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REVIEW ARTICLE

Dysregulation of Protein Synthesis and its Implications for CNS Disorders: Detection Methods, Diseases and Therapy an Update

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ABSTRACT

Protein translation is central to gene expression in the central nervous system (CNS) because it is the crucial process of converting messenger RNA (mRNA) into functional proteins, which are vital for the structure, function, and regulation of neurons and their circuits. Regulation of protein synthesis involves posttranscriptional modifications and coordination between transcription and mRNA turnover to enable rapid signaling and gene expression changes in cells of CNS. This process is highly regulated and essential for key CNS functions such as synaptic plasticity, learning, and memory. Impaired translation is linked to several CNS disorders. The present review covers basic areas of gene-regulation and deregulation to highlight the unique features of the mechanism and their relevance to CNS. Further, it updates on the current methods of detection, and CNS disorders with details of the mechanisms and proteins, pathways involved in brief. Finally, the potential of targeting the proteins and intermediates of the mechanism as therapeutic targets is discussed. In the post-Human genome sequencing era CNS disorders are implicated as major source of Human disorders. Novel methods to treat these disorders are need of the hour, thus the detail study of protein synthesis at all levels would enable positive leads towards this direction. The present review is a brief update of the current literature in this important area of biomedical research.

KEYWORDS

• Ribosome Profiling • Aminoacyl-tRNA Synthetases (ARSs) • Repeat-Associated Non-Aug (Ran) Translation

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INTRODUCTION

Although historically research has focused on transcription as the central governor of protein expression, protein translation is now increasingly being recognized as a major factor for determining protein levels within eukaryotic cells. The central nervous system (CNS) relies on efficient updating of the protein landscape for maintaining several functions. Deregulated translation can lead to aberrant protein synthesis, altered cellular functions, and disease progression. Increasing evidence suggests that impaired mRNA translation is a common feature found in numerous CNS disorders. In this review, we discuss malfunctions of translation and their contributions to development of diseases. We explore the key mechanisms contributing to the deregulation of protein translation, including functional alterations in translation factors, tRNA, mRNA, and ribosome function. Advances in detection methods are discussed. Abnormal protein synthesis leads to protein expression, disrupted cellular signaling, and perturbed cellular functions these are discussed with reference to CNS disorders. Advancements in understanding the molecular mechanisms of protein translation deregulation, coupled with the development of targeted therapies, could offer promising avenues for improving disease outcomes in various human diseases like CNS disorders which form major burden of diseases globally.

BASICS OF GENE-REGULATION AND CONTROL OF TRANSLATION

In the following paragraphs gene-regulation through transcript and translation is described in brief to highlight the major event protein and modifications to provide a background of the mechanism and its regulation. The paragraph uses chapters from books Bruce Alberts *et al.,* 2020 and De Robertis 2020 as a source.

An mRNA is exported from the nucleus after transcription, splicing, capping, and polyadenylation. The ribosome in the cytoplasm then uses the mRNA to translate its encoded information into a polypeptide chain. An mRNA is chosen for translation by a complicated process, and the effectiveness of each mRNA's recruitment is determined by a number of regulatory elements found inside the mRNA. The polyA tail at the 3 end of an mRNA and the cap structure at the 5 end are especially significant in this context. Other components include the poly-adenosine-binding protein (PABP) and the cap-binding protein eukaryotic initiation factor 4E (eIF4E), respectively, and allow the circularization of the mRNA by binding to eIF4G.

EIF4G functions as a scaffold protein, with additional binding sites for the ATP-dependent RNA helicase eIF4A and eIF3, which binds to the 40S ribosomal subunit. Next the 40S ribosome subunit is be loaded with the initiator methionine-tRNA (tRNAiMet) aided by eIF2, which binds tRNAiMet and GTP. This 'ternary complex' is subsequently delivered to the pre-initiation complex, which consists of the 40S ribosomal subunit, eIF3, and eIF1A, resulting in the 43S pre-initiation complex. This complex is attracted to the mRNA by eIF3 and eIF4G, resulting in the 48S initiation complex. The GTP bound by eIF2 is subsequently hydrolyzed to GDP, releasing eIF2 and requiring replenishment with GTP for successive rounds of initiation, which is carried out by the GTP exchange factor eIF2B. The 40S ribosomal subunit then scans the mRNA in a 5 to 3 direction until it finds an AUG start codon in the appropriate context. Finally the binding of the 60S ribosomal subunit and elongation of the polypeptide chain occurs. Figure 1 is an illustration of protein synthesis steps and machinery.

