Research article
J. Adv. Nutri. Sci. Technol. 6(1-2):1-8, 2026 **DOI:10.15228/ANST. 2026.v06.i01-2.p01**

RPS14 Haploinsufficiency, Ribosomal Stress, and Nutrient-Dependent Erythropoiesis in 5q Deletion Syndrome

[1]Sarah Usmani & [1]Joshua Guardado*
[1]Department of Biological Sciences, California State University, Long Beach, 1250 Bellflower Blvd, MS 9502, Long Beach, CA 90840-9502, United States of America
Corresponding author email: joshuaguardado76@gmail.com

Abstract
5q deletion syndrome is a subtype of myelodysplastic syndrome (MDS) characterized by macrocytic anemia and impaired erythropoiesis due to the deletion of genes on chromosome 5q. RPS14, a dosage-sensitive regulator of ribosome biogenesis within this region, plays a central role in disease pathogenesis. Reduced RPS14 expression activates p53-mediated ribosomal stress and disrupts erythroid maturation. Because ribosome biogenesis and red blood cell production are metabolically demanding processes requiring adequate micronutrients, particularly iron for hemoglobin synthesis, ribosomal insufficiency may increase susceptibility to metabolic stress. This study integrates PCR-based molecular analysis, genomic annotation, tissue-wide transcriptomic profiling, pathway analysis, and disease-associated datasets to examine RPS14 expression across physiological and hematopoietic contexts. RPS14 is ubiquitously expressed but tightly regulated, with prominent expression in hematopoietic tissues. These findings support a model in which 5q deletion syndrome reflects tissue-specific vulnerability to reduced ribosomal capacity, potentially amplified by micronutrient-dependent erythropoiesis.

Keywords: RPS14, 5q deletion syndrome, myelodysplastic syndrome, ribosome biogenesis

Highlights

- RPS14 haploinsufficiency is a key cause of erythroid failure in 5q deletion syndrome.
- RPS14 is expressed throughout the body, with higher expression in hematopoietic tissues.
- Ribosome biogenesis and erythropoiesis require high energy and adequate iron for hemoglobin synthesis.
- Reduced ribosomal capacity may make red blood cell production more sensitive to iron deficiency.

1. Introduction
5q deletion syndrome is a distinct subtype of myelodysplastic syndrome (MDS) characterized by macrocytic anemia, dysplastic megakaryocytes, and an interstitial deletion on chromosome 5q (Narla & Ebert, 2010). Among the genes within the commonly deleted region, RPS14 has been identified as a critical contributor to disease pathogenesis. RNA interference screening demonstrated that reduced expression of RPS14 recapitulates the erythroid defects observed in 5q− syndrome (Ebert et al., 2008). Subsequent murine models confirmed that RPS14 haploinsufficiency activates p53-dependent stress signaling and produces macrocytic anemia (Barlow et al., 2010).

RPS14 encodes a structural component of the 40S ribosomal subunit and is essential for proper ribosome assembly (Ebert et al., 2008). Ribosome biogenesis is among the most energetically demanding processes in the cell (Warner, 1999). Disruptions in ribosomal protein dosage impair translational capacity and induce cellular stress responses, particularly in rapidly proliferating tissues (Narla & Ebert, 2010).

Erythroid progenitors are especially sensitive to ribosomal perturbations because they require sustained, high-level protein synthesis to support hemoglobin production (Narla & Ebert, 2010). Hemoglobin synthesis is iron-dependent, and erythropoiesis is tightly regulated by systemic nutrient availability (Ganz & Nemeth, 2012). Iron deficiency alone is sufficient to impair red blood cell production (Camaschella, 2015), while vitamin B12 and folate are required for DNA synthesis and erythroid proliferation (O'Leary & Samman, 2010). Thus, effective erythropoiesis depends on coordinated ribosomal function and adequate micronutrient supply.

Although RPS14 haploinsufficiency is well established as a driver of erythroid failure in 5q deletion syndrome (Ebert et al., 2008; Barlow et al., 2010), its broader expression landscape and metabolic context remain less defined. The present study integrates genomic annotation, transcriptomic profiling, pathway analysis, and disease-associated datasets to evaluate RPS14 expression within a framework linking ribosomal genetics to nutrient-dependent hematopoiesis.

