustrated perfectly matched molecular networks and pathways, the results consistently suggest that the complex network of TDP-43 target RNAs and interacting proteins plays a pivotal role in mRNA splicing on spliceosome and translation on ribosome, by dynamically translocating themselves from the nucleus to the cytoplasm. Based on these observations, the present study would propose the systems biological view that TDP-43 serves as a molecular scaffold that coordinates RNA-dependent regulation of gene transcription and translation essential for achievement of diverse neuronal functions, including axon guidance. Therefore, even a trivial perturbation that disturbs the TDP-43-mediated molecular coordination, possibly caused by genetic and environmental insults and stresses, could deregulate robustness of the molecular network, disturb normal neuronal function, and induce neurodegeneration in ALS and FTLD.

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KEY TERMS AND DEFINITIONS

ALS: Amyotrophic lateral sclerosis (ALS) is an adult-onset fatal neurodegenerative disease characterized by generalized skeletal and bulbar muscle atrophy owing to progressive loss of cortical and spinal motor neurons. Up to 10% of ALS cases are responsible for inheritable genetic mutations of the genes, such as SOD1, FUS/TLS, TDP-43/TARDBP, OPTN, UBQLN2, and ANG.

FTLD: Frontotemporal lobar degeneration (FTLD) constitutes a group of clinically, pathologically, and genetically heterogeneous disorders characterized by remarkable atrophy of the frontotemporal cortex in the brain. Up to 40% of FTLD cases are responsible for inheritable genetic mutations of the genes, such as TAU, TDP-43/TARDBP, FUS/TLS, GRN, VCP, and CHMP2B. Substantial populations of ALS and FTLD share clinical and pathological manifestations, categorized into TDP-43 proteinopathy.

KEGG: Kyoto Encyclopedia of Genes and Genomes (KEGG) is a public database that systematically integrates genomic and chemical information to create the whole biological system *in silico*. KEGG includes 148,769 manually curated reference pathways that cover a wide range of metabolic, genetic, environmental, and cellular processes, and human diseases and drugs.

KeyMolnet: KeyMolnet is a pathway analysis tool of bioinformatics composed of knowledge-based contents on 137,300 relationships among human genes and proteins, small molecules, diseases, pathways and drugs, curated by expert biologists. By importing the list of Entrez Gene IDs, KeyMolnet automatically provides corresponding molecules as a node on networks.

IPA: Ingenuity Pathways Analysis (IPA) is a pathway analysis tool of bioinformatics composed

of knowledgebase containing approximately 2,500,000 biological and chemical interactions and functional annotations with definite scientific evidence, curated by expert biologists. By uploading the list of Entrez Gene IDs, the network-generation algorithm identifies focused genes integrated in a global molecular network.

Molecular Network: Molecular network represents the cell-wide map of complex molecular interactions extracted from high-throughput data of the genome, transcriptome and proteome illustrated with the aid of the literature-based knowledgebase of molecular pathways. The logically arranged molecular networks construct the whole system characterized by robustness that maintains the proper function of the system in the face of genetic and environmental perturbations.

Systems Biology: Systems biology is a research field to study the whole system of living organism based on the experimentally and computationally integrated molecular networks by using simulated biological models.

TDP-43: TAR DNA-binding protein-43 (TDP-43) is a nuclear protein, capable of interacting with UG/TG repeat stretches of target RNAs/DNAs, plays a key role in regulation of transcription, alternative splicing, mRNA stability and transport, and microRNA biogenesis. Abnormally phosphorylated, ubiquitinated, and aggregated TDP-43 proteins constitute a principal component of neuronal and glial cytoplasmic and nuclear inclusions in the brains of ALS and FTLD.