Translation of protein synthesis is regulated globally by two main mechanisms: interruption of the closed loop containing mRNA, eIF4F complex, eIF4B, and PABP, or decreased ternary complex formation (Olga *et al.,* 2020). The first is accomplished through a collection of inhibitor proteins that compete with eIF4G for a binding site on eIF4E, inhibiting this essential interaction. This set of eIF4E-binding proteins, known as 4E-BP1, 4E-BP2, and 4E-BP3, is phosphorylated in a pathway downstream of the mammalian target of rapamycin' (mTOR) kinase (Böhm, *et al.,* 2021). Signaling via mTOR causes the phosphorylation of 4E BPs, rendering them unable to bind eIF4E and allowing it to engage with eIF4G. In the second mechanism of global control four eIF2α-kinases (GCN2, PERK, HRI, and PKR) phosphorylate the eIF2 α subunit on serine during cellular stress, such as amino acid deprivation, viral infection, hypoxia, and DNA damage (Ryoo *et al.,* 2024; Llabata, *et al.,* 2019). Phosphorylation of serine increases the protein's affinity for eIF2B, preventing it from

carrying out guanosine nucleotide exchange with other eIF2 molecules. This reduces the amounts of ternary complexes and overall translational inhibition. In addition to these global translation mechanisms, there are several mRNA-specific mechanisms at action. The majority of examples of message-specific regulation rely on sequence elements that may or may not be organized inside the 5 and 3UTRs. IRESs, uORFs, and miR-binding sites are examples of such structures, which can act individually or in combination (Leppek *et al.,* 2018; Nandagopal and Roux 2015; Somers *et al.,* 2013).