2. Materials and Methods
2.1. Study Design and Sample Information
This study integrates a molecular validation component with in silico transcriptomic and pathway-based analyses. Genomic DNA was obtained from n = 2 healthy adult volunteers for the purpose of PCR-based amplification of the RPS14 locus. No patients diagnosed with myelodysplastic syndrome (MDS) were recruited, and no clinical samples representing del(5q) were directly analyzed for deletion status. The experimental polymerase chain reaction (PCR)

component was conducted to establish locus specificity and methodological reproducibility rather than to diagnose chromosomal abnormalities. PCR was performed following established amplification principles (Mullis & Faloona, 1987) with minor changes.

2.2. Ethical Considerations

Samples were collected from adult volunteers following informed consent for educational research purposes. No identifiable personal information was retained. This study did not involve interventional procedures, clinical patient recruitment, or analysis of protected health information. Therefore, formal institutional review board approval was not required.

2.3. Genomic DNA Extraction from Cheek Epithelial Cells

Genomic DNA was isolated from human cheek epithelial cells using the New England Biolabs (NEB) Monarch Genomic DNA Purification Kit (New England Biolabs, Ipswich, MA, USA) according to the manufacturer's protocol with minor adaptations. Prior to sample collection, participants rinsed their mouths with water and refrained from eating or drinking for at least 30 minutes to minimize contamination. All procedures were performed using appropriate personal protective equipment.

Saliva samples were collected directly into sterile 50 mL conical tubes and immediately placed on ice. For each individual sample, 500 µL of saliva was combined with 1000 µL of cold phosphate-buffered saline (PBS) and transferred to a labeled 1.5 mL microcentrifuge tube. Samples were centrifuged at 4200 rpm for 1 minute to pellet epithelial cells. The supernatant was carefully decanted into a bleach waste container, and the pellet was resuspended in 1000 µL of PBS. This wash step was repeated twice to remove residual contaminants and concentrate the cellular material.

Following the final wash, the supernatant was discarded, leaving approximately 100 µL of residual volume. Protein digestion was performed by adding 10 µL of Proteinase K and RNase A to each sample, followed by gentle inversion to ensure uniform mixing. Subsequently, 100 µL of cell lysis buffer containing guanidine hydrochloride was added, and samples were incubated at 56°C for 30 minutes. During incubation, samples were gently mixed every 5 minutes to promote complete lysis and enzymatic activity.

After incubation, 400 µL of genomic DNA binding buffer was added to each lysate, mixed thoroughly by vortexing, and 600 µL of the mixture was transferred to a silica-based purification column placed in a collection tube. Columns were centrifuged at 4200 rpm for 3 minutes, allowing genomic DNA to bind to the column matrix. The flow-through was discarded.

The bound DNA was washed twice by adding 500 µL of genomic DNA wash buffer to the column, followed by centrifugation at maximum speed for 1 minute per wash. After the final wash, columns were transferred to DNase-free 1.5 mL microcentrifuge tubes. DNA was eluted by adding 100 µL of preheated elution buffer (Tris-EDTA), incubating at room temperature for 1 minute, and centrifuging at maximum speed for 1 minute. Purified genomic DNA was stored at 4°C until downstream analysis.

2.4 Primer Preparation and PCR Amplification of RPS14

Forward and reverse primers targeting a defined region of the RPS14 gene were prepared by combining 90 µL of DNase-free water with 5 µL each of forward and reverse primer stocks in a 1.5 mL microcentrifuge tube. The primer working solution was mixed thoroughly and briefly centrifuged. Polymerase chain reaction (PCR) was performed using genomic DNA extracted from cheek cell samples. For each reaction, 1 µL of genomic DNA was added to PCR tubes. Non-template control (NTC) reactions were prepared by adding 1 µL of DNase-free water in place of DNA to monitor contamination.

A master mix was prepared containing DNase-free water, 10× PCR buffer, dNTPs, and primer working stock. Taq DNA polymerase was added last to minimize enzyme degradation. A total of 19 µL of master mix was aliquoted into each PCR tube, resulting in a final reaction volume of 20 µL. PCR amplification was carried out under the following thermal cycling conditions: initial denaturation at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 30 seconds, primer annealing at 57°C for 39 seconds, and extension at 72°C for 1 minute. A final extension step was performed at 72°C for 5 minutes, followed by a hold at 20°C. PCR products were stored at 4°C until analysis.