Table 1. Top 30 Gene Ontology Categories Enriched in the Set of TDP-43 Target RNAs and Interacting Proteins

Set	Rat TDP-43 Target RNAs			Human TDP-43 Interacting Proteins			The Integration of Human TDP-43 Target RNAs and Interacting Proteins		
Rank	GO Term	Number of Genes	p-Value after Bonferroni Correction	GO Term	Number of Genes	p-Value after Bonferroni Correction	GO Term	Number of Genes	p-Value after Bonferroni Correction
1	GO:0000166~nucleotide binding	624	7.846E-29	GO:0030529~ribonucleoprotein complex	109	9.329E-101	GO:0003723~RNA binding	333	3.995E-38
2	GO:0008104~protein localization	269	1.403E-25	GO:0003723~RNA binding	122	2.460E-98	GO:0005829~cytosol	511	5.094E-34
3	GO:0005829~cytosol	401	1.942E-25	GO:0006414~translational elongation	49	1.252E-60	GO:0000166~nucleotide binding	756	1.365E-27
4	GO:0046907~intracellular transport	214	8.087E-24	GO:0005840~ribosome	58	8.007E-55	GO:0046907~intracellular transport	286	8.787E-26
5	GO:0045184~establishment of protein localization	230	1.979E-22	GO:0006412~translation	64	4.545E-52	GO:0070013~intracellular organelle lumen	610	5.192E-25
6	GO:0015031~protein transport	228	3.148E-22	GO:0033279~ribosomal subunit	46	8.545E-49	GO:0031981~nuclear lumen	513	8.699E-24
7	GO:0016192~vesicle-mediated transport	193	5.554E-22	GO:0022626~cytosolic ribosome	40	1.429E-48	GO:0043233~organelle lumen	615	2.350E-23
8	GO:0045202~synapse	172	3.155E-21	GO:0003735~structural constituent of ribosome	50	2.898E-47	GO:0031974~membrane-enclosed lumen	624	4.034E-23
9	GO:0032553~ribonucleotide binding	494	8.206E-21	GO:0006396~RNA processing	67	1.579E-41	GO:0030529~ribonucleoprotein complex	228	1.356E-22
10	GO:0032555~purine ribonucleotide binding	493	1.296E-20	GO:0043228~non-membrane-bounded organelle	120	8.289E-36	GO:0006396~RNA processing	242	1.717E-22
11	GO:0043005~neuron projection	188	3.111E-20	GO:0043232~intracellular non-membrane-bounded organelle	120	8.289E-36	GO:0045184~establishment of protein localization	312	4.403E-22

12	GO:0070013~intracellular organelle lumen	399	9.446E-20	GO:0044445~cytosolic part	40	8.788E-36	GO:0016071~mRNA metabolic process	181	4.404E-22
13	GO:0031981~nuclear lumen	328	5.256E-19	GO:0005198~structural molecule activity	61	1.009E-28	GO:0015031~protein transport	309	8.598E-22
14	GO:0017076~purine nucleotide binding	506	6.240E-19	GO:0016071~mRNA metabolic process	46	5.746E-27	GO:0008104~protein localization	345	1.927E-21
15	GO:0043233~organelle lumen	404	6.257E-18	GO:0015934~large ribosomal subunit	26	6.441E-27	GO:0006397~mRNA processing	162	2.830E-21
16	GO:0031974~membrane-enclosed lumen	413	6.353E-18	GO:0022625~cytosolic large ribosomal subunit	21	4.693E-25	GO:0008380~RNA splicing	144	7.795E-19
17	GO:0019899~enzyme binding	195	3.107E-17	GO:0006397~mRNA processing	40	6.246E-23	GO:0032555~purine ribonucleotide binding	599	6.424E-17
18	GO:0000267~cell fraction	333	3.419E-17	GO:0005730~nucleolus	53	5.630E-21	GO:0032553~ribonucleotide binding	599	6.424E-17
19	GO:0042995~cell projection	265	9.157E-17	GO:0070013~intracellular organelle lumen	82	1.455E-20	GO:0043232~intracellular non-membrane-bounded organelle	792	1.406E-16
20	GO:0005626~insoluble fraction	271	3.683E-16	GO:0043233~organelle lumen	82	6.435E-20	GO:0043228~non-membrane-bounded organelle	792	1.406E-16
21	GO:0016071~mRNA metabolic process	116	2.963E-15	GO:0015935~small ribosomal subunit	21	1.353E-19	GO:0005730~nucleolus	269	1.642E-16
22	GO:0019904~protein domain specific binding	144	7.230E-15	GO:0008380~RNA splicing	35	1.952E-19	GO:0070727~cellular macromolecule localization	182	8.135E-16
23	GO:0006397~mRNA processing	104	8.461E-15	GO:0031974~membrane-enclosed lumen	82	2.288E-19	GO:0017076~purine nucleotide binding	615	1.439E-15
24	GO:0003723~RNA binding	175	1.066E-14	GO:0005829~cytosol	69	3.767E-19	GO:0045202~synapse	158	2.971E-15
25	GO:0005624~membrane fraction	255	1.423E-14	GO:0031981~nuclear lumen	72	3.995E-19	GO:0034613~cellular protein localization	179	5.267E-15
26	GO:0030163~protein catabolic process	142	7.059E-14	GO:0022627~cytosolic small ribosomal subunit	18	4.886E-19	GO:0016192~vesicle-mediated transport	229	3.924E-14