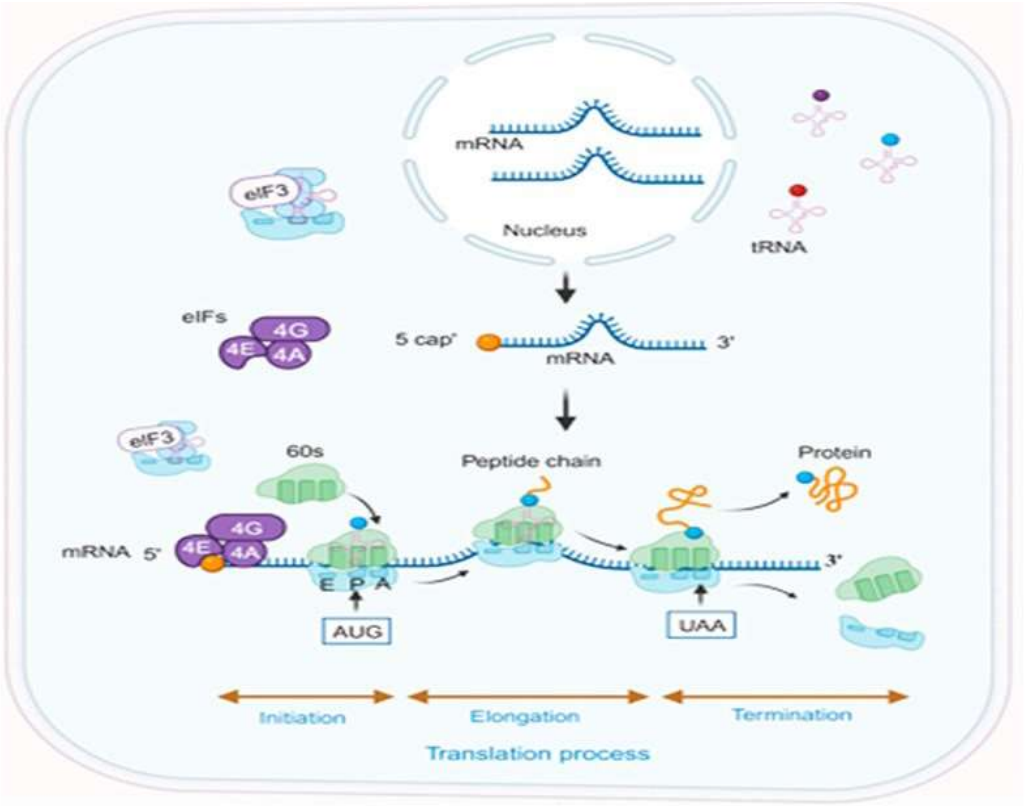

Figure 1: Overview illustrating various steps and machinery of protein synthesis

Deregulation mechanisms

These regulatory mechanisms could vary based on cellular stress, developmental stage, viral infections, and other situations due to their distinct combination and interaction (Endres *et al.,* 2015; Dong *et al.*, 2015; Gao *et al.,* 2025). In the 5′ UTR, m6A modification can enhance translation independently of 5′ cap-binding proteins, especially in response to physiological stress. Selective suppression of adenosine methylation lowers the translation efficiency of mRNAs with m6A in their 5′ UTRs. When cells are subjected to heat shock, higher levels of m6A in Hsp70 mRNA govern cap-independent translation (Meyer *et al.,* 2015). In eIF3d-mediated translation initiation, eIF3d, an eIF3 complex subunit, possesses cap-binding ability, allowing it to detect the mRNA cap structure (Lee *et al.,* 2016). IRES-mediated translation initiation is a mechanism that allows some mRNA molecules, commonly found in viruses, to start protein synthesis within a eukaryotic cell without using the typical cap-dependent translation initiation (Yang, *et al.,* 2019). This allows for the quick commencement of protein synthesis, which enables viruses to hijack cellular translation machinery and generate their own proteins inside host cells. Ribosome shunting initiation is frequently reported in plant viruses (Bamford and Mark Zuckerman 2021). Protein expression dysregulation, post-translational changes, and mutations of initiation-related proteins typically block the translation initiation process (Song, *et al.,* 2020). Deregulation of tRNA, such as changes in tRNA expression, modifications, aminoacylation, splicing, and maturation, can all lead to cellular malfunction and diseases (Orellana *et al.,* 2024). Abnormal expression or mutations of rRNA

and ribosomal proteins in the ribosome result in abnormal ribosome biogenesis, affecting several ribosome functions and limiting translation (Turi, *et al.,* 2019). Finally, short RNA molecules target certain mRNAs, such as eIFs, splicing factors, and upstream regulators, influencing their secondary structure and expression (Georgakopoulos-Soares, *et al.*, 2022). Also, miRNAs can prevent or enhance the degradation of target mRNAs by binding to their 3′ or 5′ untranslated regions (O'Brien, *et al.,* 2018).

Elongation dynamics can be influenced by a variety of environmental or cellular stressors, including oxidative stress, thermal shock, food shortage, and viral infections (Barros *et al.,* 2023; Guzikowski, *et al.,* 2022; Shcherbik and Pestov *et al.,* 2019). Deregulation of elongation, the mechanism by which ribosomes move along mRNA during protein synthesis, has a substantial impact on translation efficiency, fidelity, and protein creation. eEFs can interfere with proper function, resulting in elongation faults (Rodnina. *et al.,* 2016). Impaired eEF2 activity could cause diminished ribosome translocation, resulting in slower translation rates and possibly altering protein folding, localization, or function. Deregulation of alternative mRNA splicing results in aberrant protein isoforms that disrupt EEF1B2 production, facilitating disease development in eukaryotes (Peng, *et al.,* 2021). Errors in aminoacyl-tRNA selection and the incorporation of incorrect amino acids into the developing polypeptide chain result in faulty or non-functional proteins that contribute to cell malfunction or disease states. In addition, tRNA mutations have been linked to ribosomal stalling, premature polypeptide release, and neurodegeneration. Ribosome stalling can be caused by mRNA secondary structures, codon repetitions, uncommon codons, mRNA damage, or a lack of particular eEF availability (Ou, *et al.,* 2019).

