Global Medical Genetics 12 (2025) 100032

Contents lists available at ScienceDirect

Global Medical Genetics

journal homepage: www.keaipublishing.com/en/journals/gmg/

RNA binding proteins (RBPs) on genetic stability and diseases

Abdullahi Tunde Aborode[a], Ohilebo Abdulateef Abass[b], Shaibu Nasiru[a,b], Mary Ugunnushe Eigbobo[b], Sumana Nefishatu[b], Abdullahi Idowu[c], Zainab Tiamiyu[d], Aeshah A. Awaji[e], Nike Idowu[f], Babawale Roqeeb Busayo[g], Qasim Mehmood[h], Isreal Ayobami Onifade[i], Sodiq Fakorede[j], Ashraf Akintayo Akintola[k,*]

[a] Department of Research and Development, Healthy Africans Platform, Ibadan, Nigeria
[b] Department of Biochemistry, Ambrose Alli University Ekpoma, Nigeria
[c] Department of Biological Sciences, Purdue University Fort Wayne, USA
[d] Department of Biochemistry and Cancer Biology, Medical College of Georgia, Augusta University, USA
[e] Department of Biology, Faculty of Science, University College of Taymaa, University of Tabuk, Tabuk 71491, Saudi Arabia
[f] Department of Chemistry, University of Nebraska-Lincoln, USA
[g] University of Ilesa, Ilesa, Osun state, Nigeria
[h] Shifa Clinical Research Center, Shifa International Hospital, Islamabad, Pakistan
[i] Department of Division of Family Health, Health Research Incorporated, New York State Department of Health, USA
[j] Department of Physical Therapy, Rehabilitation Science, and Athletic Training, University of Kansas Medical Center, Kansas City, KS, USA
[k] Department of Biology Education, Teachers College & Institute for Phylogenomics and Evolution, Kyungpook National University, Daegu, South Korea

ARTICLE INFO

Keywords:
RNA binding proteins
Genetic stability
Diseases

ABSTRACT

RNA-binding proteins (RBPs) are integral components of cellular machinery, playing crucial roles in the regulation of gene expression and maintaining genetic stability. Their interactions with RNA molecules govern critical processes such as mRNA splicing, stability, localization, and translation, which are essential for proper cellular function. These proteins interact with RNA molecules and other proteins to form ribonucleoprotein complexes (RNPs), hence controlling the fate of target RNAs. The interaction occurs via RNA recognition motif, the zinc finger domain, the KH domain and the double stranded RNA binding motif (all known as RNA-binding domains (RBDs). These domains are found within the coding sequences (intron and exon domains), 5' untranslated regions (5'UTR) and 3' untranslated regions (3'UTR). Dysregulation of RBPs can lead to genomic instability, contributing to various pathologies, including cancer neurodegenerative diseases, and metabolic disorders. This study comprehensively explores the multifaceted roles of RBPs in genetic stability, highlighting their involvement in maintaining genomic integrity through modulation of RNA processing and their implications in cellular signalling pathways. Furthermore, it discusses how aberrant RBP function can precipitate genetic instability and disease progression, emphasizing the therapeutic potential of targeting RBPs in restoring cellular homeostasis. Through an analysis of current literature, this study aims to delineate the critical role of RBPs in ensuring genetic stability and their promise as targets for innovative therapeutic strategies.

* Corresponding author.
E-mail addresses: abdullahiaborodet@gmail.com (A.T. Aborode), abassohilebo@gmail.com (O.A. Abass), idowam01@pfw.edu (A. Idowu), ztiamiyu@augusta.edu (Z. Tiamiyu), aawaji@ut.edu.sa (A.A. Awaji), nidowu2@huskers.unl.edu (N. Idowu), roqeeb_babawale@unilesa.edu.ng (B.R. Busayo), qasimmehmood1051@gmail.com (Q. Mehmood), isrealonifade@gmail.com (I.A. Onifade), sfakorede@kumc.edu (S. Fakorede), ashraf.akintola@gmail.com (A.A. Akintola).

https://doi.org/10.1016/j.gmg.2024.100032
Received 29 October 2024; Received in revised form 26 November 2024; Accepted 28 November 2024

Introduction

In recent years, the regulation of gene expression at the post-transcriptional level has garnered significant attention due to its fundamental role in cellular homeostasis and its implication in a wide range of diseases [1]. This regulation occurs after transcription and before translation, influencing how genes are expressed at the RNA level [2]. Central to this regulatory framework are RNA-binding proteins (RBPs), which mediate diverse processes such as RNA splicing, transport, localization, translation, and degradation [3]. RBPs play crucial roles by interacting with RNA molecules and other proteins to form ribonucleoprotein complexes (RNPs), which control the fate of target RNAs [4], and the association of RBPs with RNA transcripts begins during transcription [5-7]. These proteins are characterized by their ability to bind RNA molecules through specific RNA-binding domains (RBDs) (such as the RNA recognition motif, the zinc finger domain, the KH domain and the double stranded RNA binding motif), which allow them to interact with diverse RNA targets, influencing their fate from synthesis to degradation [8,9]. These domains are found within the coding sequences (intron and exon domains), 5' untranslated regions (5'UTR) and 3' untranslated regions (3'UTR) of RNA [10].

The human genome contains at least 1200 confirmed RBPs (Table 1). Some important examples include serine-arginine rich proteins, human antigen R (HuR), heterogeneous nuclear ribonucleoprotein (HnRNP), TAR DNA-binding protein 43 (TDR-43), and Fragile X mental retardation protein (FMRP0) [11]. Dysregulation of RBPs has been increasingly associated with pathological conditions, particularly neurodegenerative, cancer, cardiovascular, diabetes and genetic disorders [12]. For instance, an aberrant RBP activity can lead to the misprocessing of RNA, resulting in the accumulation of disease-driving transcripts, protein misfolding and aggregation, phenomena that are often observed in cancers and neurodegenerative disorders like amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD), and spinal muscular atrophy (SMA). In these diseases, RBPs such as TDP-43, FUS, and LIN28 have been implicated in promoting oncogenic or neurotoxic effects through mechanisms like abnormal RNA splicing, stabilization of oncogenic transcripts, or aggregation of toxic protein species [13-15].

RBPs are also pivotal in maintaining genomic stability. For example, the long noncoding RNA NORAD has been shown to sequester PUMILIO proteins, thereby regulating their activity and contributing to genomic integrity [16]. Moreover, the interaction between RBPs and RNA can be modulated by genetic variations, such as single nucleotide polymorphisms (SNPs), which can affect RNA secondary structures and, consequently, RBP binding. This interplay between genetic variations and RBP functionality underscores the complexity of gene regulation and its implications for disease susceptibility.

Given the pivotal role of RBPs in disease pathogenesis, therapeutic targeting of RBPs has emerged as a promising strategy. Current approaches focus on disrupting RNA-protein interactions, modulating protein-protein complexes, and preventing RBP aggregation to restore cellular homeostasis [10]. Direct targeting strategies, including the knockdown or overexpression of specific RBPs, have been explored for their potential to modulate splicing decisions, particularly in diseases where splicing dysregulation contributes to disease pathology [17]. Additionally, indirect approaches, such as the use of small molecules, antisense oligonucleotides (ASOs), aptamers, and synthetic peptides, have shown potential in modulating RBP activity by disrupting their interactions with RNA or other proteins [7,18].

Advancements in proteomics and computational biology have facilitated the identification and characterization of novel RBPs, expanding our understanding of their diverse functions and interactions. For instance, large-scale studies have revealed that RBPs can bind thousands of RNA targets, often with overlapping functions, which complicates the dissection of their specific roles in cellular contexts. The development of predictive models for RBP-RNA interactions further enhances our ability to understand the mechanisms by which these proteins influence gene expression and stability [19]. This review provides a comprehensive view on the roles of RBPs on genetic stability, focusing on RBPs structures, examples, functions, genetic stability and therapeutic strategies.

RBPs structure & function

Structural features

RBPs structural features are diverse and play a critical role in their functionality. A comprehensive understanding of these structural features can be categorized into several key aspects: the presence of RNA-binding domains, the role of intrinsically disordered regions (IDRs), and the specific sequence and structural motifs that facilitate RNA binding.

RNA-binding domains

Most of RBPs contain several RNA-binding domains (RBDs), including different types of RNA binding motifs, very often in multiple copies, which recognize RNA sequence specifically. The current structural understanding of protein–RNA recognition mediated are four RBDs, such as the RNA recognition motif (RRM), K homology (KH) domain, double-stranded RNA-binding motif (dsRBM) and zinc finger domain [20,21].

The RRM is the most abundant RBDs in higher vertebrates (about 0.5 %− 1 % in human genes), consists of approximately 90 amino acids and is known for its ability to recognize single-stranded. The 90 amino acids long domain containing two conserved sequences of eight and six amino-acids, called RNP1 and RNP2, respectively. RRM adopts a typical $\beta_1\alpha_1\beta_2\beta_3\alpha_2\beta_4$ topology that forms a four-stranded β-sheet packed against two α-helices. The RNP1 and RNP2 sequences located in the two central β-strands, β_3 and β_1, exposes three conserved aromatic residues on the surface of the β-sheet which form the primary RNA binding surface RNA [26,20,27]. Lack of the presence of most, if not all of these aromatic residues, led to the definition of several subclass of RRMs like the quasi-RRM (qRRM), the pseudo-RRM (Ψ-RRM) or U2AF Homology Motifs (UHM) [28]. RRMs enable proteins to interact with RNA through various mechanisms, including stacking interactions with nucleobases and electrostatic interactions with the RNA backbone. The presence of multiple RRMs within a single protein can enhance binding affinity and specificity, allowing for more complex

Table 1
RBPs: their target RNA, mechanism of action, functional domain and primary function.

Protein Name	Primary Function	Subcellular Localization	RNA Targets	Mechanism of Action	PTMs	Interacting Partners	Mutations/ Variants	Functional Domains	Additional Notes
CELF	Regulates alternative splicing, mRNA translation, and stability	Nucleus, cytoplasm	pre-mRNAs, mRNAs	Binds to GU-rich sequences to regulate splicing and mRNA stability	Phospho-rylation	Splicing factors, hnRNPs	CELF mutations linked to myotonic dystrophy	RNA Recognition Motif (RRM)	Important in muscle-specific and neuron-specific splicing regulation
AUF1 (hnRNP D)	mRNA decay and stabilization	Nucleus, cytoplasm	mRNAs (AU-rich)	Binds and destabilizes ARE-containing mRNAs	Phospho-rylation	hnRNP proteins, poly(A)-binding proteins	Variants associated with autoimmune diseases	RNA Recognition Motif (RRM)	Binds AU-rich elements (ARE) in mRNA
AGO1 −4	RNA silencing via miRNA and siRNA pathways	Cytoplasm	miRNAs, siRNAs	Binds small RNAs to guide RISC to complementary mRNAs	Phospho-rylation, ubiquitination	Dicer, GW182, TRBP	Mutations linked to dysregulated RNA silencing in cancers	PAZ domain, PIWI domain	Key component of the RISC complex
Lin28A/B	miRNA regulation	Cytoplasm, nucleus	pre-let−7 miRNA	Blocks miRNA processing and regulates translation	Phospho-rylation	TRIM71, TUTase (Zcchc11)	Overexpression linked to various cancers	Cold Shock Domain (CSD), Zinc knuckle domain	Inhibits let−7 miRNA processing
HuR (ELAVL1)	Stabilization of stress response-related mRNAs	Nucleus, cytoplasm	mRNAs (inflamma-tory, cell cycle-related)	Binds to AU-rich elements to stabilize mRNAs	Phospho-rylation, methylation	hnRNPs, eIFs, mTOR	Variants linked to Alzheimer's disease	RRM domains	Stabilizes mRNAs related to cellular stress response
PUM 1&2	mRNA stability, translational control	Cytoplasm	mRNAs (specific 3' UTR motifs)	Binds to specific sequences in 3' UTR to regulate translation	Phospho-rylation	CPEB, FBF	Mutations linked to neurological disorders	PUF domain	Regulates mRNA stability via 3' UTR binding
TDP−43	RNA metabolism, alternative splicing	Nucleus, cytoplasm	mRNAs, pre-mRNAs	Regulates splicing and RNA transport, forms aggregates	Phospho-rylation, ubiquitination, cleavage	FUS, hnRNPA1	Mutations cause familial ALS and FTD	RRM domains, Glycine-rich domain	Linked to neurodegenera-tion
FMRP	Regulation of mRNA translation	Cytoplasm	mRNAs (neuronal synaptic mRNAs)	Suppresses translation of mRNAs at synapses	Phospho-rylation, methylation	CYFIP1, Dicer	FMR1 gene mutation causes Fragile X syndrome	KH domains, RGG box	Linked to Fragile X syndrome
MSI 1&2	Stem cell regulation, mRNA translational control	Nucleus, cytoplasm	mRNAs (cell cycle and stem cell regulators)	Represses translation by binding to 3' UTR of target mRNAs	Phospho-rylation, acetylation	Notch signaling components, eIF4E	Overexpression linked to leukemia and solid tumors	RRM domains	Controls cell differentiation and self-renewal
PABP (1, 2)	Regulation of poly(A) tail and mRNA stability	Cytoplasm	mRNAs (poly(A) tail)	Binds poly(A) tail and interacts with translation machinery	Phospho-rylation, methylation	eIF4G, eIF4E	Dysregulation linked to cancer and viral replication	RRM domains, Poly(A) binding domain	Bind to poly(A) tail to regulate mRNA stability
hnRNPs	Pre-mRNA processing, stability, and transport	Nucleus, cytoplasm	pre-mRNAs, mRNAs	Bind RNA to regulate splicing and nuclear export	Phospho-rylation, acetylation, ubiquitination	Spliceosome components, eIFs	Mutations linked to neurodegenerative diseases	RRM domains	Key in alternative splicing and RNA transport

(*continued on next page*)

Table 1 (*continued*)

Protein Name	Primary Function	Subcellular Localization	RNA Targets	Mechanism of Action	PTMs	Interacting Partners	Mutations/ Variants	Functional Domains	Additional Notes
IGF2BP (1, 2, 3)	Regulation of mRNA translation and localization	Cytoplasm, stress granules	mRNAs (develop-mental and oncogenic)	Binds to mRNA to regulate localization and stability	Phospho-rylation	HuR, eIF4G	Overexpression linked to cancer progression	KH domains	Control of mRNA transport and stability in the cytoplasm
STAU (1, 2)	mRNA localization and decay	Cytoplasm, stress granules	mRNAs (dendritic, synaptic mRNAs)	Facilitates mRNA transport and decay	Phospho-rylation	Upf1, eIF4E	Dysregulation linked to neurodegenerative diseases	Double-stranded RNA-binding domains	Involved in mRNA transport and decay
SRSF (1 −12)	Pre-mRNA splicing	Nucleus	pre-mRNAs	Regulates alternative splicing of pre-mRNA	Phospho-rylation	U1 snRNP, spliceosome components	Mutations linked to myelodysplastic syndromes	RRM domains, RS domain	Serine/arginine-rich proteins essential for splicing
FUS/TLS	RNA splicing, DNA repair	Nucleus, cytoplasm	pre-mRNAs, mRNAs	Regulates splicing, forms aggregates in neurodegenerative diseases	Phospho-rylation, methylation	TDP−43, SMN	Mutations in FUS gene cause familial ALS and FTD	RGG box, RRM domains	Involved in RNA metabolism and splicing, linked to neurodegenera-tion
TIA1/TIAL1	Regulation of translation and stress granule formation	Cytoplasm, stress granules	mRNAs (AU-rich)	Represses translation and forms stress granules	Phospho-rylation	G3BP1, eIFs	Mutations linked to amyotrophic lateral sclerosis (ALS)	RRM domains	Regulates translation under stress conditions
Sam68 (KHDRBS1)	Alternative splicing regulation	Nucleus, cytoplasm	pre-mRNAs	Binds to RNA and regulates alternative splicing	Phospho-rylation	Src, hnRNP proteins	Dysregulation linked to prostate cancer	KH domain	Binds RNA for splicing control
DROSHA	Primary miRNA (pri-miRNA) processing	Nucleus	pri-miRNAs	Cleaves pri-miRNAs to produce precursor miRNAs	Phosphorylati-on	DGCR8, RNA polymerase II	Variants linked to cancer and miRNA dysregulation	RNase III domains	Essential for the biogenesis of miRNAs
DGCR8	miRNA processing, cofactor for DROSHA	Nucleus	pri-miRNAs	Binds pri-miRNAs and helps DROSHA cleave them	Phosphorylati-on	DROSHA, RNA polymerase II	Linked to DiGeorge syndrome (22q11.2 deletion syndrome)	Double-stranded RNA-binding domains	Works with DROSHA in the microprocessor complex
TRBP	miRNA biogenesis, RNA silencing	Cytoplasm	siRNAs, miRNAs	Facilitates Dicer's cleavage of double-stranded RNA	Phosphorylati-on, ubiquitination	Dicer, AGO proteins	Variants linked to altered RNA silencing in cancers	dsRNA-binding domain	Interacts with Dicer in RISC loading
PTBP (1, 2)	Alternative splicing, mRNA transport	Nucleus, cytoplasm	pre-mRNAs, spliced mRNAs	Binds polypyrimidine tracts to regulate splicing	Phosphorylati-on, acetylation	Spliceosome components, hnRNPs	Dysregulation in glioblastoma and neurodegenerative diseases	RRM domains	Key role in neuron-specific splicing regulation
NANOS (1, 2, 3, 4)	Germ cell development, translational repression	Cytoplasm	mRNAs (germ cell-related)	Represses translation by binding to target mRNAs	Phosphorylati-on	PUM proteins	Variants linked to infertility and germ cell disorders	Zinc finger domain	Essential in germ cell survival and differentiation
MOV10	RNA silencing, mRNA surveillance	Cytoplasm	miRNAs, mRNAs	Unwinds RNA and assists RISC loading	Phosphorylati-on	AGO proteins, Dicer	Overexpression linked to hepatocellular carcinoma	Helicase domains	Interacts with AGO proteins in the RISC complex

(*continued on next page*)

Table 1 (*continued*)

Protein Name	Primary Function	Subcellular Localization	RNA Targets	Mechanism of Action	PTMs	Interacting Partners	Mutations/ Variants	Functional Domains	Additional Notes
YBX1	mRNA stability, translation control	Cytoplasm, nucleus	mRNAs (growth and stress-related)	Binds to Y-box sequences and regulates translation	Phosphorylation, acetylation	PABP, translation initiation factors	Overexpression associated with chemoresistance in cancers	Cold shock domain (CSD)	Involved in regulation of drug resistance genes in cancer
LARP	RNA processing, translation regulation	Cytoplasm, nucleus	pre-tRNAs, mRNAs	Bind 3' UTR of target RNAs and regulate stability	Phosphorylation, ubiquitination	Translation factors, RNA polymerase III	Overexpression linked to autoimmune diseases	La motif, RNA recognition motif	Regulate RNA polymerase III transcripts and protect 3' ends of pre-RNAs
RBFOX (1, 2, 3)	Alternative splicing regulation	Nucleus, cytoplasm	pre-mRNAs (neuronal, muscle-specific)	Binds to UGCAUG motifs to regulate splicing	Phosphorylation	hnRNPs, SR proteins	Mutations linked to autism spectrum disorders and epilepsy	RRM domains	Tissue-specific splicing regulators, especially in neurons and muscles
hnRNP A/B (A1, A2/B1)	RNA splicing, mRNA transport	Nucleus, cytoplasm	pre-mRNAs, mRNAs	Bind RNA to regulate splicing and nuclear export	Phosphorylation, acetylation, ubiquitination	Spliceosome components, eIFs	Mutations linked to neurodegenerative diseases	RRM domains	Key players in pre-mRNA splicing, RNA transport, and stability
DAZ (1, 2, 3)	Germ cell development, mRNA stability	Cytoplasm	mRNAs (spermatogenesis-related)	Binds mRNAs to regulate stability and translation	Phosphorylation	PUM proteins, translation factors	Variants linked to male infertility and azoospermia	RRM domains	Essential for spermatogenesis
QKI	RNA splicing, mRNA stability	Nucleus, cytoplasm	pre-mRNAs (oligodendrocyte-specific)	Binds to target RNA and regulates alternative splicing	Phosphorylation	hnRNPs, splicing factors	Mutations linked to schizophrenia and glioma	KH domain	Regulates mRNA splicing in oligodendrocytes, involved in myelination
Nucleolin	rRNA processing, ribosome biogenesis	Nucleus, nucleolus	rRNAs, mRNAs	Regulates rRNA processing and ribosome assembly	Phosphorylation, methylation	RNA polymerase I, ribosomal proteins	Overexpression linked to various cancers	RRM domains	Plays a key role in nucleolar organization
DCP1/DCP2	mRNA decay	Cytoplasm	mRNAs (decay targets)	Catalyze mRNA decapping to initiate mRNA decay	Phosphorylation	Lsm proteins, Xrn1	Overexpression linked to defective mRNA decay in cancers	Nudix hydrolase domain	Remove 5' cap from mRNAs to trigger degradation
Exosome complex (Exosc3, Exosc10)	RNA degradation and processing	Cytoplasm, nucleus	mRNAs, rRNAs, snRNAs	Degrades RNAs as part of quality control processes	Phosphorylation	RNA polymerase II, TRAMP complex	Mutations linked to neurological diseases (e.g., pontocerebellar hypoplasia)	RNA-binding domains	Multi-protein complex responsible for RNA degradation and quality control