27	GO:0016023~cytoplasmic membrane-bounded vesicle	196	3.197E-13	GO:0022613~ribonucleoprotein complex biogenesis	28	1.469E-17	GO:0006886~intracellular protein transport	164	7.429E-14
28	GO:0043632~modification-dependent macromolecule catabolic process	125	5.289E-13	GO:0003729~mRNA binding	20	4.647E-17	GO:0030163~protein catabolic process	240	1.039E-12
29	GO:0019941~modification-dependent protein catabolic process	125	5.289E-13	GO:0042254~ribosome biogenesis	23	1.015E-15	GO:0051603~proteolysis involved in cellular protein catabolic process	231	4.158E-12
30	GO:0044456~synapse part	115	1.839E-12	GO:0000377~RNA splicing, via transesterification reactions with bulged adenosine as nucleophile	23	1.867E-13	GO:0043632~modification-dependent macromolecule catabolic process	223	4.158E-12

Entrez Gene IDs of 4,163 rat TDP-43 target RNAs (Sephton et al., 2011), 227 human interacting proteins (Freibaum et al., 2010), and the integration of both 4,063 human TDP-43 target RNAs and 227 human interacting proteins were imported into the Functional Annotation tool of DAVID. Top 30 GO categories enriched in the gene set are listed.

Table 2. The Set of 106 Genes Concurrently Serving as Both Human TDP-43 Target RNAs and Interacting Proteins