Deregulation of termination, the final stage of protein synthesis, has a profound impact on translation fidelity and functional protein output. Abnormal termination is caused by a dysregulated read-through of the termination codon, as well as changes in the 3′ UTR of mRNA, the ribosome, and termination factor modifications (Pandit, *et al.,* 2023; Embree, *et al.,* 2022). Translation is bypassed and continues beyond the stop codon. This process, known as PTC read-through or nonsense suppression, can be caused by a number of variables, including specific genetic mutations, ribosomal context, and the existence of suppressor tRNAs (Lejeune *et al.,* 2017; Dabrowski, *et al.,* 2015). Changes in regulatory elements within the 3′ UTR of mRNA can affect translation termination efficiency, resulting in deregulated termination, abnormal protein synthesis, or changed protein levels (Cridge *et al.,* 2015). Alterations in the modification patterns of termination factors may impact their functions and subsequently affect termination efficiency and fidelity (Agris, *et al.,* 2017). Thus various machinery of the translation could be dysregulated through extrinsic and intrinsic factors could lead to a spectrum of CNS diseases.

Table 1: Brief list of proteins involved in eukaryotic protein translation

S. no	Protein involved in protein translation	Function/role	Reference
1	Eukaryotic initiation factors (eIFs)	Stabilize the formation of ribosomal preinitiation complexes around the start codon and are an important input for post-transcription gene regulation.	Jackson RJ, 2010
2	Eukaryotic release factors (eRF1)	Essential protein involved in stop codon recognition in translation, termination of translation.	Song *et al.,* 2000
3	Cap-binding protein (eukaryotic initiation factor 4E (eIF4E))	A type of RNA-binding protein that specifically recognizes and binds to the 5′ m7G cap structure of messenger RNA (mRNA).	Pelletier J, *et al.,* 1991
4	DEAD-box helicase	ATP-dependent protein that unwinds RNA, playing a central role in translation.	*Linder et al., 1989*
5	PERK kinase	Regulates translation by phosphorylating the eIF2α subunit of the eukaryotic initiation factor 2 (eIF2).	*Shi Y et al.,1998*
6	mTOR	The protein is a key regulator of translation, influencing both general and specific mRNA translation.	Mitra *et al.,* 2015
7	Peptidyl-tRNA hydrolase (Pth)	Essential enzyme that cleaves the ester bond linking the peptide to the tRNA.	Tomasi *et al.,* 2023
8	Peptidyl transferase	Facilitates the aminolysis reaction that joins amino acids during protein synthesis.	Tirumalai *et al.,* 2021

METHODS OF PROTEIN TRANSLATION ANALYSIS

The following paragraph compiles few methods of protein translation, describing the protocol involved brief and their applications.

Polysome Profiling

One or more ribosomes recruit identical mRNA, and the translation rate is restricted by the start rate. Thus, ribosome density on a certain mRNA indicates translational state. Polysome profiling is a technique from the 1960s that uses sucrose density gradient ultracentrifugation and fractionation (Drysdale and Munro, 1967). mRNAs attached to different numbers of ribosomes can be separated using centrifugation (King and Gerber, 2016). Polysomes and monosomes are frequently separated using a normal linear sucrose gradient (typically 50% sucrose) produced by a gradient maker. Gradients are separated into fractions, some of which contain translating mRNAs coupled with polysomes and monosomes, as well as the supernatant containing free mRNAs, 60S and 40S ribosomal subunits. The height of polysome peaks of the curve and the area under each peak indicate ribosome translational activity. Northern blot, RT qPCR, as well as the high-throughput microarray or RNA-seq approaches are then used to identify mRNAs in the separated components. Initiation inhibition causes ribosome "runoff," leading to decomposition of polysome and elevated levels of free ribosomal subunits. Elongation inhibition enhances polysomalsize (Liang *et al.,* 2018).