(*continued on next page*)

Table 1 (*continued*)

Protein Name	Primary Function	Subcellular Localization	RNA Targets	Mechanism of Action	PTMs	Interacting Partners	Mutations/ Variants	Functional Domains	Additional Notes
Gemin proteins (2, 3, 4)	snRNP assembly, RNA splicing	Nucleus	snRNAs	Involved in the assembly of snRNPs required for splicing	Phosphorylation	SMN, snRNP proteins	Mutations in Gemin genes linked to spinal muscular atrophy	RNA-binding domains	Essential components of the SMN complex that assembles snRNPs
CIRP	RNA stabilization under stress conditions	Cytoplasm	mRNAs (stress-related)	Stabilizes mRNAs under stress conditions	Phosphorylation	Translation factors, hnRNPs	Overexpression associated with cancer	Cold shock domain (CSD)	Involved in stress response, stabilizes mRNAs during cold shock
RBM20	Alternative splicing regulation in cardiac tissues	Nucleus	pre-mRNAs (cardiac-specific)	Regulates alternative splicing in cardiac muscle	Phosphorylation	hnRNPs, splicing factors	Variants linked to dilated cardiomyopathy	RRM domains	Regulates splicing of titin (TTN), key for cardiac function
SND1	mRNA degradation, miRNA biogenesis	Cytoplasm	miRNAs, mRNAs	Facilitates RNA-induced silencing and degradation	Phosphorylation, acetylation	AGO proteins, Dicer	Overexpression linked to cancer and viral infections	Nuclease domain	Part of RISC, involved in RNA silencing and degradation
Sm proteins (SmB/B', SmD1, SmD2, SmD3, SmE, SmF, SmG)	mRNA splicing, degradation	Nucleus, cytoplasm	snRNAs, mRNAs	Bind RNAs and assist in splicing or degradation processes	Phosphorylation	U6 snRNA, Xrn1	Dysregulation linked to cancer and neurodegenerative diseases	Sm domains	Form a heptameric complex involved in splicing and mRNA decay
ZBP1	mRNA localization, translation control	Cytoplasm	β-actin mRNA	Binds to zipcode sequences and controls mRNA localization	Phosphorylation	hnRNPs, translation factors	Dysregulation linked to metastasis and neurodevelopmental disorders	RNA-binding domains	Involved in the localization of β-actin mRNA
NOVA (1, 2)	Alternative splicing in neurons	Nucleus, cytoplasm	pre-mRNAs (neuron-specific)	Binds to YCAY motifs and regulates splicing	Phosphorylation	hnRNPs, splicing factors	Mutations linked to paraneoplastic neurological disorders	KH domains	Regulates splicing of neuron-specific pre-mRNAs
TIA1/TIAL1	Stress granule formation, translational repression	Cytoplasm	mRNAs (stress-related)	Represses translation and promotes stress granule formation	Phosphorylation, acetylation	hnRNPs, splicing factors	Mutations linked to neurodegenerative diseases	RRM domains	Key regulators of stress granules and mRNA storage
hnRNPK	RNA splicing, transcription regulation	Nucleus, cytoplasm	pre-mRNAs, mRNAs	Binds RNA and DNA to regulate splicing and transcription	Phosphorylation, acetylation	Spliceosome components, transcription factors	Overexpression linked to cancer	RRM domains	Multifunctional protein involved in RNA splicing and transcription regulation

(*continued on next page*)

Table 1 (*continued*)

Protein Name	Primary Function	Subcellular Localization	RNA Targets	Mechanism of Action	PTMs	Interacting Partners	Mutations/ Variants	Functional Domains	Additional Notes
TTP	mRNA decay, inflammation regulation	Cytoplasm	mRNAs (inflammatory cytokines)	Binds to AU-rich elements in mRNAs and promotes degradation	Phosphorylation	mRNA decay factors, e.g., CCR4-NOT complex	Variants linked to dysregulated inflammation	Zinc finger domain	Regulates mRNA stability, especially inflammatory cytokines (e.g., TNF-α)
METTL3/METTL14	mRNA methylation	Nucleus	mRNAs, long non-coding RNAs	Methylate mRNA at specific adenosine residues	Phosphorylation, acetylation	WTAP, YTHDF proteins	Overexpression linked to cancer	Methyltransferase domain	Catalyze m6A modification on mRNA, involved in gene expression regulation
YTHDF/YTHDC	m6A recognition, mRNA stability	Cytoplasm, nucleus	m6A-modified mRNAs	Recognize m6A modifications and regulate RNA fate	Phosphorylation	METTL3/ METTL14, translation factors	Overexpression linked to cancer and obesity	YTH domain	Bind to m6A-modified mRNAs and regulate stability, translation, or decay
SF3B1	Pre-mRNA splicing	Nucleus	pre-mRNAs (spliceosomal)	Involved in recognition of branch point during splicing	Phosphorylation	U2 snRNP, splicing factors	Mutations linked to myelodysplastic syndromes	RNA-binding domains	Essential component of the U2 snRNP involved in 3' splice site recognition
CstF64	mRNA 3' end processing	Nucleus	pre-mRNAs (3' UTR)	Binds to 3' UTRs and promotes cleavage and polyadenylation	Phosphorylation	Polyadenylation machinery, CPSF proteins	Variants linked to neurodevelopmental disorders and cancer	RRM domains	Involved in cleavage and polyadenylation of pre-mRNAs

* *Note*: **PTMs:** Post-Translational Modifications, **AUF1:** AU-rich element binding factor 1, **TDP-43:** Transactive response (TAR) DNA-binding protein 43, **Lin28A/B:** Lin-28 homolog A/B, **PUM:** PUMILIO, **FMRP:** Fragile X mental retardation protein, **MSI:** Musashi, **PABP:** Poly(A)-binding proteins, **IGF2BP:** Insulin-like growth factor 2 mRNA-binding protein, **hnRNPs:** Heterogeneous nuclear ribonucleoproteins, **HuR (ELAVL1):** Human antigen R (Embryonic lethal abnormal vision-like protein 1), **AGO:** Argonaute, **STAU:** Staufen, **SRSF:** Serine/arginine-rich splicing factor, **FUS/TLS:** Fused in sarcoma / Translocated in liposarcoma, **TIA1/TIAL1:** T-cell intracellular antigen 1 / TIA-like protein 1, **Sam68 (KHDRBS1):** Src-associated in mitosis of 68 kDa (KH domain-containing, RNA-binding, signal transduction-associated protein 1), **DROSHA:** Drosha ribonuclease III, **DGCR8:** DiGeorge syndrome critical region 8, **TRBP:** TAR RNA-binding protein, **PTBP:** Polypyrimidine tract-binding protein, **MOV10:** Moloney leukemia virus 10 homolog, **YBX1:** Y-box binding protein 1, **LARP:** La-related protein, **RBFOX:** RNA-binding Fox, **hnRNP:** Heterogeneous nuclear ribonucleoproteins, **DAZ:** Deleted in azoospermia, **QKI:** Quaking, **CIRP:** Cold-inducible RNA-binding protein, **RBM20:** RNA-binding motif protein 20, **SND:** Staphylococcal nuclease and Tudor domain-containing protein, **ZBP:** Zipcode binding protein, **NOVA:** Neuro-oncological ventral antigen, **TIA1/TIAL1:** T-cell intracellular antigen 1 / TIA-like protein 1, **TTP:** Tristetraprolin, **METTL3/METTL14:** Methyltransferase-like protein 3/14, **YTHDF/YTHDC:** YTH domain family proteins/YTH domain-containing protein, **SF3B1:** Splicing factor 3B subunit 1, **CstF64:** Cleavage stimulation factor 64 kDa subunit, **CELF:** CUGBP and ETR-3-like factors.

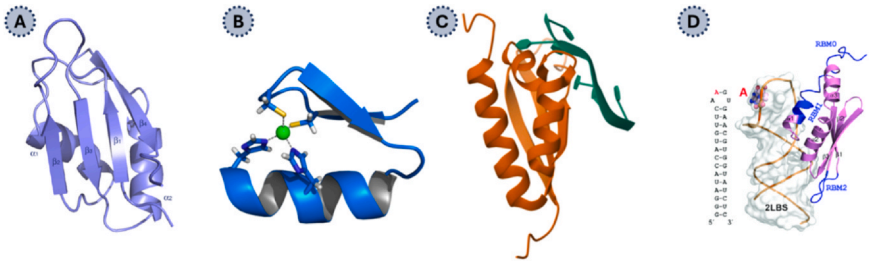

Fig. 1. Structure of various RBDs. **a.** Ribbon structure of RRM (PDB: 2CQI; [22]). **b.** Cartoon representation of the Cys2His2 zinc finger motif (PDB: 1A1L). *The zinc ion (green) is coordinated by two histidine and two cysteine amino acid residues* [23] **c.** Crystal Structure of KH domain (PDB: 1ZZI; [24]). d. NMR structure of isolated dsRBD in complex with the AAGU tetraloop (PDB: 2LBS; [25]).

interactions with RNA molecules. This is particularly evident in proteins like TDP-43 and FUS, which contain multiple RRMs that can bind to adjacent or separate RNA elements [12,29-31].

Zinc finger (ZnF) is another domain found in RBPs. In a single RBP, this motif can be found alone, as a repeated domain or even in combination with other types of RBDs. A classical ZnF is about 30 amino acids long and displays a ββα protein fold in which a β-hairpin and an α-helix are pinned together by a Zn^{2+} ion. These domains are classified depending on the amino acids that interact with this ion (e.g., C2H2, CCCH or CCCC) and were initially described as DNA binding motifs. They were found interacting specifically with dsDNA bases located in major grooves via side chains of residues present in their α-helix [32]. With regards to RBP. the interaction typically involves contacts between amino acid side chains in the α-helical region of the ZnF and the RNA molecule. This is similar to how they interact with DNA but adapted for the unique structures of RNA [33,34]. Different types of zinc fingers can engage with RNA through various mechanisms. For example, C2H2 zinc fingers may use both backbone interactions and base-specific contacts to achieve binding [35].

The hnRNP K homology (KH) domain is approximately 70 amino acids long. It is found in proteins with different functions including splicing, transcriptional regulation and translational control. Two versions of the KH fold have been reported, the Types I and II found in eukaryotic and prokaryotic proteins, respectively. The Type I has a βααββα topology and is characterized by a β-sheet composed of three antiparallel β-strands packed against three α-helices [36,37]. The β1- and β2-strands are parallel to each other and the β3-strand is antiparallel to both. In addition, a "GXXG loop" containing the (I/L/V)-I-G-X-X-G-X-X-(I/L/V) conserved motif, located between the α1 and α2 helices, and a β2-β3 loop variable in length (3 to over 60 amino acids) and sequence, are also found in this motif. The KH Type II fold differs from the Type I by a αββααβ topology and a characteristic β-sheet in which the central strand (β2) is parallel to β3 and antiparallel to β1 [36,37]. Although both KH motif folds are known for interacting with RNA or ssDNA targets, only few structures of these domains bound to nucleic acid molecules have been deposed in the Protein Data Bank [38,39] and most of them concern the eukaryotic Type I KH domain.

Contrary to the three families of RBDs described, dsRBMs were first described as recognizing RNA shape rather than RNA sequence [40]. The dsRBM typically adopts an αβββα fold, which is crucial for its function in binding structured RNA molecules [41]. Each dsRBM consists of approximately 65–70 amino acids and can recognize specific features of the dsRNA structure, particularly in the minor groove of the RNA helix [42]. The recognition of dsRNA by dsRBMs is largely believed to be shape-dependent, although recent findings suggest that sequence-specific recognition may also occur through direct readout mechanisms [43].

Intrinsically disordered regions

In contrast to these structured domains, a significant proportion of RBPs also possess intrinsically disordered regions (IDRs). IDRs are segments of proteins that lack a stable three-dimensional structure under physiological conditions [44]. These regions are increasingly recognized for their critical roles in the function of RBPs, particularly in mediating interactions with RNA and other proteins [45]. IDRs enable RBPs to engage with multiple RNA targets through a flexible binding mechanism. This flexibility allows IDRs to adapt their conformation to fit various RNA structures, enhancing the protein's capacity to recognize and bind different RNA sequences or structures [46,47].

Many RBPs contain multiple RNA-binding modules connected by IDRs. These linkers can influence the spatial arrangement and effective concentration of these modules, thereby affecting the overall binding affinity and specificity for RNA [48]. The dynamic nature of IDRs allows for a range of conformations, which can facilitate interactions with non-contiguous binding sites on RNA molecules [46]. DRs can also play regulatory roles within RBPs. For example, they can modulate the affinity of the protein for its RNA target by undergoing conformational changes upon binding to other proteins or ligands. This autoinhibition mechanism is crucial for maintaining proper cellular functions, especially in processes like gene regulation and signaling [49].

Research has identified two primary binding modes utilized by disordered protein regions when interacting with RNA. These modes reflect different strategies for recognition and suggest that IDRs may accommodate a broader range of substrates compared to structured domains [47]. The charge distribution within IDRs significantly influences their interaction with RNA. For instance, negatively charged IDRs can enhance the target search process by accelerating the binding kinetics of RBPs to their RNA targets, due to favourable electrostatic interactions [50].

Specific sequence and structural motifs

Moreover, the specific sequence and structural motifs recognized by RBPs are critical for their binding specificity. Studies have shown that RBPs often exhibit preferences for particular RNA sequences and secondary structures, such as hairpin loops and bulges [51,52]. For instance, proteins with KH domains tend to favor large hairpin loops, indicating a structural preference that guides their binding interactions [51]. Furthermore, the sequence context of RNA can significantly influence RBP binding, with certain RBPs showing a strong preference for specific nucleotide arrangements [52,53]. This specificity is essential for the precise regulation of gene expression, as it determines which RNA molecules are targeted by RBPs in a cellular context.

Functions

The RBPs facilitate critical steps in RNA metabolism, including splicing, transport, stability, translation, and degradation (Fig. 2), thereby playing a pivotal role in determining the fate of RNA molecules within the cell [1,54,55,20,56].

One of the primary functions of RBPs is to regulate mRNA stability and translation. For instance, PUF family proteins bind specifically to the 3' untranslated region (3' UTR) of target mRNAs, influencing their stability and translational efficiency [56,57]. This sequence-specific binding allows RBPs to modulate the expression of genes in response to various cellular signals, thereby participating in the regulation of metabolic pathways and developmental processes [56,58]. Additionally, RBPs are involved in the nonsense-mediated decay (NMD) pathway, which is crucial for eliminating faulty mRNAs, thus maintaining cellular RNA quality [59,54,55].

Moreover, RBPs play a significant role in RNA splicing, a process that is essential for the maturation of precursor mRNA into functional mRNA. They interact with spliceosomal components to facilitate the removal of introns and the joining of exons [1,20]. This splicing regulation is particularly important in generating protein diversity through alternative splicing, which allows a single gene to produce multiple protein isoforms [60]. Furthermore, RBPs are implicated in the transport of mRNAs from the nucleus to the cytoplasm, ensuring that mRNAs are properly localized for translation [54,55].

In addition to their roles in mRNA metabolism, RBPs also interact with non-coding RNAs, such as microRNAs (miRNAs), to regulate gene expression. This interaction can lead to the degradation of target mRNAs or inhibition of their translation, further emphasizing the multifaceted regulatory roles of RBPs in cellular homeostasis [61]. The importance of RBPs is underscored by their involvement in various diseases, including cancer, where dysregulation of RBP activity can lead to aberrant gene expression profiles [60,62].

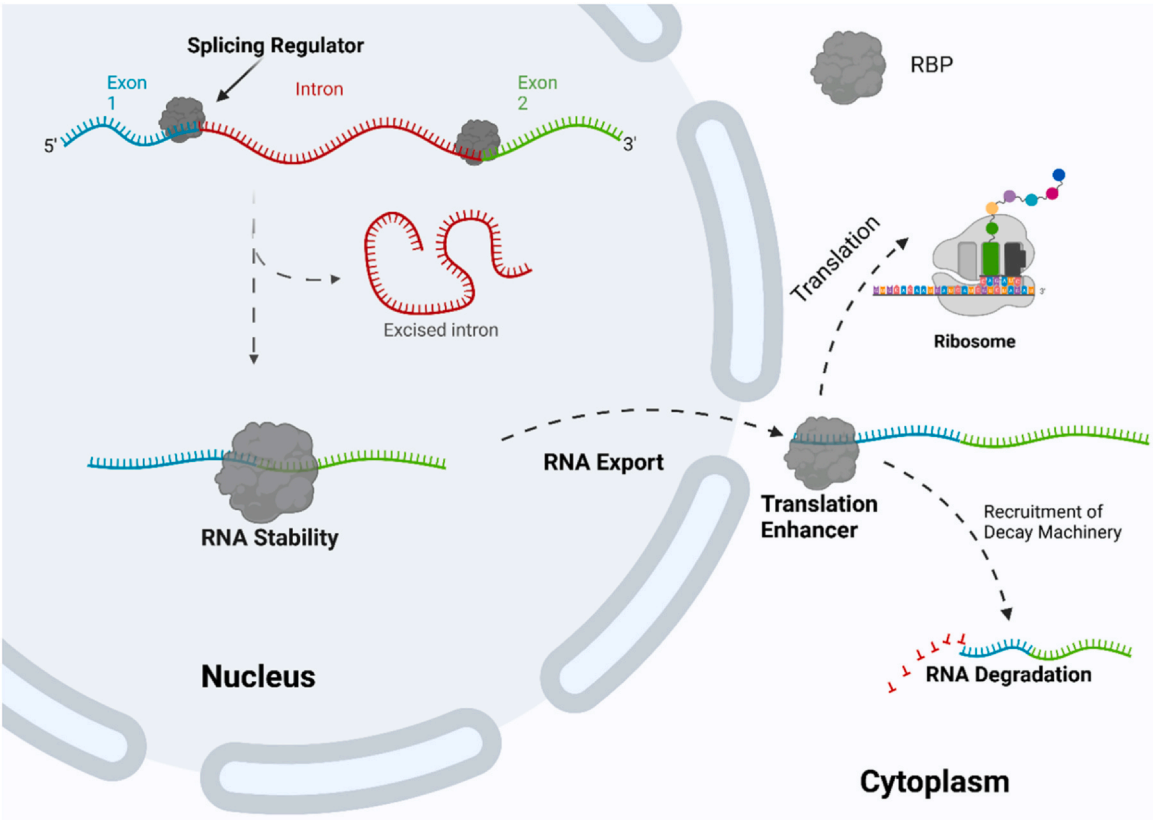

Fig. 2. Schematic diagram summarizing the various roles of RBPs.