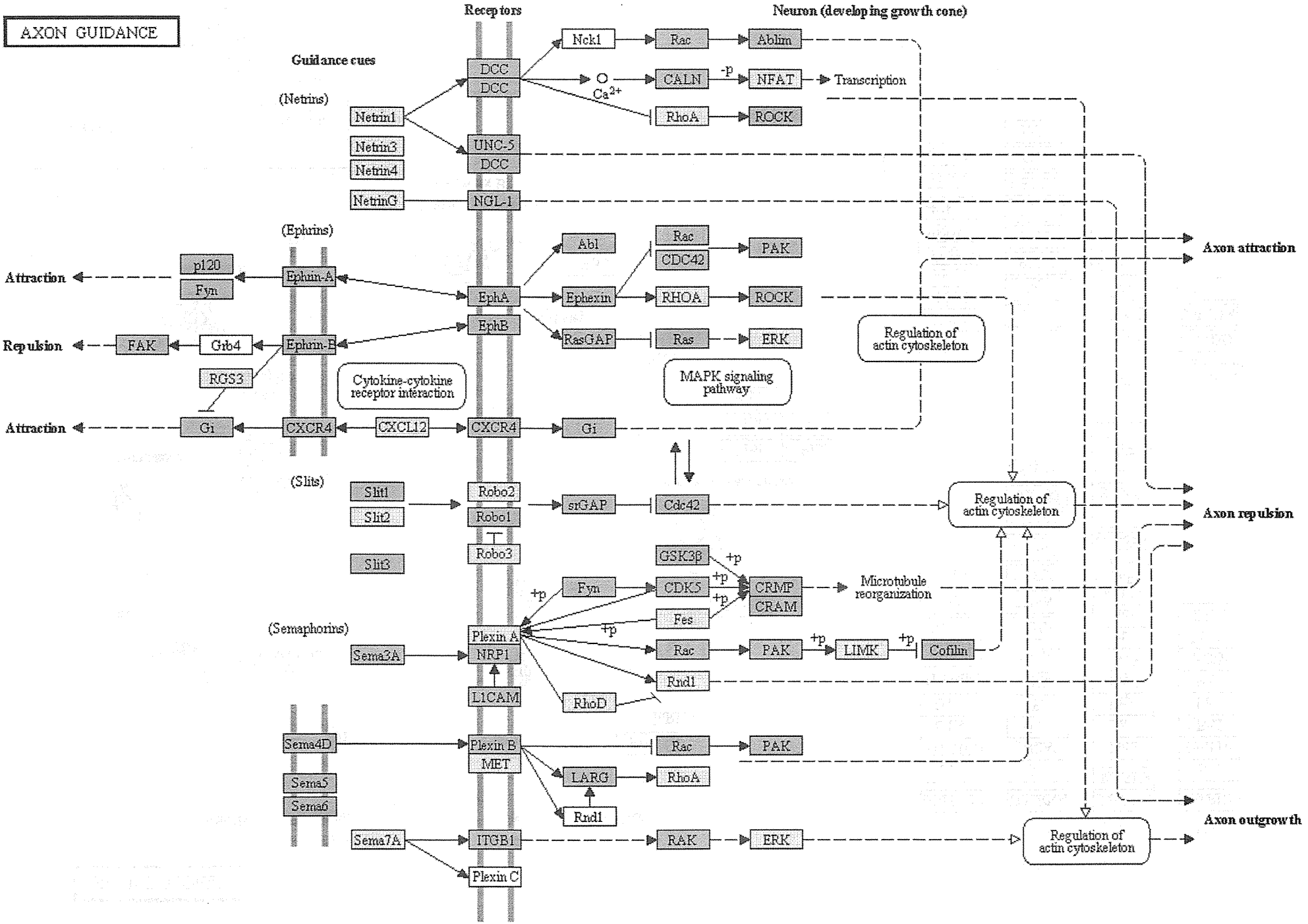
Entrez Gene ID	Gene Symbol	Gene Name
103	ADAR	adenosine deaminase, RNA-specific
444	ASPH	aspartate beta-hydroxylase
11273	ATXN2L	ataxin 2-like
51637	C14orf166	chromosome 14 open reading frame 166
81627	C1orf25	chromosome 1 open reading frame 25
4076	CAPRIN1	cell cycle associated protein 1
988	CDC5L	CDC5 cell division cycle 5-like (S. pombe)
10658	CELF1	CUG triplet repeat, RNA binding protein 1
8531	CSDA	cold shock domain protein A
7818	DAP3	death associated protein 3
10521	DDX17	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17
9188	DDX21	DEAD (Asp-Glu-Ala-Asp) box polypeptide 21
1654	DDX3X	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked
1655	DDX5	DEAD (Asp-Glu-Ala-Asp) box polypeptide 5
79009	DDX50	DEAD (Asp-Glu-Ala-Asp) box polypeptide 50
1656	DDX6	DEAD (Asp-Glu-Ala-Asp) box polypeptide 6
22907	DHX30	DEAH (Asp-Glu-Ala-His) box polypeptide 30
170506	DHX36	DEAH (Asp-Glu-Ala-His) box polypeptide 36
1660	DHX9	DEAH (Asp-Glu-Ala-His) box polypeptide 9
27292	DIMT1L	DIM1 dimethyladenosine transferase 1-like (S. cerevisiae)
10049	DNAJB6	DnaJ (Hsp40) homolog, subfamily B, member 6
1937	EEF1G	eukaryotic translation elongation factor 1 gamma
27161	EIF2C2	eukaryotic translation initiation factor 2C, 2
8661	EIF3A	eukaryotic translation initiation factor 3, subunit A
8662	EIF3B	eukaryotic translation initiation factor 3, subunit B
8672	EIF4G3	eukaryotic translation initiation factor 4 gamma, 3
1993	ELAVL2	ELAV (embryonic lethal, abnormal vision, Drosophila)-like 2 (Hu antigen B)