Ribosome Profiling

Ribosome profiling involves treating the ribosome-nascent peptide chain complex with nuclease to delete mRNA portions that are not occupied by ribosomes (Ingolia *et al.,* 2009). Ribosome-protected fractions (RPFs) are then obtained using sucrose density gradient centrifugation or immunopurification of ribo-tag cells (Ingolia *et al.,* 2012). Following ribosome and rRNA removal, high-throughput sequencing is employed to detect small, ribosome-protected RNA fragments ranging from 21 to 28 bp. This strategy has several advantages. High-resolution ribosome footprints (RFs) enable genome-wide investigation of translation with codon resolution and can reveal: (i) translational efficiency of all individual mRNAs as computed by ribosome profiling combined with RNA-seq; (ii) detect rare and subtle translation events (iii) uncover rich and precise ribosome positional information, such as translation initiation at non-AUG codons, identify upstream ORFs (uORFs) translation, elucidate codon usage bias and ribosome pausing(Juntawong *et al.,* 2013).

TRAP-Seq

Inada *et al.* (2002) demonstrated ribosome affinity purification sequencing (TRAP-seq) using tagged ribosomal proteins. Using animals or cells in which activated cre-recombinase under a cell-specific promoter drives expression of an affinity tag (such as His, Avi, or GFP) fused to the large ribosomal subunit, RNC-mRNAs of a specific cell type can be isolated by affinity purification with corresponding anti-tag beads. This strategy is constrained by the necessity to create stably transfected cell lines or transgenic animals for each cell type. Also, the approach may be biased by the fact that some ribosomal proteins, notably RPL10a, selectively translate only specific mRNAs (Xue and Barna, 2012), and extra ribosomal mRNAs.

Mass spectrometry

Mass spectrometry proteomics has emerged as a powerful tool for investigating dynamic changes in protein translation and identifying key players. By pulse labeling nascent peptide chains with heavy amino acid isotopes (SILAC) or click-reactive amino acids/puromycin, mass spectrometry approaches can assess protein dynamics such as degradation and synthesis (Ross, *et al.,* 2021). Quantitative proteomics with mass spectrometry can compare overall protein levels between healthy and diseased cells/tissues, revealing which proteins are over/under produced due to defects in translation (Jiang, *et al.,* 2024).

Other recent methods

In recent years, mRNA sequencing is a powerful technique for profiling the transcriptome and has emerged as a valuable tool for investigating protein translation deregulation. The method aids detection of mutations in the Kozack sequence and enables identification of the 5′ UTRs of eukaryotic mRNAs (Tsimberidou, *et al.,* 2022). Single-cell ribosome sequencing (scRibo seq) combines nuclease foot-printing, small-RNA

library construction and size enrichment to measure translation dynamics in individual cells (Michael VanInsberghe *et al.,* 2021). The method provides valuable information about protein translation dynamics during cellular differentiation, cell-to-cell heterogeneity in gene expression thus revealing defects in subpopulations of cells.

CNS disorders

Neurological tissues are sensitive to perturbations in the control of protein synthesis because CNS neurons are demanding in metabolism, and shortcomings in translation that are tolerated in other cell types become limiting in neurons (Zhou and Bian 2024). However, synapse and at the ends of long axons (dendrites) protein synthesis is localized and control neurotransmission. Translational mechanisms are efficient in controlling translation in situ and transport of mRNAs to the extremities of dendrites and axons, over long distances to meet short-term changes in local protein requirements (Das *et al.,* 2021). Brain enables experience-dependent cognition in humans and synaptic transmission is a key component of this physiological phenomenon. Changes in synaptic strength are controlled in part by rapid local translation of mRNAs at synaptic clefts (Rajgor *et al.,* 2021). Figure-2 is an illustration of context specific protein translation in the neuron. Impaired local translation regulation is to central feature in the mechanisms underlying CNS disorders. In the following paragraph CNS disorders caused due to protein translation is described briefly. The table-2 summarizes few CNS disorders and the gene and gene functions briefly.