Classes of RBPs

Several RBPs has been reported from various studies to interact with RNA through various mechanisms and domains. In the human genome there are at least 1200 verified RBPs as well as several newly discovered ones [10,63]. Some examples of RBPs that has been reported so far are presented in Table 1.

RBPS in genetic stability

The survival of cells is one of the fundamental problems linked to genome stability and integrity, and RBPs have been shown to maintaining genetic stability through their multifaceted roles in DNA Damage Response and Repair (DDR), RNA surveillance and quality control and chromatin architecture.

DDR and repair

The DDR is a critical cellular mechanism that detects and repairs DNA damage, ensuring genomic integrity and preventing diseases. This response involves a complex network of signalling pathways that coordinate the detection of damage, activation of repair mechanisms, and regulation of cell cycle progression [64]. Several studies demonstrated DNA double-strand breaks (DSBs) as a severe genomic lesion that arises from various sources and leads to breaks that may occur due to exposure to genotoxic or chemical agents such as methyl methane sulfonate. DSBs are programmed events in meiosis and antibody diversification processes. Whether the breaks are either accidental or deliberate, they significantly impact genome stability and cellular function, necessitating efficient repair mechanisms to maintain genomic integrity. Interestingly, DSBs are not always accidental; they can also be deliberately generated during certain biological processes [65-68].

RBPs play a significant role in recognizing and repairing DNA damage, contributing to the maintenance of genomic stability. These proteins are involved in various aspects of the DDR, including the detection of DNA lesions, recruitment of repair factors, and regulation of gene expression related to repair processes [69,70]. One of the key RBPs involved in the DDR is FUS (Fused in Sarcoma). FUS has been shown to localize to sites of DNA damage and is essential for the recruitment of other repair proteins, such as poly(ADP-ribose) polymerase-1 (PARP1), which is critical for the repair of DNA-DSBs [71,72]. FUS interacts with PARP and is involved in the formation of compartments enriched in damaged DNA, highlighting its role in the early stages of the DNA repair process [73].

Another RBP complex known as heterogeneous nuclear ribonucleoproteins (hnRNPs) has been identified to play an important role in DDR. hnRNP A1-U, a highly expressed cellular protein that is a subtype of hnRNPs, has been shown to be involved in cell proliferation, mRNA translation, cell cycle, and splicing [74,75]. Notably, hnRNPUL 1 and 2 protein families have been observed to associate with the MRE11-RAD50-NBS1 (MRN) complex, which is responsible for DNA-DSB sensor complex detection [76]. Remarkably, this RBPs contribute to DNA repair via other methods as moderators or executors of DNA repair or DNA lesions sensor in a role extrinsic to splicing, which are well established [77]. Mastrocola et al., [71] reported another significant RBP protein, FUS, a multifunctional RNA/DNA-binding protein that is involved in translation, mRNA transport, and splicing involved in DNA repair. This protein is less effective in repairing DSBs due to the disruption of the first stage of DDR induction.

RBMX is another RBP that has been identified as a crucial component of the DDR. It is involved in homologous recombination repair and is essential for the stabilization of repair complexes at sites of DNA damage. RBMX functions independently of ATM signalling and is essential for the recruitment of repair factors to DSBs [20,78]. Additionally, RBMX has been shown to interact with various other RBPs, indicating a network of interactions that facilitate the DDR [79]. NONO is also noteworthy in the context of DNA repair and this RBP is involved in the regulation of homologous recombination and the stabilization of mRNAs related to the DNA damage response. NONO's recruitment to damage sites is influenced by PARP activation, which underscores the interconnectedness of RNA metabolism and DNA repair mechanisms [80,81].

Moreover, hnRNP K and hnRNP A0 have been reported to play roles in the transcriptional response to DNA damage. hnRNP K is induced following DNA damage and collaborates with p53 to promote the expression of genes involved in the repair process [78], while hnRNP A0 stabilizes Gadd45α mRNA, which is crucial for the DNA damage response [78]. Finally, SFPQ (also known as PSF) has emerged as a critical RBP in the DDR. It has been shown to interact with RAD51D, a protein essential for homologous recombination, thereby linking RNA processing to DNA repair pathways [82]. SFPQ's involvement in the DDR highlights the importance of splicing factors in maintaining genomic integrity.

RNA surveillance and quality control

RNA surveillance and quality control are critical processes that ensure the fidelity of gene expression in both prokaryotic and eukaryotic cells. These mechanisms are designed to detect and eliminate faulty RNA molecules, thereby preventing the synthesis of dysfunctional proteins that could disrupt cellular functions [83]. In eukaryotes, several RNA surveillance pathways have been identified, including nonsense-mediated decay (NMD), no-go decay (NGD), and non-stop decay (NSD). These pathways are essential for maintaining mRNA quality by targeting defective transcripts for degradation.

NMD specifically recognizes mRNAs containing premature termination codons (PTCs) and facilitates their degradation, thus preventing the accumulation of truncated proteins that could be harmful to the cell [84-87]. Additionally, the ribosome-associated quality control (RQC) system plays a pivotal role in monitoring translation, detecting stalled ribosomes, and targeting both the defective mRNA and nascent polypeptides for degradation [88,89]. The interplay between transcription and translation also influences RNA quality control. In eukaryotic cells, the translation process itself can trigger mRNA decay pathways, as seen in the co-translational surveillance mechanisms that monitor mRNA integrity during translation [86,90]. One of the key RBPs involved in NMD

is UPF1, an ATP-dependent RNA helicase that is central to the NMD pathway. UPF1 is responsible for recognizing mRNAs with PTCs and facilitating their degradation. It interacts with other essential factors, such as UPF2 and UPF3, which are necessary for the assembly of the NMD complex [91,92]. UPF1's helicase activity is critical for unwinding RNA structures, allowing for the recruitment of decay machinery [93,94]. The interaction between UPF1 and other RBPs is also significant; for instance, the polypyrimidine tract-binding protein (PTBP1) can protect certain mRNAs from NMD by preventing UPF1 from binding to them, thereby regulating the stability of these transcripts [95,96]. Research has shown that various RBPs can modulate the efficiency of NMD. For example, SRSF3 has been identified as a splicing factor that regulates its own expression through a "poison cassette exon," which leads to NMD when included in the transcript [97]. Similarly, TDP-43, an RBP associated with neurodegenerative diseases, has been implicated in the regulation of cryptic splicing events that can influence NMD outcomes [98,99].

No-go decay (NGD) is vital for maintaining cellular homeostasis by preventing the accumulation of defective mRNAs that could lead to the synthesis of nonfunctional or harmful proteins. NGD is initiated when a ribosome is stalled during elongation due to various factors, such as stable RNA secondary structures, rare codons, or premature stop codons [100-102]. The core components involved in NGD include the proteins Dom34 and Hbs1, which are essential for recognizing stalled ribosomes and facilitating their disassembly. Upon ribosome stalling, Dom34 and Hbs1 promote the release of the ribosomal subunits and the drop-off of peptidyl-tRNA, effectively initiating the decay of the aberrant mRNA [101]. This mechanism not only helps in the degradation of faulty mRNAs but also plays a role in recycling ribosomal components for future rounds of translation [101,102]. RBPs such as Hbs1 and Dom34 are crucial for detecting stalled ribosomes on mRNAs that impede translation elongation. When ribosomes encounter problematic sequences that hinder their movement, these RBPs are recruited to the ribosomal complex. They promote the disassembly of the ribosome and facilitate the degradation of the defective mRNA by the exosome complex, which is responsible for RNA decay [103,104]. The interaction of RBPs with the ribosome is vital for the efficient recognition of stalled translation and subsequent mRNA degradation [105].

Non-stop decay (NSD) specifically targets mRNAs lacking a termination codon, thereby preventing the accumulation of potentially harmful, continuously translated proteins. This process is particularly important in maintaining cellular homeostasis and ensuring the fidelity of gene expression. The mechanism of NSD involves the recognition of ribosomes that have stalled during translation due to the absence of a stop codon [101,106]. The endonucleolytic cleavage of the mRNA occurs near the stalled ribosome, allowing for the rapid degradation of the transcript by the exosome complex, which is responsible for 3′ to 5′ degradation of RNA [107]. The exosome complex, a multi-subunit ribonuclease, is integral to the NSD process. It works in conjunction with the TRAMP complex, which adds poly(A) tails to the aberrant mRNAs, facilitating their recognition and degradation by the exosome [108,109]. The TRAMP complex enhances the specificity and efficiency of RNA degradation, ensuring that only defective transcripts are targeted while preserving functional RNAs [109]. Moreover, NSD has implications beyond simple RNA degradation; it also plays a role in regulating gene expression and maintaining the integrity of the transcriptome. By eliminating faulty mRNAs, NSD contributes to the overall quality control of RNA metabolism, which is essential for proper cellular function and response to environmental changes [110,111,108]. RBPs also play a role in NSD, which targets mRNAs lacking a stop codon. In this process, RBPs such as the Lsm1–7-Pat1 complex are involved in recognizing the poly(A) tail of mRNAs, which is a signal for degradation. The Lsm complex binds to the 3' end of the mRNA, facilitating its decay through the exosome pathway [112,113]. Additionally, RBPs like Nab2 have been shown to interact with exosome cofactors, enhancing the specificity and efficiency of RNA degradation [114]. This highlights the importance of RBPs in linking RNA decay pathways with the cellular machinery responsible for mRNA turnover.

Maintenance of telomeres

Telomeres, the protective caps at the ends of chromosomes, are critical for maintaining genomic stability and preventing cellular senescence [115]. The regulation of telomere length and function is a complex process involving various RBPs, notably telomeric repeat-containing RNA (TERRA) and heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1). These molecules play pivotal roles in telomere biology, influencing cellular aging and the integrity of the genome.

The role of TERRA in cellular senescence is underscored by its ability to induce premature senescence when overexpressed [116]. This is particularly significant in cancer biology, where TERRA levels can be dysregulated, leading to genomic instability and tumor progression [117]. Furthermore, TERRA's interaction with RBPs like hnRNP A1 has been shown to modulate telomerase activity, suggesting that TERRA acts as a natural inhibitor of telomerase, thereby contributing to the maintenance of telomere length and stability [118]. The interplay between TERRA and RBPs is essential for maintaining telomere integrity, as disruptions in this balance can lead to increased susceptibility to DNA damage and cellular aging [14]. In addition to TERRA, other RBPs such as SFPQ and NONO have been identified as important players in telomere stability. These proteins help suppress RNA:DNA hybrid-related telomere instability, further emphasizing the critical role of RBPs in telomere biology [119]. The regulation of TERRA and its associated RBPs is complex and context-dependent, influenced by factors such as cellular stress and the cell cycle [120]. For instance, TERRA expression is regulated in a cell-cycle-dependent manner, with implications for telomere replication and stability during cell division [121].

Across different species, the phenomenon of cellular senescence has been linked to organismal aging due to the underlying mechanisms that are thought to induce a permanent cessation of proliferation in cell populations, contributing to the aging process and other physiological changes. Grimes, Chandra [122]. Disrupted telomeres caused by telomere uncapping could promote cellular senescence indirectly and degradation of unprotected telomeres, resulting in a weaker DDR. Ghadaouia et al., [123,124]. Telomere erosion or shortening uses the breakage-fusion-bridge mechanism leading to genomic instability, and the shortening of telomere during cell division triggers the activation of the DNA repair mechanisms. This repair mechanism results in sister chromatid fusion via DNA replication, leading to chromosomal integrity compromise as well as cellular dysfunction [125]. Furthermore, the chromatid

daughter cells inherit altered genetic material due to breakage of fused chromosomes during mitosis, resulting in genomic instability due to the repeated multiple cell divisions caused by the continuous breakage-fusion-bridge cycle [126]. According to Ghadaouia et al. [123], genomic instability and secondary DNA break production occur when telomeres lose protection due to chromosomal end fusion prompting a robust DDR; therefore, the additional damage to DNA triggered by the chromosomal end fusion leads to cellular senescence and a permanent cell growth cessation. Notably, cellular senescence along with organismal aging has been linked to the gradual shortening of telomere length [127].

RBPs and diseases

RBPs has been known to play crucial roles in various cellular processes, including RNA splicing, transport, stability, and translation. Dysregulation or mutations in these proteins have been implicated in a wide range of diseases, particularly neurodegenerative disorders, cancers, diabetes, cardiovascular and genetic conditions.

Neurodegenerative diseases

One of the most significant associations of RBPs is with neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Mutations in RBPs like TDP-43 and FUS (normally localized in the nucleus, where they participate in RNA processing, splicing, and transport) have been linked to these conditions, where abnormal aggregation of these proteins in the cytoplasm is a hallmark of the diseases [128,13,15]. The aggregation of TDP-43, characterized by hyperphosphorylation and ubiquitination, forms insoluble inclusions that disrupt cellular functions [129,130]. Similarly, FUS mislocalization from the nucleus to the cytoplasm is also observed, contributing to neurodegeneration [131,132]. The aggregation of these proteins is thought to be driven by several factors, including mutations in the genes encoding them, such as TARDBP (which encodes TDP-43) and FUS, as well as the presence of hexanucleotide repeat expansions in the C9orf72 gene [133-135]. Similarly, the prion-like domains in hnRNPA2B1 and hnRNPA1 have been shown to cause multisystem proteinopathy and ALS through altered dynamics of RNA granule assembly [128].

The toxic effects of these aggregates are multifaceted. They can sequester essential cellular components, disrupt nucleocytoplasmic transport, and impair RNA metabolism, leading to cellular stress and ultimately neuronal death [130,135]. The presence of these aggregates is not only a hallmark of ALS and FTD but also correlates with disease severity and progression [136,137]. Furthermore, the G4C2 repeat expansions in C9orf72 lead to the production of toxic dipeptide repeat proteins, which further exacerbate cellular toxicity and contribute to the pathophysiology of both diseases [133,134,138].

Given the critical role of RBPs in ALS and FTD, targeting their aggregation and restoring their normal function presents a promising therapeutic strategy. Several approaches are currently being explored: *1. Gene Therapy*: Techniques such as CRISPR-Cas9 are being investigated to correct mutations in the C9orf72 gene or to eliminate the toxic repeat expansions [139]. This approach aims to restore normal protein function and prevent the formation of toxic aggregates. *2. Small Molecule Inhibitors:* Compounds that can stabilize RBPs or prevent their aggregation are under investigation. For instance, targeting the pathways involved in the post-translational modifications of TDP-43 and FUS may help mitigate their toxic effects [130,140]. *3. RNA-based Therapeutics:* Antisense oligonucleotides (ASOs) that specifically target the RNA products of the C9orf72 gene are being developed to reduce the levels of toxic dipeptide repeat proteins [134,138]. This strategy aims to decrease the overall burden of toxic proteins in affected neurons. *4. Modulation of Cellular Stress Responses:* Enhancing the cellular mechanisms that manage protein homeostasis, such as the ubiquitin-proteasome system and autophagy, may help clear aggregates and restore normal cellular function [130,140].

Cancer

Cancer is another area where RBPs have emerged as significant players. Dysregulation of RBPs can lead to aberrant splicing and expression of oncogenes and tumour suppressors, contributing to tumorigenesis [8,141]. One of the primary mechanisms by which RBPs contribute to tumorigenesis is through the stabilization of mRNA. For instance, HuR, an RBP, is known to bind to AU-rich elements in the 3' untranslated regions of target mRNAs, enhancing their stability and promoting the expression of oncogenes [142]. Similarly, the RBP LIN28 has been implicated in the regulation of let-7 microRNAs, which are tumour suppressors; aberrant expression of LIN28 leads to increased levels of oncogenic targets, thereby facilitating cancer progression [14]. Furthermore, RBPs such as CELF2 have been shown to stabilize specific mRNAs, thereby inhibiting ovarian cancer progression [143].

Alternative splicing is another critical process influenced by RBPs that can lead to tumorigenesis. RBPs such as DAP3 have been shown to regulate splicing networks, resulting in widespread changes in splicing patterns that can contribute to the cancer phenotype [144]. The dysregulation of splicing factors can lead to the production of oncogenic isoforms of proteins, further driving tumorigenesis [14]. For example, the RBP HNRNPK has been associated with promoting cancer cell proliferation and migration through its role in splicing regulation [7]. Moreover, RBPs are involved in the evasion of immune responses, which is a hallmark of cancer. They can modulate the expression of immune-related genes, thereby influencing the tumor microenvironment and immune evasion strategies [145]. For instance, the HuR has been implicated in the regulation of cytokine mRNAs, which can affect immune cell function and contribute to tumor immune evasion [146].

In terms of their potential as biomarkers and therapeutic targets, several RBPs have been identified as promising candidates. For example, the expression levels of RBPs like HuR and LIN28 have been correlated with poor prognosis in various cancers, making them potential biomarkers for disease progression [29,30,147]. Additionally, therapeutic strategies targeting RBPs are being explored, such as

the use of small molecules or RNA-based therapies to inhibit the function of oncogenic RBPs [148]. The development of RNA-PROTACs, which are designed to degrade specific RBPs, represents a novel approach to targeting these proteins in cancer therapy [148].

Cardiovascular disease

The cardiovascular system also exhibits a notable association with RBPs, where they regulate gene expression related to cardiac function and disease. For example, the RNA-binding protein Quaking has been shown to influence alternative splicing events critical for cardiac myocyte function [141]. Dysregulation of RBPs in the heart can lead to conditions such as cardiac fibrosis and arrhythmias, highlighting their importance in cardiovascular health [149]. Among the various RBPs implicated in these processes, RBFOX, CELF, RBM20, and RBM24 are notable for their contributions to cardiac functionality and pathology.

RBFOX proteins, particularly RBFOX2, are essential for proper heart development, as they regulate alternative splicing of pre-mRNAs involved in cardiac myocyte differentiation. Mutations in RBFOX2 have been linked to congenital heart defects, underscoring its significance in cardiac morphogenesis [150]. Similarly, RBM20 has been identified as a key splicing factor that regulates the alternative splicing of the Titin gene, which is crucial for cardiac muscle function. Loss-of-function mutations in RBM20 are associated with dilated cardiomyopathy (DCM), highlighting its role in maintaining cardiac structure and function [151]. The CELF family of RBPs, particularly CELF1 and CELF4, also plays a pivotal role in cardiac development and disease. These proteins are involved in the regulation of alternative splicing during embryonic development and have been shown to influence the expression of foetal-specific isoforms in heart failure [152]. The interplay between CELF proteins and other splicing factors is critical for the proper transition from foetal to adult cardiac isoforms, which is vital for normal heart function [14].

RBM24 is another RBP that has garnered attention for its role in cardiac development. It is involved in the regulation of alternative splicing during the differentiation of embryonic stem cells into cardiac lineages. Studies have demonstrated that RBM24 knockout leads to disrupted splicing and contributes to the development of cardiomyopathies [153,154]. This suggests that RBM24 is not only important for normal heart development but also for preventing pathological conditions. Moreover, the regulation of alternative splicing by RBPs is influenced by miRNAs, which can modulate the expression of splicing factors. For instance, miRNAs have been shown to coordinate the expression of CELF proteins during postnatal heart development, indicating a complex regulatory network that governs splicing transitions in the heart [155]. This interplay between RBPs and miRNAs is crucial for maintaining cardiac homeostasis and responding to stress conditions, such as hypertrophy and heart failure [156].

Diabetes

RBPs such as HuR, HNRNPD, and CELF1 have been shown to be significantly involved in the pathophysiology of diabetes. HuR levels are significantly lower in cardiac endothelial cells (CECs) of diabetic mice and patients with diabetes compared to controls [157]. HuR protein was found to increase in kidneys from OVE26 mice, a type 1 diabetic mouse model [158]. Decreased HuR contributes to the development of coronary microvascular dysfunction in diabetes through downregulation of gap junction protein Cx40 in CECs [157]. Inhibiting HuR attenuates the severity of structural abnormalities in diabetic nephropathy, such as glomerular hypertrophy, collagen type IV expression, and mesangial expansion [158].