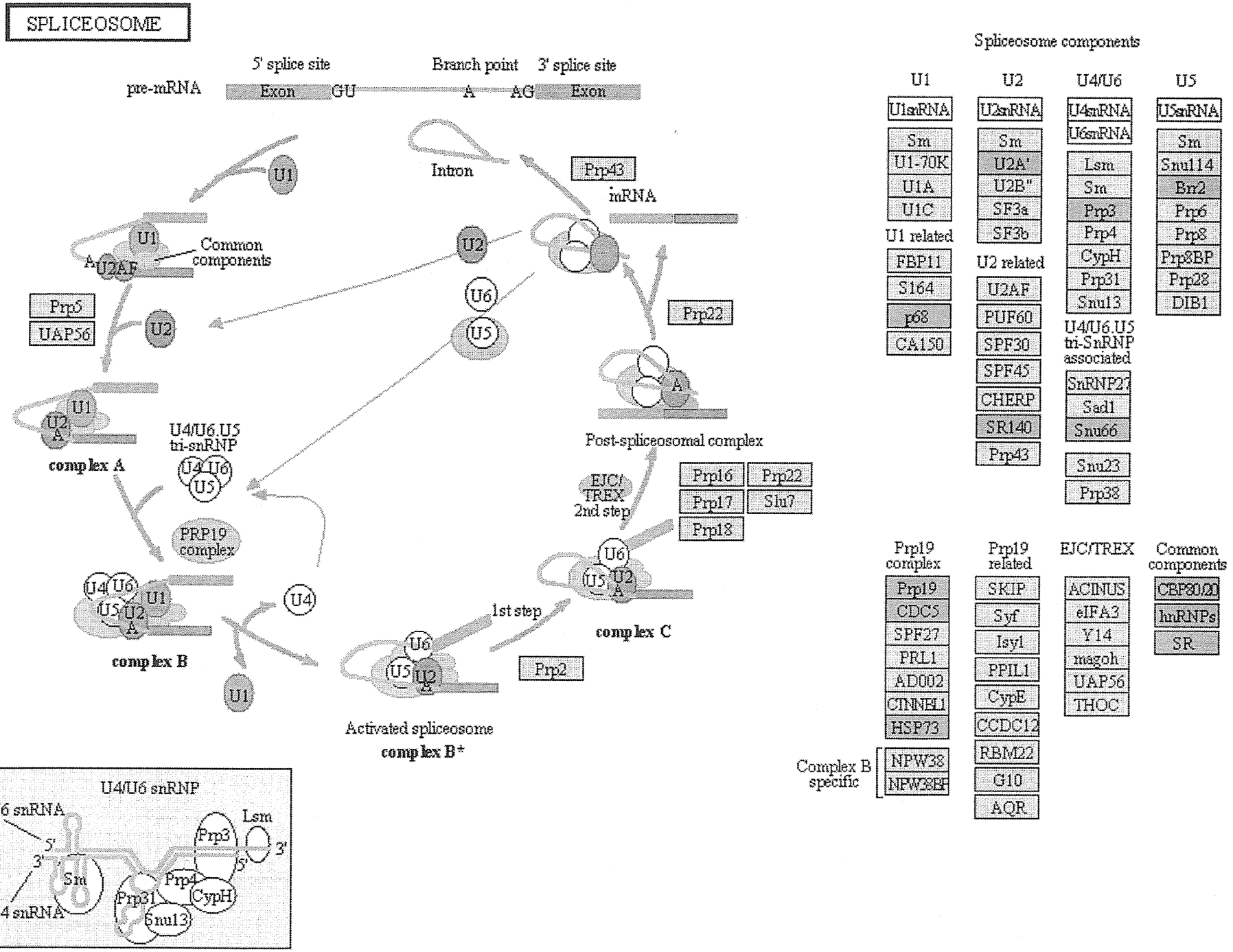
2091	FBL	fibrillarin
1968	FIF2SC	eukaryotic translation initiation factor 2, subunit 3 gamma, 52kDa
10146	G3BP1	GTPase activating protein (SH3 domain) binding protein 1
9908	G3BP2	GTPase activating protein (SH3 domain) binding protein 2
26354	GNL3	guanine nucleotide binding protein-like 3 (nucleolar)
2926	GRSF1	G-rich RNA sequence binding factor 1
9931	HELZ	helicase with zinc finger
3178	HNRNPA1	heterogeneous nuclear ribonucleoprotein A1
3181	HNRNPA2B1	heterogeneous nuclear ribonucleoprotein A2/B1
3182	HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B
3187	HNRNPH1	heterogeneous nuclear ribonucleoprotein H1 (H)
4670	HNRNPM	heterogeneous nuclear ribonucleoprotein M
10236	HNRNPR	heterogeneous nuclear ribonucleoprotein R
3192	HNRNPU	heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)
9987	HNRPDL	heterogeneous nuclear ribonucleoprotein D-like
3183	HNRPNC	heterogeneous nuclear ribonucleoprotein C (C1/C2)
3308	HSPA4	heat shock 70kDa protein 4
3309	HSPA5	heat shock 70kDa protein 5 (glucose-regulated protein, 78kDa)
10808	HSPH1	heat shock 105kDa/110kDa protein 1
3608	ILF2	interleukin enhancer binding factor 2, 45kDa
3609	ILF3	interleukin enhancer binding factor 3, 90kDa
8570	KHSRP	KH-type splicing regulatory protein
23185	LARP4B	La ribonucleoprotein domain family, member 4B
124801	LSM12	LSM12 homolog (S. cerevisiae)
51631	LUC7L2	LUC7-like 2 (S. cerevisiae)
4134	MAP4	microtubule-associated protein 4
9782	MATR3	matrin 3
4343	MOV10	Mov10, Moloney leukemia virus 10, homolog (mouse)
65080	MRPL44	mitochondrial ribosomal protein L44
51642	MRPL48	mitochondrial ribosomal protein L48
4440	MSI1	musashi homolog 1 (Drosophila)
92140	MTDH	metadherin