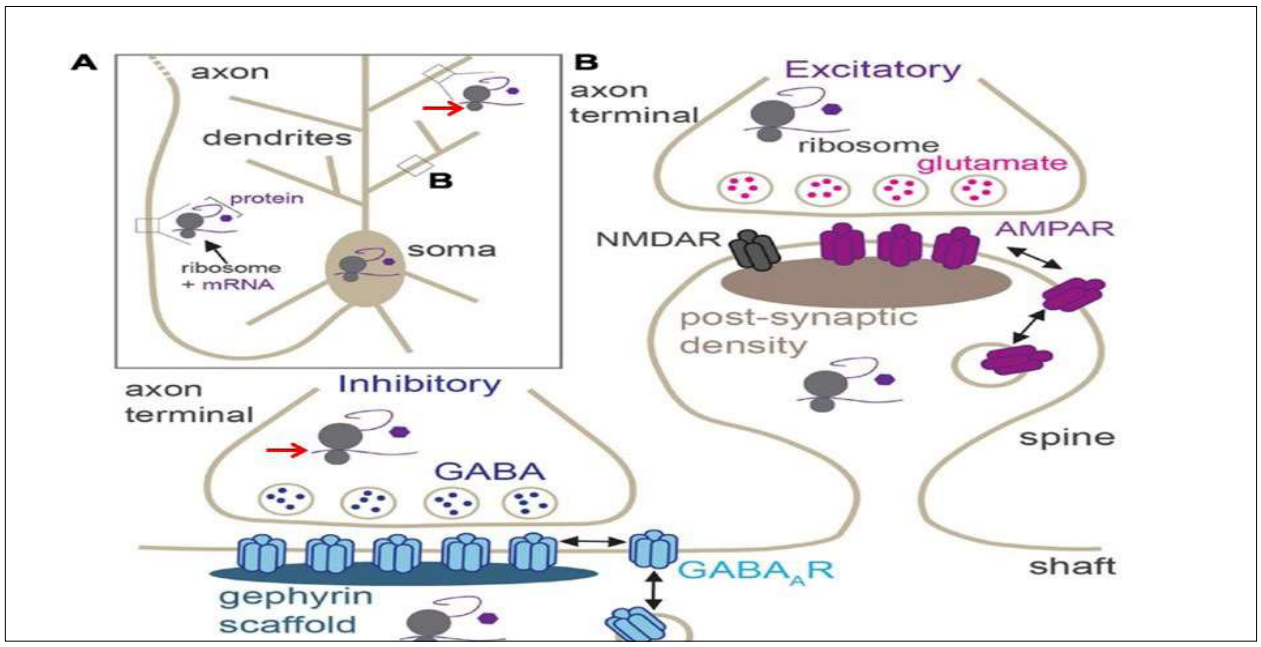

Figure 2: Illustration of protein translation at various sites in a Neuron and context dependent protein sysnthesis (Excitatory Neutransmission). Arrow head-protein synthesis

Table 2: CNS disorders of protein translation

Sl. no	Disorder	Gene	Function/cellular roles	Reference
1	ALS/FTD	*TDP-43*	Abnormal traffickingof futsch/Map1b mRNAs to neurites leading to cytoskeleton defects	Gamarra *et al.*, 2021.
2	SMA	*SMN*	Mislocalization altering neurite growth,	
3	AD	*Mapt*	Hyperphosphorylation	
4	PD	*LRRK2*	DeregulationofglobaleIF4E/4E-BP. Defectsinaxonal4E-BPdependent translation?	
5	HD	*HTT*	Impaired dendritic levels of Act bmRNA, Ago2proteinandP-bodies	
6	ASD and FXS	*FMRP*	Deregulation of local mRNAs linked to abnormal spine morphology and plasticity	
7	DS	*Dscam*	Upregulation of dendritic mRNA and protein level swith defects in dendrite branching	
8	Depression and bipolar disorder	*Bdnf*	Protein crucial for the survival, growth, and function of neurons.	