Also is the HNRNPD (heterogeneous nuclear ribonucleoprotein D), which plays a significant role in the determination of beta cell identity in response to cellular stress. In diabetes, changes in HNRNPD expression are linked to increased rates of beta cell apoptosis. Specifically, reduced HNRNPD expression is associated with the survival of pancreatic beta cells, while its overexpression can lead to apoptosis by decreasing the levels of anti-apoptotic proteins such as BCL2 and MCL1 [159,160]. In children with Type 1 Diabetes (T1DM), studies have shown that HNRNPD expression is downregulated in the blood, suggesting a potential association with disease progression. This downregulation may contribute to the vulnerability of beta cells under stress conditions, further implicating HNRNPD in the pathophysiology of T1DM [160,161].

Another RNA-binding protein, CELF1 (also known as CUGBP1), has been implicated in the pathogenesis of diabetes through its roles in alternative splicing, mRNA stability, and translation regulation. In T1DM, CELF1 protein levels are elevated in skeletal muscle and heart of type 1 diabetic mice and increased CELF1 levels correlate with abnormal alternative splicing patterns of its target genes involved in metabolism (Nutter et al., 2018). CELF1 target RNAs are aberrantly spliced in the type 1 diabetic heart, leading to abnormal gene expression [162]. For T2DM, CELF1 regulates alternative splicing of the insulin receptor, contributing to insulin resistance, CELF1 is expressed in pancreatic islets and its elevated levels in diabetic mice suppress insulin secretion in response to glucose and GLP-1 and targeting CELF1 may hold promise as a therapeutic approach for T2DM [163]. In the case of diabetic cardiomyopathy, CELF1 overexpressing mice develop dilated cardiomyopathy and heart failure, displaying reactivation of embryonic splicing patterns similar to changes observed in diabetic hearts [164,165]. Increased CELF1 protein levels in diabetic heart may contribute to diabetic cardiomyopathy [164].

Another RBP associated with diabetes is the IGF2BP2. Genome-wide association studies (GWAS) have identified that variants in the IGF2BP2 gene are associated with an increased risk of developing T2DM in several populations, Czech and Swedish [166], Iranians [167], Chinese [168]. The IGF2BP2 rs1470579C allele and rs4402960 T allele were found to be more frequent in T2D patients compared to healthy controls [169]. IGF2BP2 regulates insulin-like growth factor 2 (IGF2) translation by binding to the 5' UTR of IGF2 mRNA. IGF2 plays an important role in growth and insulin signalling pathways [168]. Variants in IGF2BP2 affect first-phase glucose-stimulated insulin secretion and the disposition index [168]. The rs4402960 variant attenuates the first phase of glucose-stimulated insulin secretion [169]. A nominally significant interaction was observed between the IGF2BP2 variant and prenatal exposure to famine on glucose levels during oral glucose tolerance test (OGTT). The presence of both the IGF2BP2 risk allele

and exposure to famine was associated with lower glucose AUC during OGTT, which seems counterintuitive considering their individual associations with increased T2DM risk [170].

Genetic disorders

In addition to forementioned diseases, RBPs are also implicated in genetic disorders. For example, mutations in the A2BP1 gene, which encodes an RNA-binding protein, have been associated with mental retardation, epilepsy, and autism. Furthermore, the role of RBPs in myotonic dystrophy is notable, where proteins like Muscleblind are recruited to CUG repeat expansions, leading to disrupted RNA processing and contributing to the disease phenotype [171,172]. The involvement of RBPs in fragile X-associated tremor/ataxia syndrome (FXTAS) further exemplifies their critical role in neurodegeneration, where RBPs like hnRNP A2/B1 mitigate neurodegeneration in models of the disease [173].

RBPs target

RBP targeting strategies focus on disrupting or modulating several key interactions and pathways, thereby restoring cellular homeostasis or countering pathogenic mechanisms. These targeting strategies include RNA-protein interactions, protein-protein interactions, affected cell pathways and protein aggregation (Fig. 3).

RNA-protein interactions

RBPs function primarily through their interaction with RNA molecules, making RNA-protein interactions a vital target for therapeutic intervention. By interfering with these interactions, it is possible to modulate the RNA-binding activity of the protein, thereby influencing the stability, localization, or translation of its target mRNAs. This approach is particularly relevant in diseases where RBPs bind and stabilize oncogenic or pathogenic transcripts. Disrupting RNA-protein interactions could thus reduce the expression of disease-driving genes [174,175].

Protein-protein interactions

Beyond binding RNA, RBPs frequently interact with other proteins, forming complexes that are necessary for their full functionality. Disrupting these protein-protein interactions can impair the activity of RBPs and the larger ribonucleoprotein complexes

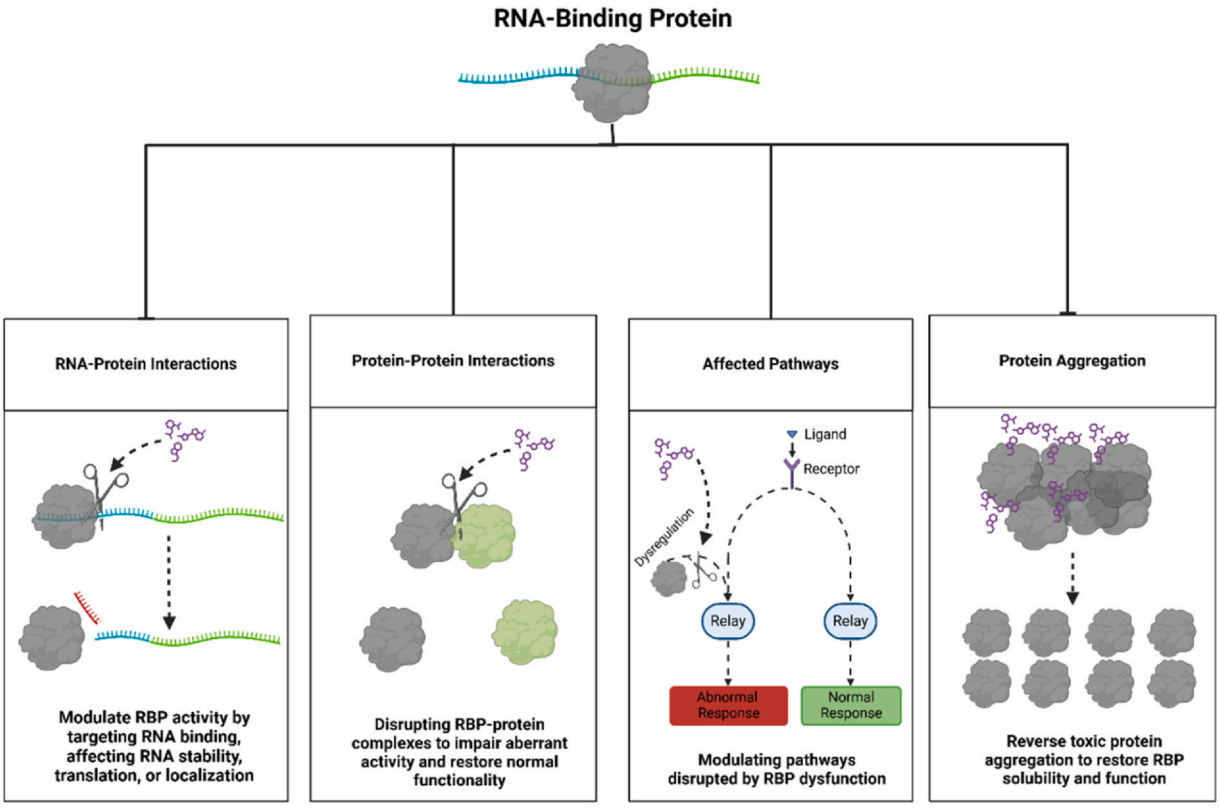

Fig. 3. Schematic diagram illustrating strategies for targeting RBPs, encompassing potential RNA-protein interactions, protein-protein interactions, protein aggregation, and associated cellular pathways.

(RNPs) in which they operate. For example, inhibiting the interaction of RBPs with co-factors essential for mRNA splicing, translation, or degradation can lead to therapeutic outcomes by blocking aberrant processing events in diseases such as cancer or neurodegenerative disorders [5,6,176].

Affected cell pathways

RBPs are central players in cellular signalling pathways and metabolic networks. Their dysregulation can lead to widespread disturbances in gene expression and cellular physiology. By targeting RBPs, therapeutic strategies aim to restore proper cellular homeostasis and rescue the normal functioning of critical pathways. This approach is often applied in diseases like cancer, where RBPs are overexpressed and promote tumorigenesis by dysregulating multiple mRNA targets involved in proliferation and apoptosis. Therapeutic modulation of RBPs can lead to the restoration of proper cell cycle control and apoptosis [177,178].

Protein aggregation

A significant challenge in targeting RBPs is their propensity to aggregate, particularly in neurodegenerative diseases like amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Certain RBPs, such as TDP-43 and FUS, misfold and aggregate in neuronal cells, leading to cellular toxicity. Strategies aimed at preventing or reversing protein aggregation have become a crucial aspect of RBP-targeted therapies. Small molecules, peptides, or oligonucleotides are being explored for their potential to disrupt these aggregates and restore RBP solubility and function, offering a promising avenue for treating aggregation-related diseases [179,180].

RBPs therapeutic strategies

Therapeutic strategies for targeting RBPs can be broadly categorized into direct and indirect approaches (Fig. 4), each offering unique mechanisms of intervention.

Direct targeting strategies

Direct approaches focus on modulating the expression or function of RBPs through overexpression or knockdown [18]. Overexpression of RBPs can enhance their activity, leading to increased binding to target RNAs. This often results in altered splicing patterns, which can have significant implications for cellular functions and disease states. For instance, RBPs that act as splicing

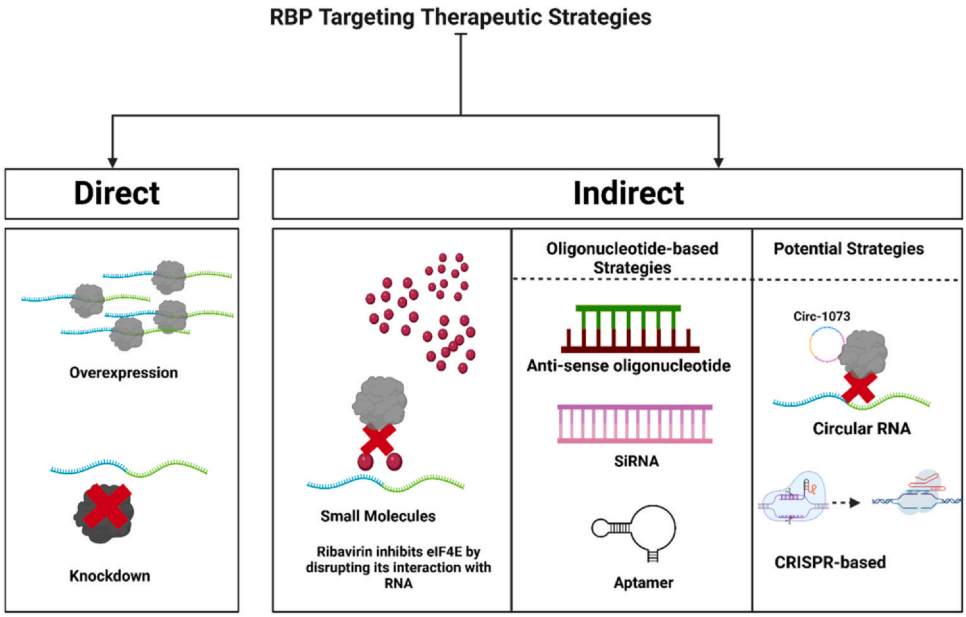

Fig. 4. The therapeutic strategies for targeting RBPs. This figure illustrates the therapeutic approaches used to target RNA-binding proteins (RBPs), categorized into direct and indirect strategies. Direct strategies involve either enhancing or suppressing RBP levels. Overexpression of RBPs, such as increasing HuR expression, can stabilize tumor suppressor mRNAs, aiding in cancer therapy. On the other hand, knockdown approaches, like the use of shRNA or siRNA, can reduce the levels of RBPs such as TDP-43, which is implicated in neurodegenerative diseases like ALS. Indirect strategies include targeting RBPs with small molecules, oligonucleotides, or novel techniques. For instance, small molecules like Ribavirin inhibit eIF4E by disrupting its interaction with the mRNA cap, reducing its pro-cancerous activity. Oligonucleotide-based strategies involve anti-sense oligonucleotides (ASOs), such as those targeting nucleolin to inhibit its activity, and siRNA, like HuR siRNA, which silences oncogenic RBPs to suppress tumor growth. Another approach, aptamers, includes examples like AS1411, which binds to nucleolin and disrupts its cancer-promoting functions. Emerging strategies such as circular RNAs, exemplified by Circ-1073, act as decoys to sequester RBPs like HuR, preventing their interaction with target mRNAs. Additionally, CRISPR-based techniques like CRISPR-Cas13 are being developed to directly degrade RBP mRNAs, such as EIF4E, while CRISPR-Cas9 is used for gene knockout of RBPs like FUS in ALS research. Together, these approaches aim to modulate RBP activity and their downstream effects, providing promising therapeutic options for cancer, neurodegeneration, and other diseases.

activators may promote exon inclusion, thereby influencing the diversity of protein isoforms produced from a single gene [18,181]. This approach is particularly relevant in diseases such as myotonic dystrophy or fragile X syndrome, where overexpression of RBPs like CELF or FMRP respectively, may compensate for functional deficits [182,183]. This strategy leverages viral vectors or plasmid-based delivery systems to achieve the desired upregulation of target RBPs [184]. Conversely, knocking down RBPs using techniques such as RNA interference (RNAi) reduces their expression levels [18]. This can disrupt normal splicing processes and lead to the exclusion of certain exons or the use of alternative splice sites, potentially contributing to disease mechanisms, especially in cancers [185]. For instance, the knockdown of overexpressed RBPs like LIN28 or hnRNPs has shown therapeutic potential by inhibiting tumour progression. The knockdown of RBPs can be achieved through various delivery systems, including short interfering RNA (siRNA) or antisense oligonucleotides (ASOs), which target specific mRNAs encoding the RBPs for degradation [185].

Indirect targeting strategies

Indirect approaches target RBPs by modulating their interactions with RNA or proteins, or by leveraging molecular tools to alter their activity or stability [7,17]. Several strategies have been explored:

i. *Circular RNA*: Circular RNAs (circRNAs) act as molecular decoys for RBPs by sequestering them and preventing their interaction with endogenous RNA targets. This approach has been proposed for RBPs involved in pathological RNA splicing or translation, where circRNAs could alleviate disease phenotypes by reducing the availability of pathogenic RBPs. For example, circRNAs could target RBPs like PTB to influence splicing decisions in diseases such as cancer and neurodegenerative disorders [186-188].
ii. Small Interfering RNA (siRNA): siRNA-based therapeutics provide a mechanism for targeting RBPs indirectly by promoting the degradation of their specific mRNA substrates. siRNA molecules have been employed to silence genes encoding RBPs, reducing their cellular abundance and consequently their pathological effects [189]. This approach has been successfully applied in models of ALS, where siRNAs targeting TDP-43 mRNA have shown neuroprotective effects by reducing the accumulation of toxic protein aggregates [190].
iii. Synthetic Peptides: Synthetic peptides can be designed to interfere with RBP functions by mimicking or disrupting protein-protein or RNA-protein interactions. These peptides can selectively bind RBPs and inhibit their ability to associate with RNA or other proteins, thus altering downstream cellular processes [20]. This approach has been used to target RBPs involved in ALS and spinal muscular atrophy (SMA), where protein aggregation and abnormal RBP interactions exacerbate disease progression [191].
iv. Oligonucleotide-Based Therapies: Oligonucleotides, such as antisense oligonucleotides (ASOs), can be designed to bind to specific RNA sequences and modulate RBP binding or RNA splicing. ASOs targeting SRSF1 and CELF1 have been explored for their ability to correct aberrant splicing patterns in myotonic dystrophy and spinal muscular atrophy [192,193]. Additionally, oligonucleotide-based therapies can influence the post-transcriptional fate of mRNAs by altering RBP recognition sites, thus restoring normal gene expression profiles [194].
v. Aptamers: Aptamers are short, single-stranded nucleic acids that fold into specific three-dimensional structures capable of binding to proteins with high specificity. Aptamers targeting RBPs can be designed to inhibit their function by competitively binding to RNA-binding domains or modulating protein conformations [195]. This strategy has been employed in preclinical models of cancer, where aptamers targeting HuR and LIN28 have shown promise in reducing tumour growth by inhibiting their oncogenic functions [196,197].
vi. Small Molecules: Small-molecule inhibitors of RBPs have garnered significant attention due to their potential for oral bioavailability and tissue penetration. High-throughput screening approaches have identified small molecules capable of disrupting RBP-RNA interactions, thus altering gene expression. In particular, small molecules targeting RBPs such as FUS and TARDBP (TDP-43) have shown promise in treating neurodegenerative diseases by reducing the aggregation of these RBPs [198,199].

Future research

Advances in research tools are crucial for furthering our understanding of RBPs and their implications on genetic stability and diseases. Techniques such as RNA interactome in regulating gene expression at the post-transcriptional level by controlling the fate of RNA in processes such as mRNA localization, translation, splicing and stability [200-202] and molecular dynamics simulations for study protein dynamics, enzyme mechanisms, and interactions between biomolecules [203-206] have already provided valuable insights into the interactions and functions of RBPs. Moving forward, the development of more sophisticated tools, like machine learning-informed RNA-binding chemical space exploration [207], can aid in identifying novel RNA-binding compounds and understanding their mechanisms of action. Additionally, the utilization of fusion proteins for enhanced small RNA loading to extracellular vesicles can revolutionize RNA delivery systems, enabling targeted and efficient delivery of therapeutic RNAs to specific tissues [208]. The integration of computational biology with experimental techniques, as demonstrated in the prediction of RNA-protein binding sites using deep learning, can enhance our ability to predict and understand RBP interactions [209]. Furthermore, the construction of a versatile RNA-binding protein using designer proteins showcases the potential of integrating protein engineering with RNA manipulation technologies for future therapeutic applications. Such integrative approaches can lead to a more holistic understanding of the roles of RBPs in genetic stability and diseases [210]. The field of personalized medicine is not left out, as it holds great promise in leveraging the knowledge of RBPs for tailored therapeutic interventions. Understanding the binding preferences of RBPs to RNA editing events [211] and the dysregulated expression patterns of circular RNAs in cancer [212], can provide valuable information for developing personalized treatment strategies. Moreover, the optimization of protein-targeted medicines into RNA-specific small molecules has the potential for personalized RNA-targeted therapies [213]. By incorporating information on individual

genetic variations and RNA profiles, personalized medicine can offer more effective and precise treatments, as seen in the success of personalized cancer nanomedicine [214].

Conclusion

In conclusion, RNA-binding proteins are pivotal in maintaining genetic stability within the cellular context. Their diverse functions in RNA metabolism and gene regulation underscore their significance in preserving genomic integrity. The dysregulation of RBPs is intricately linked to various diseases characterized by genetic instability, thereby presenting a compelling case for their investigation in the context of pathophysiology. As research progresses, the understanding of RBPs' roles will not only enhance our comprehension of genetic stability but also unveil novel therapeutic avenues to combat diseases rooted in RBP dysfunction. Future studies should focus on elucidating the specific mechanisms by which RBPs influence genomic stability, as well as exploring targeted interventions that could restore normal RBP function in disease states. This knowledge will ultimately contribute to the development of innovative strategies aimed at mitigating the effects of genetic instability and improving patient outcomes in a range of disorders.