4686	NCBP1	nuclear cap binding protein subunit 1, 80kDa
4691	NCL	nucleolin
51491	NOP16	NOP16 nucleolar protein homolog (yeast)
10528	NOP56	NOP56 ribonucleoprotein homolog (yeast)
51602	NOP58	NOP58 ribonucleoprotein homolog (yeast)
4869	NPM1	nucleophosmin (nucleolar phosphoprotein B23, numatrin)
10482	NXF1	nuclear RNA export factor 1
26986	PABPC1	poly(A) binding protein, cytoplasmic 1
8761	PABPC4	poly(A) binding protein, cytoplasmic 4 (inducible form)
26227	PHGDH	phosphoglycerate dehydrogenase
5317	PKP1	plakophilin 1 (ectodermal dysplasia/skin fragility syndrome)
54814	QPCTL	glutaminyl-peptide cyclotransferase-like
9584	RBM39	RNA binding motif protein 39
9921	RNF10	ring finger protein 10
4736	RPL10A	ribosomal protein L10a
6144	RPL21	ribosomal protein L21
6146	RPL22	ribosomal protein L22
6160	RPL31	ribosomal protein L31
6124	RPL4	ribosomal protein L4
6133	RPL9	ribosomal protein L9
6205	RPS11	ribosomal protein S11
6218	RPS17	ribosomal protein S17
6222	RPS18	ribosomal protein S18
6228	RPS23	ribosomal protein S23
6229	RPS24	ribosomal protein S24
6189	RPS3A	ribosomal protein S3A
6201	RPS7	ribosomal protein S7
6203	RPS9	ribosomal protein S9
3921	RPSA	ribosomal protein SA
9092	SART1	squamous cell carcinoma antigen recognized by T cells
26135	SERBP1	SERPINE1 mRNA binding protein 1
79085	SLC25A23	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23

23020	SNRNP200	small nuclear ribonucleoprotein 200kDa (U5)
6732	SRPK1	SRSF protein kinase 1
6431	SRSF6	serine/arginine-rich splicing factor 6
6432	SRSF7	serine/arginine-rich splicing factor 7
6741	SSB	Sjogren syndrome antigen B (autoantigen La)
6780	STAU1	staufen, RNA binding protein, homolog 1 (Drosophila)
10492	SYNCRIP	synaptotagmin binding, cytoplasmic RNA interacting protein
23435	TARDBP	TAR DNA binding protein
7150	TOP1	topoisomerase (DNA) I
9100	USP10	ubiquitin specific peptidase 10
7415	VCP	valosin-containing protein
84305	WIBG	within bgcn homolog (Drosophila)
22803	XRN2	5'-3' exoribonuclease 2
9877	ZC3H11A	zinc finger CCCH-type containing 11A
23567	ZNF346	zinc finger protein 346