Missense mutations in any one of the five subunits of eIF2B, the guanosine nucleotide-exchange factor is responsible for recharging eIF2, can cause vanishing white matter disease (VWM) (Moon *et al.,* 2018). VWM is a leukoencephalopathy with vanishing white matter caused by dysfunctional translational control. The symptoms typically appear following mild infections or head trauma, indicating a role for cell stress (Knaap *et al.,* 2025-Genereviewes). CNS diseases are caused by mutations in aminoacyl-tRNA synthetases (ARSs), the enzymes responsible for loading amino acids onto tRNA molecules, which is a early step in protein synthesis (Meyer-Schuman and Antonellis 2017). Defects in translation elongation are also known to cause neurological symptoms such as epilepsy, microcephaly and ataxias. In Mice lacking eEF1A2 exhibit the 'wasted' phenotype, in which neurodegeneration occurs as eEF1A expression in the brain shifts from isoform 1 to isoform 2 in seizures (Davies *et al.,* 2017). Fragile X Mental Retardation Protein (FMRP) is a RNA-binding protein proposed to play a role in specific translational regulation of the subset of mRNAs with which it interacts (Chen and Joseph 2015). Internal ribosome entry is used to initiate translation in a large number of mRNAs and IRES-mediated translation is involved in a number of neurological disorders such as muscular dystrophies (Marques *et al.,* 2022). The expression of many miRs is restricted to particular areas of the CNS and several studies suggest that miRs are involved in key stages of neurogenesis, survival and synaptic plasticity (Rashidi *et al.,* 2023). In Huntington's disease (HD), miR-9 and miR-9 levels are decreased, and miR-9 has been shown to target the REST transcription silencer (REST) transcription silencer (Dong and Cong 2021). In Alzheimer's disease (AD) MiR-106 levels are decreased and APP is targeted by the miR-20 family miRNA (miR-106) in neuronal cell lines (Wang *et al.,* 2023). SNPs in the miRNA machinery have been associated with major depressive disorder (MDD), including SNPs within pre-miR-30e, AGO1, and DGCR8, the latter being part of the microprocessor complex and a component of miRNA biogenesis (Lopizzo, *et al.,* 2019). mTORC1 has also been linked to schizophrenia (SZ) via the serotonin receptor 5-HT6 (Meffre, *et al.,* 2012). Several lines of evidence suggest that activation of mTORC1 signaling is beneficial for the treatment of MDD (Gururajan and van den Buuse 2014).

Expansions of short nucleotide sequence repeats account for more than 50 neurological or neuromuscular diseases and the pathogenic mechanism among those diseases varies based on repeat sequence, length, and the genetic context (Paulson 2018). A unique phenomenon of the repeat expansion is the non-canonical translation of the repeat-containing RNA, recognized as repeat-associated non-AUG (RAN) translation (Goodman and Bonini 2020). The secondary structures of the expanded RNA repeats are important for the non-canonical translation initiation that does not require the AUG start codon, and sometimes the 5'-cap as well (Kearse and Wilusz 2017). The translation of the RNA repeats in all possible reading frames generates various poly-peptide proteins, which contribute to disease pathogenesis. RAN translation is detected in fragile X-associated tremor/ataxia syndrome (FXTAS) (CGG•CCG), myotonic dystrophy type 2 (CCTG•CAGG), spinocerebellar ataxias type example- SCA31 (TGGAA•TTCCA) (Banez-Coronel and Ranum 2019). Translation defects in Amotrophic lateral sclerosis (ALS) demonstrate that the GGGGCC repeat containing RNA transcripts in the cytoplasm are spliced introns, but not the un-spliced pre-mRNAs (Cheng *et al.,* 2019). Cytoplasmic repeats containing introns mainly exist in circular form, due to the defective debranching of spliced lariat intron induced by the repeat. The repeated RNA has been shown to form both hairpin and G-quadruplex structures (Cammas *et al.* 2016). It is demonstrated that both CAG•CTG and CGG•CCG repeats have a propensity to undergo frameshifting, resulting in the production of frameshifted proteins (Wojciechowska *et al.,* 2014). It has been shown that the translation of CGG repeats located in the 5' UTR of FMR1 requires the 5' 7-methylguanosine (m7G) cap on the mRNA. However, as the spliced circular intron is exported to the cytoplasm, the cap-independent translation initiation is important for C9ORF72 repeat expansion (van 't Spijker, *et al.,* 2023). RNA secondary structure is important for RAN translation, and RNA helicases are also implicated in RAN translation (Georgakopoulos-Soares, *et al.,* 2022).