References

[1] A. Corbett, Post-transcriptional regulation of gene expression and human disease, Curr. Opin. Cell Biol. 52 (2018) 96–104, https://doi.org/10.1016/j.ceb.2018.02.011.
[2] E. Dassi, Handshakes and fights: the regulatory interplay of RNA-binding proteins, Front Mol. Biosci. 4 (2017) 67.
[3] M.E. Leonart, Understanding RNA-binding proteins, Semin. Cancer Biol. 86 (Pt 3) (2022) 135–136, https://doi.org/10.1016/j.semcancer.2022.06.015.
[4] Adamek, M. (2023). Molecular grammar of rna-binding protein interactions in formation and function of ribonucleoprotein complexes. 〈https://doi.org/10.55295/psl.2023.ii15〉.
[5] M. Corley, M.C. Burns, G.W. Yeo, How RNA-binding proteins interact with RNA: molecules and mechanisms, Mol. Cell 78 (1) (2020) 9–29, https://doi.org/10.1016/j.molcel.2020.03.011 PMID: 32243832; PMCID: PMC7202378.
[6] M. Corley, M.C. Burns, G.W. Yeo, How RNA-binding proteins interact with RNA: molecules and mechanisms, Mol. Cell 78 (1) (2020) 9–29, https://doi.org/10.1016/j.molcel.2020.03.011.
[7] Y. Li, W. Zhou, Q. Jie, T. Pan, J. Shi, T. Jiang, Y. Ma, Single-Cell Rna Bind. Protein Regul. Netw. Anal. Reveal Oncog. hnrnpk-myc Signal. Pathw. Cancer (2022), https://doi.org/10.21203/rs.3.rs-1919283/v1.
[8] M. Hentze, A. Castelló, T. Schwarzl, T. Preiß, A brave new world of rna-binding proteins, Nat. Rev. Mol. Cell Biol. 19 (5) (2018) 327–341, https://doi.org/10.1038/nrm.2017.130.
[9] Q. Li, C. Kang, Targeting rna-binding proteins with small molecules: perspectives, pitfalls and bifunctional molecules, Febs Lett. 597 (16) (2023) 2031–2047, https://doi.org/10.1002/1873-3468.14710.
[10] S. Kelaini, C. Chan, V.A. Cornelius, A. Margariti, RNA-binding proteins hold key roles in function, dysfunction, and disease, Biology 10 (2021) 366.
[11] A. Smirnov, Research progress in RNA-binding proteins, Int. J. Mol. Sci. 24 (1) (2022) 58, https://doi.org/10.3390/ijms24010058.
[12] S. Agrawal, P.H. Kuo, L.Y. Chu, et al., RNA recognition motifs of disease-linked RNA-binding proteins contribute to amyloid formation, Sci. Rep. 9 (2019) 6171, https://doi.org/10.1038/s41598-019-42367-8.
[13] M. Ramaswami, J. Taylor, R. Parker, Altered ribostasis: RNA-protein granules in degenerative disorders, Cell 154 (4) (2013) 727–736, https://doi.org/10.1016/j.cell.2013.07.038.
[14] E. Wang, A. Ward, J. Cherone, J. Giudice, T. Wang, D. Treacy, C. Burge, Antagonistic regulation of mrna expression and splicing by celf and mbnl proteins, Genome Res. 25 (6) (2015) 858–871, https://doi.org/10.1101/gr.184390.114.
[15] H. Zhou, M. Mangelsdorf, J. Liu, L. Zhu, J. Wu, RNA-binding proteins in neurological diseases, Sci. China Life Sci. 57 (4) (2014) 432–444, https://doi.org/10.1007/s11427-014-4647-9.
[16] P. Lee, J. Chiang, C. Chen, Y. Chien, W. Chen, C. Huang, H. Lee, Calreticulin regulates vascular endothelial growth factor-a mrna stability in gastric cancer cells, Plos One 14 (11) (2019) e0225107, https://doi.org/10.1371/journal.pone.0225107.
[17] T.N. Shukla, J. Song, Z.T. Campbell, Molecular entrapment by RNA: an emerging tool for disrupting protein-RNA interactions in vivo, RNA Biol. 17 (4) (2020) 417–424, https://doi.org/10.1080/15476286.2020.1717059 Epub 2020 Jan 28. PMID: 31957541; PMCID: PMC7237136.
[18] Y. Tao, Q. Zhang, H. Wang, et al., Alternative splicing and related RNA binding proteins in human health and disease, Sig Transduct. Target Ther. 9 (2024) 26, https://doi.org/10.1038/s41392-024-01734-2.
[19] D. Ray, K. Ha, K. Nie, H. Zheng, T. Hughes, Q. Morris, Rnacompete methodology and application to determine sequence preferences of unconventional rna-binding proteins, Methods 118-119 (2017) 3–15, https://doi.org/10.1016/j.ymeth.2016.12.003.
[20] H. Qin, H. Ni, Y. Liu, Y. Yang, T. Xi, X. Li, L. Zheng, Rna-binding proteins in tumor progression, J. Hematol. Oncol. 13 (1) (2020), https://doi.org/10.1186/s13045-020-00927-w.
[21] W. Wang, R. Zhang, N. Feng, L. Zhang, N. Liu, Overexpression of rbm34 promotes tumor progression and correlates with poor prognosis of hepatocellular carcinoma, J. Clin. Transl. Hepatol. 000 (000) (2022), https://doi.org/10.14218/jcth.2022.00166.
[22] Dardel, F. (2016). Structure of an RNA recognition motif (RRM), showing the fold with the typical with beta-alpha-beta-beta-alpha-beta architecture. Available at: 〈https://en.wikipedia.org/wiki/RNA_recognition_motif#/media/File:RRM.png〉.
[23] S. Thomas, Cartoon Represent. zinc-Finger motif Proteins (2007) (Available at: 〈https://en.wikipedia.org/wiki/Zinc_finger#/media/File:Zinc_finger_rendered.png〉).
[24] P.H. Backe, A.C. Messias, R.B. Ravelli, M. Sattler, S. Cusack, X-ray crystallographic and NMR studies of the third KH domain of hnRNP K in complex with single-stranded nucleic acids, Structure 13 (7) (2005) 1055–1067.
[25] C. Petibon, M. Malik Ghulam, M. Catala, S. Abou Elela, Regulation of ribosomal protein genes: an ordered anarchy, Wiley Interdiscip. Rev.: RNA 12 (3) (2021) e1632.
[26] C. Maris, C. Dominguez, F.H. Allain, The RNA recognition motif, a plastic RNA-binding platform to regulate posttranscriptional gene expression, FEBS J. 272 (2005) 2118–2131.
[27] J.C. Venter, M.D. Adams, E.W. Myers, et al., The sequence of the human genome, Science 291 (2001) 1304–1351.
[28] A. Clery, M. Blatter, F.H. Allain, RNA recognition motifs: boring? Not quite, Curr. Opin. Struc Biol. 18 (2008) 290–298.
[29] F. Chen, Q. Wang, Y. Zhou, The construction and validation of an rna binding protein-related prognostic model for bladder cancer, BMC Cancer 21 (1) (2021), https://doi.org/10.1186/s12885-021-07930-5.
[30] X. Chen, Z. Yang, W. Wang, K. Qian, M. Liu, J. Wang, M. Wang, Structural basis for RNA recognition by the N-terminal tandem RRM domains of human RBM45, Nucleic Acids Res. 49 (5) (2021) 2946–2958.
[31] Y.S. Tsai, S.M. Gomez, Z. Wang, Prevalent RNA recognition motif duplication in the human genome, RNA 20 (5) (2014) 702–712, https://doi.org/10.1261/rna.044081.113 Epub 2014 Mar 25. PMID: 24667216; PMCID: PMC3988571.
[32] S.A. Wolfe, L. Nekludova, C.O. Pabo, DNA recognition by Cys2His2 zinc finger proteins, Annu Rev. Bioph Biom. 29 (2000) 183–212.
[33] M.K. Darby, RNA Binding by Single Zinc Fingers, in: S. Iuchi, N. Kuldell (Eds.), Zinc Finger Proteins. Molecular Biology Intelligence Unit, Springer, Boston, MA, 2005, https://doi.org/10.1007/0-387-27421-9_11.

[34] T.M. Hall, Multiple modes of RNA recognition by zinc finger proteins, Curr. Opin. Struct. Biol. 15 (3) (2005) 367–373, https://doi.org/10.1016/j.sbi.2005.04.004 PMID: 15963892.
[35] R.S. Brown, Zinc finger proteins: getting a grip on RNA, Curr. Opin. Struct. Biol. 15 (1) (2005) 94–98.
[36] N.V. Grishin, KH domain: one motif, two folds, Nucleic Acids Res 29 (2001) 638–643.
[37] R. Valverde, L. Edwards, L. Regan, Structure and function of KH domains, FEBS J. 275 (2008) 2712–2726.
[38] B. Beuth, S. Pennell, K.B. Arnvig, et al., Structure of a mycobacterium tuberculosis NusA-RNA complex, EMBO J. 24 (2005) 3576–3587.
[39] M.Z. Jia, S. Horita, K. Nagata, et al., An archaeal Dim2-like protein, aDim2p, forms a ternary complex with a/eIF2 alpha and the 3′ end fragment of 16S rRNA. J. Mol. Biol. 398 (2010) 774–785.
[40] R. Stefl, L. Skrisovska, F.H. Allain, RNA sequence- and shape-dependent recognition by proteins in the ribonucleoprotein particle, EMBO Rep. 6 (2005) 33–38.
[41] K.Y. Chang, A. Ramos, The double-stranded RNA-binding motif, a versatile macromolecular docking platform, FEBS J. 272 (2005) 2109–2117.
[42] G. Masliah, P. Barraud, F.H. Allain, RNA recognition by double-stranded RNA binding domains: a matter of shape and sequence, Cell Mol. Life Sci. 70 (11) (2013) 1875–1895, https://doi.org/10.1007/s00018-012-1119-x.
[43] W. Xinlei, V. Lela, R.K. Hye, S. Klaus, M. Sua, Dynamic profiling of double-stranded RNA binding proteins, Nucleic Acids Res. 43 (15) (2015) 7566–7576.
[44] L. Yuan, D. Protter, M. Rosen, R. Parker, Formation and maturation of phase-separated liquid droplets by rna-binding proteins, Mol. Cell 60 (2) (2015) 208–219, https://doi.org/10.1016/j.molcel.2015.08.018.
[45] S. Sohrabi-Jahromi, J. Söding, Thermodynamic modeling reveals widespread multivalent binding by rna-binding proteins, Bioinformatics 37 (ement_1) (2021) i308–i316, https://doi.org/10.1093/bioinformatics/btab300.
[46] D.S.M. Ottoz, L.E. Berchowitz, The role of disorder in RNA binding affinity and specificity, Open Biol. 10 (12) (2020) 200328, https://doi.org/10.1098/rsob.200328 Epub 2020 Dec 23. PMID: 33352065; PMCID: PMC7776568.
[47] A. Zeke, É. Schád, T. Horváth, R. Abukhairan, B. Szabó, A. Tantos, Deep structural insights into RNA-binding disordered protein regions, Wiley Inter. Rev. RNA 13 (5) (2022) e1714, https://doi.org/10.1002/wrna.1714 Epub 2022 Jan 30. PMID: 35098694; PMCID: PMC9539567.
[48] P. Malaney, O. Benitez, X. Zhang, S.M. Post, Assessing the role of intrinsic disorder in RNA-binding protein function: hnRNP K as a case study, Methods 208 (2022) 59–65.
[49] C. Qiu, Z. Zhang, R.N. Wine, et al., Intra- and inter-molecular regulation by intrinsically-disordered regions governs PUF protein RNA binding, Nat. Commun. 14 (2023) 7323, https://doi.org/10.1038/s41467-023-43098-1.
[50] W. Xi, S.B. Lavi, M.G. Harry, Y. Binhan, L. Yaakov, I. Junji, Negatively charged, intrinsically disordered regions can accelerate target search by DNA-binding proteins, Nucleic Acids Res. 51 (10) (2023) 4701–4712.
[51] D. Domínguez, P. Freese, M. Alexis, A. Su, M. Hochman, T. Palden, C. Burge, Sequence, structure, and context preferences of human rna binding proteins, Mol. Cell 70 (5) (2018) 854–867.e9, https://doi.org/10.1016/j.molcel.2018.05.001.
[52] J. Taliaferro, N. Lambert, P. Sudmant, D. Domínguez, J. Merkin, M. Alexis, C. Burge, Rna sequence context effects measured in vitro predict in vivo protein binding and regulation, Mol. Cell 64 (2) (2016) 294–306, https://doi.org/10.1016/j.molcel.2016.08.035.
[53] A. Jolma, J. Zhang, E. Mondragón, E. Morgunova, T. Kivioja, K. Laverty, J. Taipale, Binding specificities of human rna-binding proteins toward structured and linear rna sequences, Genome Res. 30 (7) (2020) 962–973, https://doi.org/10.1101/gr.258848.119.
[54] T. Glisovic, J.L. Bachorik, J. Yong, G. Dreyfuss, "RNA-binding proteins and post transcriptional gene regulation", FEBS Lett. 582 (14) (2008) 1977–1986, https://doi.org/10.1016/j.febslet.2008.03.004.
[55] T. Glisovic, J. Bachorik, J. Yong, G. Dreyfuss, Rna-binding proteins and post-transcriptional gene regulation, Febs Lett. 582 (14) (2008) 1977–1986, https://doi.org/10.1016/j.febslet.2008.03.004.
[56] M. Wang, L. Ogé, M. Pérez-Garcia, L. Hamama, S. Sakr, The puf protein family: overview on puf rna targets, biological functions, and post transcriptional regulation, Int. J. Mol. Sci. 19 (2) (2018) 410, https://doi.org/10.3390/ijms19020410.
[57] C. Marondedze, L. Thomas, N. Serrano, K. Lilley, C. Gehring, The rna-binding protein repertoire of Arabidopsis thaliana, Sci. Rep. 6 (1) (2016), https://doi.org/10.1038/srep29766.
[58] P. Tam, I. Barrette-Ng, D. Simon, M. Tam, A. Ang, D. Muench, The puf family of rna-binding proteins in plants: phylogeny, structural modeling, activity and subcellular localization, BMC Plant Biol. 10 (1) (2010), https://doi.org/10.1186/1471-2229-10-44.
[59] T. Brazão, J. Demmers, W. IJcken, J. Strouboulis, M. Fornerod, L. Romão, F. Grosveld, A new function of rod1 in nonsense-mediated mrna decay, Febs Lett. 586 (8) (2012) 1101–1110, https://doi.org/10.1016/j.febslet.2012.03.015.
[60] X. Liang, W. Chen, H. Shi, X. Gu, Y. Li, Y. Qi, J. Liu, Ptbp3 contributes to the metastasis of gastric cancer by mediating cav1 alternative splicing, Cell Death Dis. 9 (5) (2018), https://doi.org/10.1038/s41419-018-0608-8.
[61] S. Cao, L. Xiao, J. Wang, G. Chen, Y. Liu, The rna-binding protein hur regulates intestinal epithelial restitution by modulating caveolin-1 gene expression, Biochem. J. 478 (1) (2021) 247–260, https://doi.org/10.1042/bcj20200372.
[62] J. Li, S. Deng, J. Vieira, J. Thomas, V. Costa, C. Tseng, P. Yu, Rbpmetadb: a comprehensive annotation of mouse rna-seq datasets with perturbations of rna-binding proteins (2018), https://doi.org/10.1101/326116.
[63] A. Quattrone, E. Dassi, The architecture of the human RNA-binding protein regulatory network, iScience 21 (2019) 706–719.
[64] M. Mirza-Aghazadeh-Attari, S.G. Darband, M. Kaviani, A. Mihanfar, J. Aghazadeh Attari, B. Yousefi, M. Majidinia, DNA damage response and repair in colorectal cancer: defects, regulation and therapeutic implications, DNA Repair 69 (2018) 34–52, https://doi.org/10.1016/j.dnarep.2018.07.005.
[65] S. Keeney, J. Lange, N. Mohibullah, Self-organization of meiotic recombination initiation: general principles and molecular pathways, Annu. Rev. Genet. 48 (1) (2014) 187–214, https://doi.org/10.1146/annurev-genet-120213-092304.
[66] J. Li, H. Sun, Y. Huang, Y. Wang, Y. Liu, X. Chen, Pathways and assays for DNA double-strand break repair by homologous recombination, Acta Biochim. Et. Biophys. Sin. 51 (9) (2019) 879–889, https://doi.org/10.1093/abbs/gmz076.
[67] V.E. Provasek, J. Mitra, V.H. Malojirao, M.L. Hegde, DNA double-strand breaks as pathogenic lesions in neurological disorders, Int. J. Mol. Sci. 23 (9) (2022) 4653, https://doi.org/10.3390/ijms23094653.
[68] Y.-L. Wang, W.-W. Zhao, J. Shi, X.-B. Wan, J. Zheng, X.-J. Fan, Liquid-liquid phase separation in DNA double-strand breaks repair, Cell Death Dis. 14 (11) (2023) 746, https://doi.org/10.1038/s41419-023-06267-0.
[69] G. Gurunathan, Z. Yu, Y. Coulombe, J. Masson, S. Richard, Arginine methylation of hnrnpul1 regulates interaction with nbs1 and recruitment to sites of dna damage, Sci. Rep. 5 (1) (2015), https://doi.org/10.1038/srep10475.
[70] H. Zhang, J. Jiang, J. Ma, S. Dai, T. Xu, H. Li, A. Yasui, The role of hnrpul1 involved in dna damage response is related to parp1, Plos One 8 (4) (2013) e60208, https://doi.org/10.1371/journal.pone.0060208.
[71] A. Mastrocola, S. Kim, A. Trinh, L. Rodenkirch, R. Tibbetts, The rna-binding protein fused in sarcoma (fus) functions downstream of poly(adp-ribose) polymerase (parp) in response to dna damage, J. Biol. Chem. 288 (34) (2013) 24731–24741, https://doi.org/10.1074/jbc.m113.497974.
[72] M. Sukhanova, A. Singatulina, D. Pastré, O. Lavrik, Fused in sarcoma (fus) in dna repair: tango with poly(adp-ribose) polymerase 1 and compartmentalisation of damaged dna, Int. J. Mol. Sci. 21 (19) (2020) 7020, https://doi.org/10.3390/ijms21197020.
[73] A. Singatulina, L. Hamon, M. Sukhanova, B. Desforges, V. Joshi, A. Bouhss, D. Pastré, Parp-1 activation directs fus to dna damage sites to form parg-reversible compartments enriched in damaged dna, Cell Rep. 27 (6) (2019) 1809–1821.e5, https://doi.org/10.1016/j.celrep.2019.04.031.
[74] T. Geuens, D. Bouhy, V. Timmerman, The hnRNP family: Insights into their role in health and disease, Hum. Genet. 135 (8) (2016) 851–867, https://doi.org/10.1007/s00439-016-1683-5.
[75] S.J. Park, H. Lee, D.S. Jo, Y.K. Jo, J.H. Shin, H.B. Kim, H.M. Seo, D.C. Rubinsztein, J.-Y. Koh, E.K. Lee, D.-H. Cho, Heterogeneous nuclear ribonucleoprotein A1 post-transcriptionally regulates Drp1 expression in neuroblastoma cells, Biochim. Et. Biophys. Acta (BBA) - Gene Regul. Mech. 1849 (12) (2015) 1423–1431, https://doi.org/10.1016/j.bbagrm.2015.10.017.
[76] M. Kai, Roles of RNA-binding proteins in DNA damage response, Int. J. Mol. Sci. 17 (3) (2016) 310, https://doi.org/10.3390/ijms17030310.