The set of 106 genes concurrently serving as both human TDP-43 target RNAs and interacting proteins are listed in an alphabetical order. The genes with Entrez Gene IDs of 3921, 4736, 6124, 6133, 6144, 6146, 6160, 6189, 6201, 6203, 6205, 6218, 6222, 6228, and 6229 are located on "Ribosome", while those with 988, 1655, 3178, 3183, 3192, 4670, 4686, 6431, 6432, 9092, and 23020 are located on "Splicesome" of KEGG pathways.


AXON GUIDANCE
Receptors
Neuron (developing growth cone)
Guidance cues
(Netrins)
Netrin1
Netrin3
Netrin4
NetrinG
DCC
DCC
UNC-5
DCC
NGL-1
Nck1
Rac
Ablim
CALN
-p
NFAT
Transcription
Ca2+
RhoA
ROCK
(Ephrins)
Attraction
p120
Fyn
Ephrin-A
EphA
Abl
Rac
CDC42
PAK
Ephexin
RHOA
ROCK
Repulsion
FAK
Grb4
Ephrin-B
EphB
RasGAP
Ras
ERK
RGS3
Cytokine-cytokine receptor interaction
MAPK signaling pathway
Regulation of actin cytoskeleton
Attraction
Gi
CXCR4
CXCL12
CXCR4
Gi
(Slits)
Slit1
Slit2
Slit3
Robo2
Robo1
Robo3
srGAP
Cdc42
Regulation of actin cytoskeleton
GSK3β
+p
Fyn
CDK5
CRMP
CRAM
Microtubule reorganization
Fes
(Semaphorins)
Plexin A
Sema3A
NRP1
L1CAM
Rac
PAK
LIMK
Cofilin
Rnd1
RhoD
Sema4D
Sema5
Sema6
Plexin B
MET
Rac
PAK
LARG
RhoA
Rnd1
Sema7A
ITGB1
Plexin C
RAK
ERK
Regulation of actin cytoskeleton
Axon attraction
Axon repulsion
Axon outgrowth


SPLICEOSOME
5' splice site
Branch point
3' splice site
pre-mRNA
Exon
GU
A
AG
Exon
Intron
mRNA
Common components
Prp5
UAP56
Prp22
complex A
U4/U6.U5 tri-snRNP
Post-spliceosomal complex
EJC/TREX 2nd step
Prp16
Prp22
Prp17
Slu7
Prp18
PRP19 complex
complex B
complex C
1st step
Prp2
Activated spliceosome
complex B*
U4/U6 snRNP
U6 snRNA
U4 snRNA
Sm
Lsm
Prp3
Prp4
CypH
Prp31
Snu13
Spliceosome components
U1
U2
U4/U6
U5
U1snRNA
U2snRNA
U4snRNA
U6snRNA
U5snRNA
Sm
U1-70K
U1A
U1C
U1 related
FBP11
S164
p68
CA150
U2A'
U2B"
SF3a
SF3b
U2 related
U2AF
PUF60
SPF30
SPF45
CHERP
SR140
Prp43
Lsm
Prp3
Prp4
CypH
Prp31
Snu13
U4/U6.U5 tri-SnRNP associated
SnRNP27
Sad1
Snu66
Snu23
Prp38
Snu114
Brr2
Prp6
Prp8
Prp8BP
Prp28
DIB1
Prp19 complex
Prp19
CDC5
SPF27
PRL1
AD002
CTNNBL1
HSP73
Complex B specific
NPW38
NPW38BP
Prp19 related
SKIP
Syf
Isy1
PPIL1
CypE
CCDC12
RBM22
G10
AQR
EJC/TREX
ACINUS
eIFA3
Y14
magoh
UAP56
THOC
Common components
CBP80/20
hnRNPs
SR