Protein translation as potential therapeutic target

Emerging and promising therapeutic strategies in various neurological disorders

presently involve the translation regulatory mechanisms. An extensive preclinical model represents eEF2K as an interesting therapeutic target for both AD and PD (Knight *et al.,* 2020). Inhibition in eEF2K rescues cognitive defects in neurological disorders (Wang, *et al.,* 2024). Branaplam a small molecule RNA splicing modulator, is known to promote changes in alternative splicing and stabilize the interaction between the spliceosome unit and SMN 2 Pre-mRNA. Increase in the production of functional SMN protein focused on the splicing of survival motor neuron 2 (SMN2) mRNA towards the pivotal clinical investigation in spinal muscular atrophy (SMA) (Florian Krach *et al.,* 2025). Similarly, Mimosine, a target of eIF3a effects on protein synthesis and cell cycle progression (Dong and Zhang 2003). Everolimus and Temsirolimus are targets of mTOR (Klümpen *et al.,* 2010). Cheng *et al.,* 2018 demonstrate inhibition of PERK and the downstream signaling events of phospho-eIF2α by inhibitors GSK260641 and ISRIB in a cellular model of the hexanucleotide expansion of C9ORF72. Ridaforolimus (Sirolimus), a macrolide and an mTOR inhibitor, showed a positive result in the animal model study (MacKeigan and Krueger 2015). An allosteric inhibitor, rapamycin targets the mTOR complex I, which promote the diffusion of the effect on the cell signaling pathway through serine-threonine kinase. This pathway governs metabolism, growth and proliferation, autophagy and protein synthesis. Other small molecule inhibitors, includes PP242, Torin1, torin2, and PP30, however structurally different to rapamycin and rapalogs and does not rely on FKBP cooperation (Tramutola, A *et al.,* 2017)

Protein kinases regulate diverse cellular functions through the orchestrated propagation and amplification of cellular stimuli into distinct biological responses through coordinated signal transduction cascades. Several kinases are targets for several CNS disorders. Such as the MLK1, MLK2 and MLK3 in PD(Moreno *et al.,* 2023) and PKS–T in Bipolar disorder (Saxena, *et al.,* 2017) and DAPK1 in AD (Xu, *et al.,* 2018). Thus proteins and mechanism in protein translations are potential targets of CNS drugs.

CONCLUSION

De *novo* protein synthesis by the ribosome and its multitude of co-factors must occur in a tightly regulated manner to ensure that the correct proteins are produced spatiotemporally and, in some cases, also in the proper location in eukaryotic cells. Protein synthesis is especially critical to the development, survival, and proper functioning of neurons due to their unique cellular architecture which requires specific spatiotemporal regulation. A key factor in many CNS diseases is the misfolded proteins aggregate into toxic clumps which damage neurons and altered cellular functions. Several recent studies have highlighted the importance of canonical translational control in regulating behaviors associated with neuropsychiatric and mood disorders. Development of novel technologies encompassing diverse areas neuroscience, genomics, bioinformatics and experimental approaches have enabled advances in understanding the molecular mechanism of translation regulation at different steps and at the genome-wide level. Thus this area of cell biology is gaining importance both from basic and clinical researchers.

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