[77] B. Mikolaskova, M. Jurcik, I. Cipakova, M. Kretova, M. Chovanec, L. Cipak, Maintenance of genome stability: the unifying role of interconnections between the DNA damage response and RNA-processing pathways, Curr. Genet. 64 (5) (2018) 971–983, https://doi.org/10.1007/s00294-018-0819-7.
[78] B. Adamson, A. Smogorzewska, F. Sigoillot, R. King, S. Elledge, A genome-wide homologous recombination screen identifies the rna-binding protein rbmx as a component of the dna-damage response, Nat. Cell Biol. 14 (3) (2012) 318–328, https://doi.org/10.1038/ncb2426.
[79] M. Marchesini, Y. Ogoti, E. Fiorini, A. Samur, L. Nezi, M. D'Anca, S. Colla, Ilf2 is a regulator of rna splicing and dna damage response in 1q21-amplified multiple myeloma, Cancer Cell 32 (1) (2017) 88–100.e6, https://doi.org/10.1016/j.ccell.2017.05.011.
[80] J. Krietsch, M. Caron, J. Gagné, C. Éthier, J. Vignard, M. Vincent, J. Masson, Parp activation regulates the rna-binding protein nono in the dna damage response to dna double-strand breaks, Nucleic Acids Res. 40 (20) (2012) 10287–10301, https://doi.org/10.1093/nar/gks798.
[81] M. Yuan, C. Eberhart, M. Kai, Rna binding protein rbm14 promotes radio-resistance in glioblastoma by regulating dna repair and cell differentiation, Oncotarget 5 (9) (2014) 2820–2826, https://doi.org/10.18632/oncotarget.1924.
[82] C. Rajesh, D. Baker, A. Pierce, D. Pittman, The splicing-factor related protein sfpq/psf interacts with rad51d and is necessary for homology-directed repair and sister chromatid cohesion, Nucleic Acids Res. 39 (1) (2010) 132–145, https://doi.org/10.1093/nar/gkq738.
[83] Y. Zhao, X. Ye, M. Shehata, W. Dunker, Z. Xie, J. Karijolich, The RNA quality control pathway nonsense-mediated mRNA decay targets cellular and viral RNAs to restrict KSHV, Nat. Commun. 11 (1) (2020), https://doi.org/10.1038/s41467-020-17151-2.
[84] J. Miller, D. Pearce, Nonsense-mediated decay in genetic disease: friend or foe? Mutat. Res. /Rev. Mutat. Res. 762 (2014) 52–64, https://doi.org/10.1016/j.mrrev.2014.05.001.
[85] S. Nasif, Inhibition of nonsense-mediated mrna decay reduces the tumorigenicity of human fibrosarcoma cells, Nar. Cancer 5 (3) (2023), https://doi.org/10.1093/narcan/zcad048.
[86] C. Shoemaker, R. Green, Translation drives mrna quality control, Nat. Struct. Mol. Biol. 19 (6) (2012) 594–601, https://doi.org/10.1038/nsmb.2301.
[87] J. Weischenfeldt, J. Waage, G. Tian, J. Zhao, I. Damgaard, J. Jakobsen, B. Porse, Mammalian tissues defective in nonsense-mediated mrna decay display highly aberrant splicing patterns, Genome Biol. 13 (5) (2012) R35, https://doi.org/10.1186/gb-2012-13-5-r35.
[88] A. Garzia, S. Jafarnejad, C. Meyer, C. Chapat, T. Gogakos, P. Morozov, N. Sonenberg, The e3 ubiquitin ligase and rna-binding protein znf598 orchestrates ribosome quality control of premature polyadenylated mrnas, Nat. Commun. 8 (1) (2017), https://doi.org/10.1038/ncomms16056.
[89] E. Sundaramoorthy, M. Leonard, R. Mak, J. Liao, A. Fulzele, E. Bennett, Znf598 and rack1 regulate mammalian ribosome-associated quality control function by mediating regulatory 40s ribosomal ubiquitylation, Mol. Cell 65 (4) (2017) 751–760.e4, https://doi.org/10.1016/j.molcel.2016.12.026.
[90] I. Morozov, M. Jones, P. Gould, V. Crome, J. Wilson, A. Hall, M. Caddick, Mrna 3′ tagging is induced by nonsense-mediated decay and promotes ribosome dissociation, Mol. Cell. Biol. 32 (13) (2012) 2585–2595, https://doi.org/10.1128/mcb.00316-12.
[91] S. Lee, G. Pratt, F. Martínez, G. Yeo, J. Lykke-Andersen, Target discrimination in nonsense-mediated mrna decay requires upf1 atpase activity, Mol. Cell 59 (3) (2015) 413–425, https://doi.org/10.1016/j.molcel.2015.06.036.
[92] M.W.-L. Popp, L.E. Maquat, The dharma of nonsense-mediated mRNA decay in mammalian cells, Mol. Cells 37 (1) (2014) 1–8, https://doi.org/10.14348/molcells.2014.2193.
[93] F. Fiorini, D. Bagchi, H. Hir, V. Croquette, Human upf1 is a highly processive rna helicase and translocase with rnp remodelling activities, Nat. Commun. 6 (1) (2015), https://doi.org/10.1038/ncomms8581.
[94] Y. Kim, L. Maquat, Upfront and center in rna decay: upf1 in nonsense-mediated mrna decay and beyond, Rna 25 (4) (2019) 407–422, https://doi.org/10.1261/rna.070136.118.
[95] S. Fritz, S. Ranganathan, C. Wang, J. Hogg, The rna-binding protein ptbp1 promotes atpase-dependent dissociation of the rna helicase upf1 to protect transcripts from nonsense-mediated mrna decay, J. Biol. Chem. 295 (33) (2020) 11613–11625, https://doi.org/10.1074/jbc.ra120.013824.
[96] Z. Ge, B. Quek, K. Beemon, J. Hogg, Polypyrimidine tract binding protein 1 protects mrnas from recognition by the nonsense-mediated mrna decay pathway, Elife (2016) 5, https://doi.org/10.7554/elife.11155.
[97] M. Änkö, M. Müller-McNicoll, H. Brandl, T. Curk, Č. Gorup, I. Henry, K. Neugebauer, The rna-binding landscapes of two sr proteins reveal unique functions and binding to diverse rna classes, Genome Biol. 13 (3) (2012) R17, https://doi.org/10.1186/gb-2012-13-3-r17.
[98] J. Humphrey, W. Emmett, P. Fratta, A. Isaacs, V. Plagnol, Quantitative analysis of cryptic splicing associated with tdp-43 depletion, BMC Med. Genom. 10 (1) (2017), https://doi.org/10.1186/s12920-017-0274-1.
[99] E. Tank, C. Figueroa-Romero, L. Hinder, K. Bedi, H. Archbold, X. Li, S. Barmada, Abnormal rna stability in amyotrophic lateral sclerosis, Nat. Commun. 9 (1) (2018), https://doi.org/10.1038/s41467-018-05049-z.
[100] Y. Harigaya, R. Parker, No-go decay: a quality control mechanism for rna in translation, Wiley Interdiscip. Rev. - Rna 1 (1) (2010) 132–141, https://doi.org/10.1002/wrna.17.
[101] C. Shoemaker, D. Eyler, R. Green, Dom34:hbs1 promotes subunit dissociation and peptidyl-trna drop-off to initiate no-go decay, Science 330 (6002) (2010) 369–372, https://doi.org/10.1126/science.1192430.
[102] T. Tsuboi, K. Kuroha, K. Kudo, S. Makino, E. Inoue, I. Kashima, T. Inada, Dom34:hbs1 plays a general role in quality-control systems by dissociation of a stalled ribosome at the 3′ end of aberrant mrna, Mol. Cell 46 (4) (2012) 518–529, https://doi.org/10.1016/j.molcel.2012.03.013.
[103] J. Lin, Y. Zhang, W. Frankel, Z. Ouyang, Pras: predicting functional targets of rna binding proteins based on clip-seq peaks, Plos Comput. Biol. 15 (8) (2019) e1007227, https://doi.org/10.1371/journal.pcbi.1007227.
[104] N. Mukherjee, H. Wessels, S. Lebedeva, M. Sajek, M. Ghanbari, A. Garzia, U. Ohler, Deciphering human ribonucleoprotein regulatory networks, Nucleic Acids Res. 47 (2) (2018) 570–581, https://doi.org/10.1093/nar/gky1185.
[105] Y. Yang, A. Crofts, N. Crofts, T. Okita, Multiple rna binding protein complexes interact with the rice prolamine rna cis-localization zipcode sequences, Plant Physiol. 164 (3) (2014) 1271–1282, https://doi.org/10.1104/pp.113.234187.
[106] K. Nishiura, S. Kawashima, T. Nagai, Y. Oishi, N. Hosoda, H. Imataka, S. Hoshino, Dom34 mediates targeting of exogenous rna in the antiviral oas/rnase l pathway, Nucleic Acids Res. 47 (1) (2018) 432–449, https://doi.org/10.1093/nar/gky1087.
[107] M. Doma, R. Parker, Endonucleolytic cleavage of eukaryotic mrnas with stalls in translation elongation, Nature 440 (7083) (2006) 561–564, https://doi.org/10.1038/nature04530.
[108] C. Kilchert, S. Wittmann, L. Vasiljeva, The regulation and functions of the nuclear rna exosome complex, Nat. Rev. Mol. Cell Biol. 17 (4) (2016) 227–239, https://doi.org/10.1038/nrm.2015.15.
[109] K. Pan, Z. Huang, J. Lee, C. Wong, Current perspectives on the role of tramp in nuclear rna surveillance and quality control, Res. Rep. Biochem. 111 (2015), https://doi.org/10.2147/rrbc.s58509.
[110] M. Fasken, A. Corbett, Process or perish: quality control in mrna biogenesis, Nat. Struct. Mol. Biol. 12 (6) (2005) 482–488, https://doi.org/10.1038/nsmb945.
[111] O. Isken, L. Maquat, Quality control of eukaryotic mrna: safeguarding cells from abnormal mrna function, Genes Dev. 21 (15) (2007) 1833–3856, https://doi.org/10.1101/gad.1566807.
[112] E. Aikio, Complementary analysis of proteome-wide proteomics reveals changes in rna binding protein-profiles during prostate cancer progression, Cancer Rep. 6 (10) (2023), https://doi.org/10.1002/cnr2.1886.
[113] T. Stenum, A. Kumar, F. Sandbaumhüter, J. Kjellin, J. Jerlström-Hultqvist, P. Andrén, E. Holmqvist, Rna interactome capture in Escherichia coli globally identifies rna-binding proteins, Nucleic Acids Res. 51 (9) (2023) 4572–4587, https://doi.org/10.1093/nar/gkad216.
[114] S. Panja, S. Woodson, Hexamer to monomer equilibrium of e. coli hfq in solution and its impact on rna annealing, J. Mol. Biol. 417 (5) (2012) 406–412, https://doi.org/10.1016/j.jmb.2012.02.009.
[115] N. Srinivas, S. Rachakonda, R. Kumar, Telomeres and telomere length: a general overview, Cancers 12 (3) (2020) 558, https://doi.org/10.3390/cancers12030558.
[116] A. Maicher, L. Kastner, M. Dees, B. Luke, Deregulated telomere transcription causes replication-dependent telomere shortening and promotes cellular senescence, Nucleic Acids Res. 40 (14) (2012) 6649–6659, https://doi.org/10.1093/nar/gks358.

[117] L. Catto, Telomeric repeat-containing rna is dysregulated in acute myeloid leukemia, Blood Adv. 7 (22) (2023) 7067–7078, https://doi.org/10.1182/bloodadvances.2023010658.
[118] S. Redon, I. Zemp, J. Lingner, A three-state model for the regulation of telomerase by TERRA and hnRNPA1, Nucleic Acids Res. 41 (19) (2013) 9117–9128, https://doi.org/10.1093/nar/gkt695.
[119] E. Petti, V. Buemi, A. Zappone, O. Schillaci, P. Broccia, R. Dinami, S. Schoeftner, Sfpq and nono suppress rna:dna-hybrid-related telomere instability, Nat. Commun. 10 (1) (2019), https://doi.org/10.1038/s41467-019-08863-1.
[120] H. Chu, C. Cifuentes-Rojas, B. Kesner, E. Aeby, H. Lee, C. Wei, J. Lee, Terra rna antagonizes atrx and protects telomeres, Cell 170 (1) (2017) 86–101.e16, https://doi.org/10.1016/j.cell.2017.06.017.
[121] A. Bah, H. Wischnewski, V. Shchepachev, C. Azzalin, The telomeric transcriptome of schizosaccharomyces pombe, Nucleic Acids Res. 40 (7) (2011) 2995–3005, https://doi.org/10.1093/nar/gkr1153.
[122] A. Grimes, S.B.C. Chandra, Significance of cellular senescence in aging and cancer, Cancer Res. Treat. 41 (4) (2009) 187, https://doi.org/10.4143/crt.2009.41.4.187.
[123] S. Ghadaouia, M.A. Olivier, A. Martinez, N. Malaquin, G.B. Cardin, F. Rodier, Telomeric dysfunction triggers an unstable growth arrest leading to irreparable genomic lesions and entry into cellular senescence (2018), https://doi.org/10.1101/442533.
[124] J.W. Lee, E.B.B. Ong, Genomic instability and cellular senescence: lessons from the budding yeast, Front. Cell Dev. Biol. 8 (2021) 619126, https://doi.org/10.3389/fcell.2020.619126.
[125] J. Soudet, P. Jolivet, M.T. Teixeira, Elucidation of the DNA end-replication problem in Saccharomyces cerevisiae, Mol. Cell 53 (6) (2014) 954–964, https://doi.org/10.1016/j.molcel.2014.02.030.
[126] H. Tanaka, M.-C. Yao, Palindromic gene amplification—An evolutionarily conserved role for DNA inverted repeats in the genome, Nat. Rev. Cancer 9 (3) (2009) 216–224, https://doi.org/10.1038/nrc2591.
[127] B.A. Avin, C.B. Umbricht, M.A. Zeiger, Human telomerase reverse transcriptase regulation by DNA methylation, transcription factor binding and alternative splicing (Review), Int. J. Oncol. 49 (6) (2016) 2199–2205, https://doi.org/10.3892/ijo.2016.3743.
[128] H. Kim, N. Kim, Y. Wang, E. Scarborough, J. Moore, Z. Diaz, J. Taylor, Mutations in prion-like domains in hnrnpa2b1 and hnrnpa1 cause multisystem proteinopathy and als, Nature 495 (7442) (2013) 467–473, https://doi.org/10.1038/nature11922.
[129] M. Cao, B. Ryan, J. Wu, M. Curtis, R. Faull, M. Dragunow, E. Scotter, A panel of tdp-43-regulated splicing events verify loss of tdp-43 function in amyotrophic lateral sclerosis brain tissue (2023), https://doi.org/10.1101/2023.02.03.527079.
[130] A. Prasad, V. Bharathi, V. Sivalingam, A. Girdhar, B. Patel, Molecular mechanisms of tdp-43 misfolding and pathology in amyotrophic lateral sclerosis, Front. Mol. Neurosci. 12 (2019), https://doi.org/10.3389/fnmol.2019.00025.
[131] J. Higelin, M. Demestre, S. Putz, J. Delling, C. Jacob, A. Lutz, T. Boeckers, Fus mislocalization and vulnerability to dna damage in als patients derived hipscs and aging motoneurons, Front. Cell. Neurosci. 10 (2016), https://doi.org/10.3389/fncel.2016.00290.
[132] Z. Sun, Z. Diaz, X. Fang, M. Hart, A. Chesi, J. Shorter, A. Gitler, Molecular determinants and genetic modifiers of aggregation and toxicity for the als disease protein fus/tls, Plos Biol. 9 (4) (2011) e1000614, https://doi.org/10.1371/journal.pbio.1000614.
[133] V. Kumar, G. Hasan, M. Hassan, Unraveling the role of rna mediated toxicity of c9orf72 repeats in c9-ftd/als, Front. Neurosci. 11 (2017), https://doi.org/10.3389/fnins.2017.00711.
[134] K. Mayl, Y. Lee, Disease mechanisms and therapeutic approaches in c9orf72 als-ftd, Biomedicines 9 (6) (2021) 601, https://doi.org/10.3390/biomedicines9060601.
[135] K. Zhang, J. Daigle, K. Cunningham, A. Coyne, K. Ruan, J. Grima, T. Lloyd, Stress granule assembly disrupts nucleocytoplasmic transport, Cell 173 (4) (2018) 958–971.e17, https://doi.org/10.1016/j.cell.2018.03.025.
[136] F. Gao, S. Almeida, R. López-González, Dysregulated molecular pathways in amyotrophic lateral sclerosis–frontotemporal dementia spectrum disorder, Embo J. 36 (20) (2017) 2931–2950, https://doi.org/10.15252/embj.201797568.
[137] A. Montuschi, B. Iazzolino, A. Calvo, C. Moglia, L. Lopiano, G. Restagno, A. Chiò, Cognitive correlates in amyotrophic lateral sclerosis: a population-based study in italy, J. Neurol. Neurosurg. Psychiatry 86 (2) (2014) 168–173, https://doi.org/10.1136/jnnp-2013-307223.
[138] K. Trageser, E. Yang, C. Smith, R. Iban-Arias, T. Oguchi, M. Sebastian-Valverde, G. Pasinetti, Inflammasome-mediated neuronal-microglial crosstalk: a therapeutic substrate for the familial c9orf72 variant of frontotemporal dementia/amyotrophic lateral sclerosis, Mol. Neurobiol. 60 (7) (2023) 4004–4016, https://doi.org/10.1007/s12035-023-03315-w.
[139] M. Pribadi, Z. Yang, T. Kim, E. Swartz, A. Huang, J. Chen, G. Coppola, Crispr-cas9 Target. deletion thec9orf72repeat Expans. Mutat. corrects Cell. phenotypes Patient-Deriv. ips Cells (2016), https://doi.org/10.1101/051193.
[140] L. Dratch, J. Owczarzak, W. Mu, K. Cousins, L. Massimo, M. Grossman, L. Erby, The lived experience of reconstructing identity in response to genetic risk of frontotemporal degeneration and amyotrophic lateral sclerosis, J. Genet. Couns. 33 (3) (2023) 515–527, https://doi.org/10.1002/jgc4.1749.
[141] R. Bruin, T. Rabelink, A. Zonneveld, E. Veer, Emerging roles for rna-binding proteins as effectors and regulators of cardiovascular disease, Eur. Heart J. (2017) ehw567, https://doi.org/10.1093/eurheartj/ehw567.
[142] K. Masuda, Y. Kuwano, Diverse roles of rna-binding proteins in cancer traits and their implications in gastrointestinal cancers, Wiley Interdiscip. Rev. - Rna 10 (3) (2018), https://doi.org/10.1002/wrna.1520.
[143] Q. Guo, Y. Wu, X. Guo, L. Cao, F. Xu, H. Zhao, X. Wu, The rna-binding protein celf2 inhibits ovarian cancer progression by stabilizing fam198b, Mol. Ther. — Nucleic Acids 23 (2021) 169–184, https://doi.org/10.1016/j.omtn.2020.10.011.
[144] J. Han, Ö. An, X. Ren, Y. Song, S. Tang, H. Shen, L. Chen, Multilayered control of splicing regulatory networks by dap3 leads to widespread alternative splicing changes in cancer, Nat. Commun. 13 (1) (2022), https://doi.org/10.1038/s41467-022-29400-7.
[145] G. Hu, Q. Jiang, L. Liu, H. Peng, Y. Wang, S. Li, Z. Liu, Integrated analysis of rna-binding proteins associated with the prognosis and immunosuppression in squamous cell carcinoma of head and neck, Front. Genet. 11 (2021), https://doi.org/10.3389/fgene.2020.571403.
[146] D. Lujan, J. Ochoa, R. Hartley, Cold-inducible rna binding protein in cancer and inflammation, Wiley Interdiscip. Rev. - Rna 9 (2) (2018), https://doi.org/10.1002/wrna.1462.
[147] C. He, F. Huang, K. Zhang, J. Wei, K. Hu, M. Liang, Establishment and validation of an rna binding protein-associated prognostic model for ovarian cancer, J. Ovarian Res. 14 (1) (2021), https://doi.org/10.1186/s13048-021-00777-1.
[148] A. Ghidini, A. Cléry, F. Halloy, F. Allain, J. Hall, Rna-protacs: degraders of rna-binding proteins, Angew. Chem. 60 (6) (2020) 3163–3169, https://doi.org/10.1002/anie.202012330.
[149] S. Chothani, S. Schäfer, E. Adami, S. Viswanathan, A.A. Widjaja, S.R. Langley, J. Tan, M. Wang, N.M. Quaife, C. Jian Pua, G. D'Agostino, S. Guna Shekeran, B.L. George, S. Lim, E. Yiqun Cao, S. van Heesch, F. Witte, L.E. Felkin, E.G. Christodoulou, J. Dong, S. Blachut, G. Patone, P.J.R. Barton, N. Hubner, S.A. Cook, O.J.L. Rackham, Widespread translational control of fibrosis in the human heart by RNA-binding proteins, Circulation 140 (11) (2019) 937–951, https://doi.org/10.1161/CIRCULATIONAHA.119.039596 Epub 2019 Jul 9. PMID: 31284728; PMCID: PMC6749977.
[150] L. Qiao, L. Xu, Y. Liu, J. Wynn, R. Hernan, X. Zhou, C. Wk, Rare De. novo Var. 827 Congenit. diaphragmatic hernia probands implicate lonp1 alyref N. Candidate risk Genes (2021), https://doi.org/10.1101/2021.06.01.21257928.
[151] D. Shi, Rna-binding proteins in cardiomyopathies, J. Cardiovasc. Dev. Dis. 11 (3) (2024) 88, https://doi.org/10.3390/jcdd11030088.
[152] M. D'Antonio, J. Nguyen, T. Arthur, H. Matsui, M. Donovan, A. D'Antonio-Chronowska, K. Frazer, In heart failure reactivation of rna-binding proteins is associated with the expression of 1,523 fetal-specific isoforms, Plos Comput. Biol. 18 (2) (2022) e1009918, https://doi.org/10.1371/journal.pcbi.1009918.
[153] J. Liu, X. Kong, M. Zhang, X. Yang, X. Xu, Rna binding protein 24 deletion disrupts global alternative splicing and causes dilated cardiomyopathy, Protein Cell 10 (6) (2018) 405–416, https://doi.org/10.1007/s13238-018-0578-8.
[154] T. Zhang, L. Yu, J. Liu, Z. Zhang, W. Fu, L. Guo, X. Xiao-hong, Rbm24 regulates alternative splicing switch in embryonic stem cell cardiac lineage differentiation, Stem Cells 34 (7) (2016) 1776–1789, https://doi.org/10.1002/stem.2366.

[155] A. Kalsotra, K. Wang, P. Li, T. Cooper, Microrna coordinate an alternative splicing network during mouse postnatal heart development, Genes Dev. 24 (7) (2010) 653–658, https://doi.org/10.1101/gad.1894310.

[156] P. Ortiz-Sánchez, M. Villalba-Orero, M. López-Olañeta, J. Larrasa-Alonso, F. Sánchez-Cabo, C. Martí-Gómez, E. Lara-Pezzi, Loss of srsf3 in cardiomyocytes leads to decapping of contraction-related mrnas and severe systolic dysfunction, Circ. Res. 125 (2) (2019) 170–183, https://doi.org/10.1161/circresaha.118.314515.

[157] R. Si, J.T.O. Cabrera, A. Tsuji-Hosokawa, R. Guo, M. Watanabe, L. Gao, Y.S. Lee, J.S. Moon, B.T. Scott, J. Wang, A.W. Ashton, J.N. Rao, J.Y. Wang, J.X. Yuan, A. Makino, HuR/Cx40 downregulation causes coronary microvascular dysfunction in type 2 diabetes, JCI Insight 6 (21) (2021) e147982, https://doi.org/10.1172/jci.insight.147982 PMID: 34747371; PMCID: PMC8663561.

[158] Q. Shi, D.Y. Lee, D. Féliers, H.E. Abboud, M.A. Bhat, Y. Gorin, Interplay between RNA-binding protein HuR and Nox4 as a novel therapeutic target in diabetic kidney disease, Mol. Metab. 36 (2020) 100968, https://doi.org/10.1016/j.molmet.2020.02.011 Epub 2020 Feb 28. PMID: 32240965; PMCID: PMC7115155.

[159] N. Jeffery, D. Chambers, B.M. Invergo, R.M. Ames, L.W. Harries, Changes to the identity of EndoC-βH1 beta cells may be mediated by stress-induced depletion of HNRNPD, Cell Biosci. 11 (1) (2021) 144, https://doi.org/10.1186/s13578-021-00658-6 PMID: 34301309; PMCID: PMC8305497.

[160] V. Kumar, A. Kumar, M. Kumar, et al., NFκB (RelA) mediates transactivation of hnRNPD in oral cancer cells, Sci. Rep. 12 (2022) 5944, https://doi.org/10.1038/s41598-022-09963-7.

[161] L. Qian, H. Shi, M. Ding, Comparative analysis of gene expression profiles in children with type 1 diabetes mellitus, Mol. Med. Rep. 19 (2019) 3989–4000, https://doi.org/10.3892/mmr.2019.10099.

[162] K. Belanger, C.A. Nutter, J. Li, S. Tasnim, P. Liu, P. Yu, M.N. Kuyumcu-Martinez, CELF1 contributes to aberrant alternative splicing patterns in the type 1 diabetic heart, Biochem. Biophys. Res. Commun. 503 (4) (2018) 3205–3211.

[163] W. Qin, J.J. Shi, R.Y. Chen, et al., Curriculum vitae of CUG binding protein 1 (CELF1) in homeostasis and diseases: a systematic review, Cell Mol. Biol. Lett. 29 (2024) 32, https://doi.org/10.1186/s11658-024-00556-y.

[164] C.A. Nutter, M.N. Kuyumcu-Martinez, Emerging roles of RNA-binding proteins in diabetes and their therapeutic potential in diabetic complications, Wiley Inter. Rev. RNA 9 (2) (2018), https://doi.org/10.1002/wrna.1459.

[165] S.K. Verma, V. Deshmukh, P. Liu, C.A. Nutter, R. Espejo, M.L. Hung, M.N. Kuyumcu-Martinez, Reactivation of fetal splicing programs in diabetic hearts is mediated by protein kinase C signaling, J. Biol. Chem. 288 (49) (2013) 35372–35386.

[166] T. Gu, E. Horová, A. Möllsten, N.A. Seman, H. Falhammar, M. Prázný, H.F. Gu, IGF2BP2 and IGF2 genetic effects in diabetes and diabetic nephropathy, J. Diabetes Complicat. 26 (5) (2012) 393–398.

[167] S. Sargazi, M.H. Nia, R. Saravani, M.J. Shahroudi, D. Jahantigh, M. Shakiba, IGF2BP2 polymorphisms as genetic biomarkers for either schizophrenia or type 2 diabetes mellitus: a case-control study, Gene Rep. 20 (2020) 100680.

[168] L.F. Zhang, Q. Pei, G.P. Yang, Y.C. Zhao, Y.F. Mu, Q. Huang, Y.L. Zhu, The effect of IGF2BP2 gene polymorphisms on pioglitazone response in Chinese type 2 diabetes patients, Pharmacology 94 (3-4) (2014) 115–122.

[169] P. Rao, H. Wang, H. Fang, Q. Gao, J. Zhang, M. Song, Y. Zhou, Y. Wang, W. Wang, Association between IGF2BP2 polymorphisms and Type 2 diabetes mellitus: a case-control study and meta-analysis, Int J. Environ. Res Public Health 13 (6) (2016) 574, https://doi.org/10.3390/ijerph13060574 PMID: 27294943; PMCID: PMC4924031.

[170] M. van Hoek, J.G. Langendonk, S.R. de Rooij, E.J. Sijbrands, T.J. Roseboom, Genetic variant in the IGF2BP2 gene may interact with fetal malnutrition to affect glucose metabolism, Diabetes 58 (6) (2009) 1440–1444.

[171] J. Hong, M. Ami, S. Maurice S, M. Richard T, T. Charles A, Myotonic dystrophy type 1 is associated with nuclear foci of mutant RNA, sequestration of muscleblind proteins and deregulated alternative splicing in neurons, Hum. Mol. Genet. 13 (24) (2004) 3079–3088.

[172] S. Paul, W. Dansithong, S.P. Jog, I. Holt, S. Mittal, J.D. Brook, G.E. Morris, L. Comai, S. Reddy, Expanded CUG repeats Dysregulate RNA splicing by altering the stoichiometry of the muscleblind 1 complex, J. Biol. Chem. 286 (44) (2011) 38427–38438, https://doi.org/10.1074/jbc.M111.255224 Epub 2011 Sep 7. PMID: 21900255; PMCID: PMC3207417.

[173] S. Hutten, D. Dormann, hnRNPA2/B1 function in neurodegeneration: it'sa gain, not a loss, Neuron 92 (4) (2016) 672–674.

[174] J. Mattay, Current technical approaches to study RNA–Protein interactions in mRNAs and long non-coding RNAs, BioChem 3 (1) (2022) 1–14.

[175] N.N. Salim, S.S. Ganaie, A. Roy, S. Jeeva, M.A. Mir, Targeting a novel RNA-protein interaction for therapeutic intervention of hantavirus disease, J. Biol. Chem. 291 (47) (2016) 24702–24714, https://doi.org/10.1074/jbc.M116.750729 Epub 2016 Oct 12. PMID: 27733686; PMCID: PMC5114419.

[176] A. Fradera-Sola, E. Nischwitz, M.E. Bayer, K. Luck, F. Butter, RNA-dependent interactome allows network-based assignment of RNA-binding protein function, Nucleic Acids Res 51 (10) (2023) 5162–5176, https://doi.org/10.1093/nar/gkad245 PMID: 37070168; PMCID: PMC10250244.

[177] Y. Li, D.J. McGrail, N. Latysheva, S. Yi, M.M. Babu, N. Sahni, Pathway perturbations in signaling networks: linking genotype to phenotype, Semin Cell Dev. Biol. 99 (2020) 3–11, https://doi.org/10.1016/j.semcdb.2018.05.001 Epub 2018 May 10. PMID: 29738884; PMCID: PMC6230320.

[178] D. Medina-Cleghorn, D.K. Nomura, Exploring metabolic pathways and regulation through functional chemoproteomic and metabolomic platforms, Chem. Biol. 21 (9) (2014) 1171–1184, https://doi.org/10.1016/j.chembiol.2014.07.007 PMID: 25237861; PMCID: PMC4171689.

[179] N.E. Farrawell, I.A. Lambert-Smith, S.T. Warraich, I.P. Blair, D.N. Saunders, D.M. Hatters, J.J. Yerbury, Distinct partitioning of ALS associated TDP-43, FUS and SOD1 mutants into cellular inclusions, Sci. Rep. 5 (2015) 13416, https://doi.org/10.1038/srep13416 PMID: 26293199; PMCID: PMC4544019.

[180] E. Pokrishevsky, L. Grad, N. Cashman, TDP-43 or FUS-induced misfolded human wild-type SOD1 can propagate intercellularly in a prion-like fashion, Sci. Rep. 6 (2016) 22155, https://doi.org/10.1038/srep22155.

[181] Y. Wang, S.X. Chen, X. Rao, Y. Liu, Modulator-dependent RBPs changes alternative splicing outcomes in kidney cancer, Front. Genet. 11 (2020) 265.

[182] D.S. Berger, A.N. Ladd, Repression of nuclear CELF activity can rescue CELF-regulated alternative splicing defects in skeletal muscle models of myotonic dystrophy, PLoS Curr. 4 (2012) RRN1305, https://doi.org/10.1371/currents.RRN1305 PMID: 22453899; PMCID: PMC3286860.

[183] A.N. Ladd, N. Charlet, T.A. Cooper, The CELF family of RNA binding proteins is implicated in cell-specific and developmentally regulated alternative splicing, Mol. Cell Biol. 21 (4) (2001) 1285–1296, https://doi.org/10.1128/MCB.21.4.1285-1296.2001 PMID: 11158314; PMCID: PMC99581.

[184] S.E. Ahmadi, M. Soleymani, F. Shahriyary, M.R. Amirzargar, M. Ofoghi, M.D. Fattahi, M. Safa, Viral vectors and extracellular vesicles: innate delivery systems utilized in CRISPR/Cas-mediated cancer therapy, Cancer Gene Ther. 30 (7) (2023) 936–954.

[185] O. Rogoyski, A.P. Gerber, RNA-binding proteins modulate drug sensitivity of cancer cells, Emerg. Top. Life Sci. 5 (5) (2021) 681–685, https://doi.org/10.1042/ETLS20210193 PMID: 34328175; PMCID: PMC8726047.

[186] A. Das, T. Sinha, S. Shyamal, A.C. Panda, Emerging role of circular RNA-protein interactions, Noncoding RNA 7 (3) (2021) 48, https://doi.org/10.3390/ncrna7030048 PMID: 34449657; PMCID: PMC8395946.

[187] H.J. Hwang, Y.K. Kim, Molecular mechanisms of circular RNA translation, Exp. Mol. Med. (2024) 1–9.

[188] Z. Wei-Yi, Z.R. Cai, J. Liu, W. De-Shen, H.Q. Ju, X. Rui-Hua, Circular RNA: metabolism, functions and interactions with proteins, Mol. Cancer 19 (2020) 1.

[189] S. Hong, RNA binding protein as an emerging therapeutic target for cancer prevention and treatment, J. Cancer Prev. 22 (4) (2017) 203–210, https://doi.org/10.15430/JCP.2017.22.4.203 Epub 2017 Dec 30. PMID: 29302577; PMCID: PMC5751837.

[190] B. Portz, B.L. Lee, J. Shorter, FUS and TDP-43 phases in health and disease, Trends Biochem Sci. 46 (2021) 550–563.

[191] J.D. Laver, K. Ancevicius, P. Sollazzo, J.T. Westwood, S.S. Sidhu, H.D. Lipshitz, C.A. Smibert, Synthetic antibodies as tools to probe RNA-binding protein function, Mol. Biosyst. 8 (6) (2012) 1650–1657, https://doi.org/10.1039/c2mb00007e Epub 2012 Apr 5. PMID: 22481296.

[192] P. Khan, J.A. Siddiqui, I. Lakshmanan, A.K. Ganti, R. Salgia, M. Jain, M.W. Nasser, RNA-based therapies: a cog in the wheel of lung cancer defense, Mol. Cancer 20 (2021) 1–24.

[193] T.C. Roberts, R. Langer, M.J.A. Wood, Advances in oligonucleotide drug delivery, Nat. Rev. Drug Discov. 19 (2020) 673–694.

[194] J.P. Bost, H. Barriga, M.N. Holme, A. Gallud, M. Maugeri, D. Gupta, S. El-Andaloussi, Delivery of oligonucleotide therapeutics: chemical modifications, lipid nanoparticles, and extracellular vesicles, ACS nano 15 (9) (2021) 13993–14021.

[195] A.R. Julio, K.M. Backus, New approaches to target RNA binding proteins, Curr. Opin. Chem. Biol. 62 (2021) 13–23, https://doi.org/10.1016/j.cbpa.2020.12.006 Epub 2021 Jan 31. PMID: 33535093; PMCID: PMC8823266.

[196] X. Lu, J. Zhong, L. Liu, W. Zhang, S. Zhao, L. Chen, F. Ge, The function and regulatory mechanism of RNA-binding proteins in breast cancer and their future clinical treatment prospects, Front. Oncol. 12 (2022) 929037.
[197] Y. Xu, Y. Yuan, D.Q. Fu, Y. Fu, S. Zhou, W.T. Yang, Z. Tang, The aptamer-based RNA-PROTAC, Bioorg. Med. Chem. 86 (2023) 117299.
[198] A.K. Jaiswal, M.L. Thaxton, G.M. Scherer, J.P. Sorrentino, N.K. Garg, D.S. Rao, Small molecule inhibition of RNA binding proteins in haematologic cancer, RNA Biol. 21 (1) (2024) 1–14, https://doi.org/10.1080/15476286.2024.2303558 Epub 2024 Feb 8. PMID: 38329136; PMCID: PMC10857685.
[199] K.I. Takayama, S. Matsuoka, S. Adachi, T. Honma, M. Yoshida, T. Doi, K. Shin-Ya, M. Yoshida, H. Osada, S. Inoue, Identification of small-molecule inhibitors against the interaction of RNA-binding protein PSF and its target RNA for cancer treatment, PNAS Nexus 2 (6) (2023) pgad203, https://doi.org/10.1093/pnasnexus/pgad203 PMID: 37388923; PMCID: PMC10304769.
[200] M.S. Badar, S. Shamsi, J. Ahmed, M.A. Alam, Molecular Dynamics Simulations: Concept, Methods, and Applications, in: N. Rezaei (Ed.), Transdisciplinarity. Integrated Science, 5 Springer, Cham, 2022, https://doi.org/10.1007/978-3-030-94651-7_7.
[201] S.A. Hollingsworth, R.O. Dror, Molecular dynamics simulation for all, Neuron 99 (6) (2018) 1129–1143, https://doi.org/10.1016/j.neuron.2018.08.011 PMID: 30236283; PMCID: PMC6209097.
[202] Z. Zhang, S. Balzarini, B. Parmar, K. Boonen, A. Vandeperre, K. Geuten, Rna Inter. capture brachypodium Reveals a Flower. Plant core rbpome (2020), https://doi.org/10.21203/rs.3.rs-23468/v1.
[203] D. Essegian, T. Cunningham, C. Zerio, E. Chapman, J. Schatz, S. Schürer, Molecular dynamics simulations identify tractable lead-like phenyl-piperazine scaffolds as eif4a1 atp-competitive inhibitors, Acs Omega 6 (38) (2021) 24432–24443, https://doi.org/10.1021/acsomega.1c02805.
[204] J. Kang, Q. Tang, J. He, L. Li, N. Yang, S. Yu, M. Wang, Y. Zhang, J. Lin, T. Cui, Y. Hu, P. Tan, J. Cheng, H. Zheng, D. Wang, X. Su, W. Chen, Y. Huang, RNAInter v4.0: RNA interactome repository with redefined confidence scoring system and improved accessibility, Nucleic Acids Res. 50 (D1) (2022) D326–D332, https://doi.org/10.1093/nar/gkab997.
[205] J.I. Perez-Perri, B. Rogell, T. Schwarzl, et al., Discovery of RNA-binding proteins and characterization of their dynamic responses by enhanced RNA interactome capture, Nat. Commun. 9 (2018) 4408, https://doi.org/10.1038/s41467-018-06557-8.
[206] S. Singh, S. Shyamal, A.C. Panda, Detecting RNA-RNA interactome, Wiley Inter. Rev. RNA 13 (5) (2022) e1715, https://doi.org/10.1002/wrna.1715 Epub 2022 Feb 8. PMID: 35132791.
[207] K. Yazdani, D. Jordan, M. Yang, C. Fullenkamp, J. Schneekloth, D. Calabrese, R. Khan, Machine learning informs rna-binding chemical space**, Angew. Chem. 135 (11) (2023), https://doi.org/10.1002/ange.202211358.
[208] M. Eshaghi, O. Neustroeva, I. Chowdhury, P. Laitinen, M. Väänänen, N. Korvenlaita, T. Turunen, Construction of fusion protein for enhanced small rna loading to extracellular vesicles, Genes 14 (2) (2023) 261, https://doi.org/10.3390/genes14020261.
[209] J. Yan, M. Zhu, A review about rna–protein-binding sites prediction based on deep learning, Ieee Access 8 (2020) 150929–150944, https://doi.org/10.1109/access.2020.3014996.
[210] Y. Yagi, T. Teramoto, S. Kaieda, T. Imai, T. Sasaki, M. Yagi, T. Nakamura, Construction of a versatile, programmable rna-binding protein using designer ppr proteins and its application for splicing control in mammalian cells, Cells 11 (22) (2022) 3529, https://doi.org/10.3390/cells11223529.
[211] X. Hu, Q. Zou, L. Yao, X. Yang, Survey of the binding preferences of rna-binding proteins to rna editing events, Genome Biol. 23 (1) (2022), https://doi.org/10.1186/s13059-022-02741-8.
[212] N. DeSouza, Dysregulated expression patterns of circular rnas in cancer: uncovering molecular mechanisms and biomarker potential, Biomolecules 14 (4) (2024) 384, https://doi.org/10.3390/biom14040384.
[213] S. Meyer, Optimization of a protein-targeted medicine into an rna-specific small molecule, Acs Chem. Biol. 18 (11) (2023) 2336–2342, https://doi.org/10.1021/acschembio.3c00476.
[214] A. López-Estévez, Personalized cancer nanomedicine: overcoming biological barriers for intracellular delivery of biopharmaceuticals, Adv. Mater. 36 (14) (2023), https://doi.org/10.1002/adma.202309355.

Further reading

[1] Aggarwal G., Banerjee S., Jones S., Pavlack M., Benchaar Y., Bélanger J., .Nguyen A., (2022). Antisense oligonucleotides targeting Mir-29b binding site in the grn mrna increase progranulin translation doi: 10.1101/2022.01.12.476053.
[2] A. Aguilera, T. García-Muse, R Loops: from transcription byproducts to threats to genome stability, Mol. Cell 46 (2) (2012) 115–124, https://doi.org/10.1016/j.molcel.2012.04.009.
[3] U. Ala, Rna-binding protein transcripts as potential biomarkers for detecting primary sclerosing cholangitis and for predicting its progression to cholangiocarcinoma, Front. Mol. Biosci. 11 (2024), https://doi.org/10.3389/fmolb.2024.1388294.
[4] A. Andigema, Viral hijacking of host rna-binding proteins: implications for viral replication and pathogenesis, J. Clin. Lab. Res. 7 (5) (2024) 01–06, https://doi.org/10.31579/2768-0487/136.
[5] Baeza-Centurion, P. (2024). Deep indel mutagenesis reveals the regulatory and modulatory architecture of alternative exon splicing. 〈https://doi.org/10.1101/2024.04.21.590414〉.
[6] N. Bettin, Terra transcripts localize at long telomeres to regulate telomerase access to chromosome ends, Sci. Adv. 10 (24) (2024), https://doi.org/10.1126/sciadv.adk4387.
[7] X. Chen, Rna-binding proteins signature is a favorable biomarker of prognosis, immunotherapy and chemotherapy response for cervical cancer, Cancer Cell Int. 24 (1) (2024), https://doi.org/10.1186/s12935-024-03257-w.
[8] A. Colantoni, J. Rupert, A. Vandelli, G. Tartaglia, E. Zacco, Zooming in on protein–rna interactions: a multi-level workflow to identify interaction partners, Biochem. Soc. Trans. 48 (4) (2020) 1529–1543, https://doi.org/10.1042/bst20191059.
[9] A.H. Corbett, Post-transcriptional regulation of gene expression and human disease, Curr. Opin. Cell Biol. 52 (2018) 96–104.
[10] E. Cusanelli, P. Chartrand, Telomeric repeat-containing rna terra: a noncoding rna connecting telomere biology to genome integrity, Front. Genet. 6 (2015), https://doi.org/10.3389/fgene.2015.00143.
[11] N. Cyrielle, Viral hijacking of host rna-binding proteins: implications for viral replication and pathogenesis (2024), https://doi.org/10.20944/preprints202404.0436.v1.
[12] M. Delgado, B. Cárdenas, N. Farran, M. Fernández, Metabolic reprogramming of liver fibrosis, Cells 10 (12) (2021) 3604, https://doi.org/10.3390/cells10123604.
[13] H. Feng, S. Bao, S. Weyn-Vanhentenryck, A. Khan, J. Wong, A. Shah, C. Zhang, Modeling rna-binding protein specificity in vivo by precisely registering protein-rna crosslink sites (2018), https://doi.org/10.1101/428615.
[14] M. Feretzaki, P. Nunes, J. Lingner, Expression and differential regulation of human terra at several chromosome ends, Rna 25 (11) (2019) 1470–1480, https://doi.org/10.1261/rna.072322.119.
[15] M. Flamand, K. Ke, R. Tamming, K. Meyer, Single-molecule identification of the target rnas of different rna binding proteins simultaneously in cells, Genes Dev. (2022), https://doi.org/10.1101/gad.349983.122.
[16] W. Fu, X. Lei, Q. Lu, J. Zhang, J. Guo, J. Zhao, X. Hu, Ube2k regulated by igf2bp3 promotes cell proliferation and stemness in pancreatic ductal adenocarcinoma, Int. J. Oncol. 62 (4) (2023), https://doi.org/10.3892/ijo.2023.5500.
[17] M. Gagliardi, A. Ashizawa, The challenges and strategies of antisense oligonucleotide drug delivery, Biomedicines 9 (4) (2021) 433, https://doi.org/10.3390/biomedicines9040433.
[18] F. Gebauer, T. Schwarzl, J. Valcárcel, M.W. Hentze, RNA-binding proteins in human genetic disease, Nat. Rev. Genet 22 (2021) (2021) 185–198, https://doi.org/10.1038/s41576-020-00302-y.

[19] R. Giambruno, E. Grzybowska, N. Fawzi, D. Dormann, Editorial: the role of protein post-translational modifications in protein-rna interactions and rnp assemblies, Front. Mol. Biosci. 8 (2022), https://doi.org/10.3389/fmolb.2021.831810.
[20] L. Guo, C. Fare, J. Shorter, Therapeutic dissolution of aberrant phases by nuclear-import receptors, Trends Cell Biol. 29 (4) (2019) 308–322, https://doi.org/10.1016/j.tcb.2018.12.004.
[21] X. Guo, Y. Sun, T. Azad, H. Rensburg, J. Luo, Y. Sm, L. Xue, Rox8 promotes microrna-dependent yki messenger rna decay, Proc. Natl. Acad. Sci. 117 (48) (2020) 30520–30530, https://doi.org/10.1073/pnas.2013449117.
[22] L. Han, C. Huang, S. Zhang, The rna-binding protein sorbs2 suppresses hepatocellular carcinoma tumourigenesis and metastasis by stabilizing rora mrna, Liver Int. 39 (11) (2019) 2190–2203, https://doi.org/10.1111/liv.14202.
[23] X. Hua, J. Chen, S. Ge, H. Xiao, L. Zhang, C. Liang, Integrated analysis of the functions of rna binding proteins in clear cell renal cell carcinoma, Genomics 113 (1) (2021) 850–860, https://doi.org/10.1016/j.ygeno.2020.10.016.
[24] T. Jackson, P. Kochanek, Rna binding motif 5 (rbm5) in the cns—moving beyond cancer to harness rna splicing to mitigate the consequences of brain injury, Front. Mol. Neurosci. 13 (2020), https://doi.org/10.3389/fnmol.2020.00126.
[25] J. Jiang, X. Chai, N. Manavski, R. Williams-Carrier, B. He, A. Brachmann, W. Chi, An rna chaperone–like protein plays critical roles in chloroplast mrna stability and translation in arabidopsis and maize, Plant Cell 31 (6) (2019) 1308–1327, https://doi.org/10.1105/tpc.18.00946.
[26] P. Kordowitzki, I. Silanes, A. Guío-Carrión, M. Blasco, Dynamics of telomeric repeat-containing rna expression in early embryonic cleavage stages with regards to maternal age, Aging 12 (16) (2020) 15906–15917, https://doi.org/10.18632/aging.103922.
[27] H.A. Lewis, K. Musunuru, K.B. Jensen, et al., Sequence-specific RNA binding by a nova KH domain: implications for paraneoplastic disease and the fragile X syndrome, Cell 100 (2000) 323–332.
[28] W. Li, X. Deng, J. Chen, RNA-binding proteins in regulating mRNA stability and translation: roles and mechanisms in cancer, Semin Cancer Biol. 86 (Pt 2) (2022) 664–677, https://doi.org/10.1016/j.semcancer.2022.03.025 Epub 2022 Apr 2. PMID: 35381329; PMCID: PMC9526761.
[29] J. Li, T. Pan, L. Chen, Q. Wang, Z. Chang, W. Zhou, Y. Zhang, Alternative splicing perturbation landscape identifies rna binding proteins as potential therapeutic targets in cancer, Mol. Ther. — Nucleic Acids 24 (2021) 792–806, https://doi.org/10.1016/j.omtn.2021.04.005.
[30] W. Li, X. Deng, J. Chen, RNA-binding proteins in regulating mRNA stability and translation: roles and mechanisms in cancer, Semin. Cancer Biol. 86 (Pt 2) (2022) 664–677, https://doi.org/10.1016/j.semcancer.2022.03.025.
[31] L. Lin, Z. Liu, J. Tian, X. Zhang, Y. Zhang, M. Yang, C. Hu, Integrated analysis of nine prognostic rna-binding proteins in soft tissue sarcoma, Front. Oncol. 11 (2021), https://doi.org/10.3389/fonc.2021.633024.
[32] T. Lin, Targeting igf2bp3 enhances antileukemic effects of menin-mll inhibition in mll-af4 leukemia, Blood Adv. 8 (2) (2024) 261–275, https://doi.org/10.1182/bloodadvances.2023011132.
[33] W. Lin, Q. Wang, Y. Chen, N. Wang, Q. Ni, C. Qi, Y. Zhu, Identification of a 6-rbp gene signature for a comprehensive analysis of glioma and ischemic stroke: cognitive impairment and aging-related hypoxic stress, Front. Aging Neurosci. 14 (2022), https://doi.org/10.3389/fnagi.2022.951197.
[34] J. Liu, L. Wang, Z. Wang, J.-P. Liu, Roles of telomere biology in cell senescence, replicative and chronological ageing, Cells 8 (1) (2019) 54, https://doi.org/10.3390/cells8010054.
[35] L. Liu, T. Li, G. Song, Q. He, Y. Yin, J. Lu, X. Shen, Insight into novel rna-binding activities via large-scale analysis of lncrna-bound proteome and idh1-bound transcriptome, Nucleic Acids Res. 47 (5) (2019) 2244–2262, https://doi.org/10.1093/nar/gkz032.
[36] M. Liu, B. Lu, Y. Fan, X. He, S. Shen, C. Jiang, Q. Zhang, Tribe uncovers the role of dis3 in shaping the dynamic transcriptome in malaria parasites, Front. Cell Dev. Biol. 7 (2019), https://doi.org/10.3389/fcell.2019.00264.
[37] X. Liu, J. Chen, W. Chen, Y. Xu, Y. Shen, X. Xu, Targeting igf2bp3 in cancer, Int. J. Mol. Sci. 24 (11) (2023) 9423, https://doi.org/10.3390/ijms24119423.
[38] V. Lodde, M. Floris, E. Zoroddu, I. Zarbo, M. Idda, rna-binding proteins in autoimmunity: from genetics to molecular biology, Wiley Interdiscip. Rev. - Rna 14 (4) (2023), https://doi.org/10.1002/wrna.1772.
[39] D. Lu, M.A. Searles, A. Klug, Crystal structure of a zinc-finger-RNA complex reveals two modes of molecular recognition, Nature 426 (2003) 96–100.
[40] L. Luan, F. Lu, X. Wang, Y. Wang, W. Wang, Y. Yang, S. He, The predictive value of rna binding proteins in colon adenocarcinoma, J. Gastrointest. Oncol. 12 (4) (2021) 1543–1557, https://doi.org/10.21037/jgo-21-318.
[41] S. Maifata, F. Ghani, R. Hod, N. Zakaria, Membr. glomerulonephritis: role Retin. -Bind. Protein Monit. Progn. (2021), https://doi.org/10.20944/preprints202108.0109.v1.
[42] A.S. Mastrocola, S.H. Kim, A.T. Trinh, L.A. Rodenkirch, R.S. Tibbetts, The RNA-binding protein fused in sarcoma (FUS) functions downstream of poly(ADP-ribose) polymerase (PARP) in response to DNA damage, J. Biol. Chem. 288 (34) (2013) 24731–24741, https://doi.org/10.1074/jbc.m113.497974.
[43] C. Mei, P. Song, W. Zhang, H. Zhou, X. Li, Z. Liu, Aberrant rna splicing events driven by mutations of rna-binding proteins as indicators for skin cutaneous melanoma prognosis, Front. Oncol. 10 (2020), https://doi.org/10.3389/fonc.2020.568469.
[44] L. Méteignier, R. Ghandour, K. Meierhoff, A. Zimmerman, J. Chicher, N. Baumberger, ... K. Hammani, The arabidopsis mterf-repeat mda1 protein plays a dual function in transcription and stabilization of specific chloroplast transcripts within the psbe and ndhh operons, N. Phytol. 227 (5) (2020) 1376–1391, https://doi.org/10.1111/nph.16625.
[45] B. Ozdilek, V. Thompson, N. Ahmed, C. White, R. Batey, J. Schwartz, Intrinsically disordered rgg/rg domains mediate degenerate specificity in rna binding, Nucleic Acids Res. 45 (13) (2017) 7984–7996, https://doi.org/10.1093/nar/gkx460.
[46] X. Pan, Y. Yang, C. Xia, A. Mirza, H. Shen, Recent methodology progress of deep learning for rna–protein interaction prediction, Wiley Interdiscip. Rev. - Rna 10 (6) (2019), https://doi.org/10.1002/wrna.1544.
[47] A. Parra, C. Johnston, Emerging roles of rna-binding proteins in neurodevelopment, J. Dev. Biol. 10 (2) (2022) 23, https://doi.org/10.3390/jdb10020023.
[48] G. Pepe, F. Ballesio, M. Adinolfi, M. Pietrosanto, E. Sangiovanni, I. Vitale, M. Helmer-Citterich, Brio: a web server for rna sequence and structure motif scan, Nucleic Acids Res. 49 (W1) (2021) W67–W71, https://doi.org/10.1093/nar/gkab400.
[49] M. Popp, L. Maquat, Organizing principles of mammalian nonsense-mediated mrna decay, Annu. Rev. Genet. 47 (1) (2013) 139–165, https://doi.org/10.1146/annurev-genet-111212-133424.
[50] D. Puri, S. Samaddar, S. Banerjee, A. Ghosh-Roy, Musleblind-1 Regul. Micro Cytoskelet. C. elegans mechanosensory Neuron tubulin mrnas. (2022), https://doi.org/10.1101/2022.09.07.506915.
[51] W. Qin, Curriculum vitae of cug binding protein 1 (celf1) in homeostasis and diseases: a systematic review, Cell. Mol. Biol. Lett. 29 (1) (2024), https://doi.org/10.1186/s11658-024-00556-y.
[52] Y. Qin, W. Sun, Z. Wang, W. Dong, L. He, T. Zhang, H. Zhang, Rbm47/snhg5/foxo3 axis activates autophagy and inhibits cell proliferation in papillary thyroid carcinoma, Cell Death Dis. 13 (3) (2022), https://doi.org/10.1038/s41419-022-04728-6.
[53] Z. Que, Functional role of rbp in osteosarcoma: regulatory mechanism and clinical therapy, Anal. Cell. Pathol. 2023 (2023) 1–16, https://doi.org/10.1155/2023/9849719.
[54] R. Rahman, W. Xu, H. Jin, M. Rosbash, Identification of rna-binding protein targets with hypertribe, Nat. Protoc. 13 (8) (2018) 1829–1849, https://doi.org/10.1038/s41596-018-0020-y.
[55] D. Sanya, C. Cava, D. Onésime, Roles of rna-binding proteins in neurological disorders, covid-19, and cancer, Hum. Cell 36 (2) (2022) 493–514, https://doi.org/10.1007/s13577-022-00843-w.
[56] C. Shotwell, J. Cleary, J. Berglund, The potential of engineered eukaryotic rna-binding proteins as molecular tools and therapeutics, Wiley Interdiscip. Rev. - Rna 11 (1) (2019), https://doi.org/10.1002/wrna.1573.
[57] I. Silanes, M. d'Alcontres, M. Blasco, Terra transcripts are bound by a complex array of rna-binding proteins, Nat. Commun. 1 (1) (2010), https://doi.org/10.1038/ncomms1032.
[58] H. Swahn, M. Olmer, M. Lotz, Rna-binding proteins that are highly expressed and enriched in healthy cartilage but suppressed in osteoarthritis, Front. Cell Dev. Biol. 11 (2023), https://doi.org/10.3389/fcell.2023.1208315.

[59] Y. Tan, X. Sun, Y. Xu, B. Tang, S. Xu, D. Lu, X. Wu, Small molecule targeting celf1 rna-binding activity to control hsc activation and liver fibrosis, Nucleic Acids Res. 50 (5) (2022) 2440–2451, https://doi.org/10.1093/nar/gkac139.
[60] K. Tsuda, K. Kuwasako, M. Takahashi, et al., Structural basis for the sequence-specific RNA-recognition mechanism of human CUG-BP1 RRM3, Nucleic Acids Res 37 (2009) 5151–5166.
[61] K. Walters, M. Sajek, A. Issaian, A. Baldwin, E. Harrison, E. Murphy, N. Mukherjee, Small Mol. Inhib. Mult. Rna Bind. Proteins Under musashi-2 Indep. phenotypes (2022), https://doi.org/10.1101/2022.09.20.508735.
[62] K. Walters, M. Sajek, E. Murphy, A. Issaian, A. Baldwin, E. Harrison, N. Mukherjee, Small-molecule ro-08-2750 interacts with many rna-binding proteins and elicits musashi2-independent phenotypes, Rna 29 (10) (2023) 1458–1470, https://doi.org/10.1261/rna.079605.123.
[63] C. Wang, L. Zhao, S. Lu, Role of TERRA in the regulation of telomere length, Int. J. Biol. Sci. 11 (3) (2015) 316–323, https://doi.org/10.7150/ijbs.10528.
[64] C. Wang, L. Zhao, S. Lü, Role of terra in the regulation of telomere length, Int. J. Biol. Sci. 11 (3) (2015) 316–323, https://doi.org/10.7150/ijbs.10528.
[65] J. Wang, Q. Liu, Y. Shyr, Dysregulated transcription across diverse cancer types reveals the importance of rna-binding protein in carcinogenesis, BMC Genom. 16 (S7) (2015), https://doi.org/10.1186/1471-2164-16-s7-s5.
[66] T. Wang, G. Wang, D. Hao, X. Liu, D. Wang, N. Ning, X. Li, Aberrant regulation of the lin28a/lin28b and let-7 loop in human malignant tumors and its effects on the hallmarks of cancer, Mol. Cancer 14 (1) (2015), https://doi.org/10.1186/s12943-015-0402-5.
[67] Z. Yang, L. Lan, X. Wu, L. Xu, M. Buechner, Rna-binding proteins msi-1 (musashi) and exc-7 (hur) regulate serotonin-mediated behaviors inc, elegans (2019), https://doi.org/10.1101/748509.
[68] Z. Yang, Z. Zhou, R. Wei, X. Chu, H. Zhang, T. Fan, J. He, The rna-binding protein pcbp1 represses lung adenocarcinoma progression by stabilizing dkk1 mrna and subsequently downregulating β-catenin, J. Transl. Med. 20 (1) (2022), https://doi.org/10.1186/s12967-022-03552-y.
[69] Y. Yao, X. Li, W. Chen, H. Liu, L. Mi, D. Ren, A. Mo, P. Lu, ATM promotes RAD51-mediated meiotic DSB repair by inter-sister-chromatid recombination in arabidopsis, Front. Plant Sci. 11 (2020) 839, https://doi.org/10.3389/fpls.2020.00839.
[70] C. Yi, C. He, DNA repair by reversal of DNA damage, Cold Spring Harb. Perspect. Biol. 5 (1) (2013) a012575, https://doi.org/10.1101/cshperspect.a012575.
[71] S. Zhang, X. Yang, M. Jiang, L. Ma, J. Hu, H. Zhang, Post-transcriptional control by rna-binding proteins in diabetes and its related complications, Front. Physiol. 13 (2022), https://doi.org/10.3389/fphys.2022.953880.
[72] C. Zhou, Unraveling the role of rna-binding proteins, with a focus on rps5, in the malignant progression of hepatocellular carcinoma, Int. J. Mol. Sci. 25 (2) (2024) 773, https://doi.org/10.3390/ijms25020773.
[73] Zhou, H. (2022). Design of bifunctional antisense oligonucleotides for exon inclusion., 53–62. ⟨https://doi.org/10.1007/978–1-0716–2010-6_3⟩.
[74] Z. Zhu, A. He, L. Lin, C. Xu, T. Cai, L. Jian, Biological functions and prognostic value of rna binding proteins in clear cell renal cell carcinoma, J. Cancer 11 (22) (2020) 6591–6600, https://doi.org/10.7150/jca.49175.