2.5. Agarose Gel Electrophoresis

PCR products were analyzed by agarose gel electrophoresis to verify amplification specificity and product size. A 2.5% agarose gel was prepared using 0.5× Tris-borate-EDTA (TBE) buffer. Prior to loading, 4 µL of 6× loading dye was added to each PCR reaction. For each sample, 8 µL of the PCR loading dye mixture was loaded into individual wells, along with a DNA ladder for size estimation.

Electrophoresis was conducted at 100–107 V for approximately 45 minutes. Following electrophoresis, gels were stained in a solution containing ethidium bromide for 15 minutes and visualized under ultraviolet (UV) illumination. Successful amplification of the RPS14 target region was confirmed by the presence of a single, sharp DNA band at the expected

amplicon size in all experimental samples, while no amplification was detected in non-template control lanes, indicating high reaction specificity and absence of detectable contamination.

2.6 Transcriptomic and Tissue Expression Analysis

RPS14 protein and transcript expression data were obtained from publicly available genomic resources, including Ensembl and the Genotype-Tissue Expression (GTEx) database. Normalized RNA expression values were evaluated across hematopoietic and non-hematopoietic tissues, with emphasis on whole blood, spleen, and lymphoid-derived samples. Analyses focused on the distribution of relative expression and population-level stability.

2.7 Pathway Mapping

Functional localization of RPS14 within the human ribosome was assessed using the KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway hsa03010 (Ribosome). Positioning within the 40S small ribosomal subunit was examined to contextualize its role in ribosome assembly and translational initiation.

2.8 Disease-Associated Expression Datasets

RPS14 transcript levels were analyzed in publicly available gene expression datasets derived from bone marrow mesenchymal stromal cells of myelodysplastic syndrome (MDS) subtypes and healthy controls. Normalized expression values were extracted and grouped according to diagnostic category (Control, RCMD, RAEB). Comparative analysis assessed subtype-specific differences in ribosomal gene expression within the bone marrow microenvironment.

2.9 Statistical Analysis

Statistical analyses were performed using non-parametric methods due to small sample sizes. Group differences in RPS14 expression across Control, RCMD, and RAEB samples were evaluated using the Kruskal–Wallis test. Planned pairwise comparisons between diagnostic groups were conducted using two-tailed Mann–Whitney U tests. Effect size was calculated using the rank-biserial correlation. Statistical significance was defined as $p < 0.05$.

Analyses of GTEx and Ensembl tissue datasets were descriptive and based on reported normalized expression values.

3. Results and Discussion

3.1 Molecular Amplification of the RPS14 Locus

Targeted PCR amplification was performed using gene-specific primers designed from Ensembl reference sequences. Genomic DNA isolated from cheek epithelial cells produced amplicons of the expected size on agarose gel electrophoresis, confirming amplification of the RPS14 locus. Conventional PCR confirms the presence of a locus but does not detect chromosomal deletions, quantify gene dosage, or assess haploinsufficiency. No quantitative PCR, copy number variation analysis, or functional erythroid assays were performed. Therefore, this molecular analysis serves as technical validation of the RPS14 genomic region and does not directly assess deletion status in 5q− myelodysplastic syndrome (Ebert et al., 2008).

RPS14 encodes a structural component of the 40S ribosomal subunit and is required for proper ribosome assembly (Warner, 1999). Even partial reductions in gene dosage may impair translational efficiency and activate p53-mediated stress pathways (Ebert et al., 2008; Barlow et al., 2010). Because ribosome biogenesis is metabolically demanding and tightly linked to erythropoiesis, this framework supports investigation of how ribosomal insufficiency may interact with micronutrient availability.

3.2 Tissue-Level Distribution of RPS14 Expression

Protein expression data from Ensembl demonstrate that RPS14 is broadly expressed across human tissues, with elevated levels in the spleen, small intestine, forebrain, and pulmonary artery (Fig. 1).

The spleen plays a central role in erythrocyte turnover and iron recycling, while the small intestine is the primary site of dietary iron absorption (Camaschella, 2015). These findings indicate that RPS14 is active in metabolically and hematologically relevant tissues, consistent with its essential function in ribosome assembly and protein synthesis (Warner, 1999).

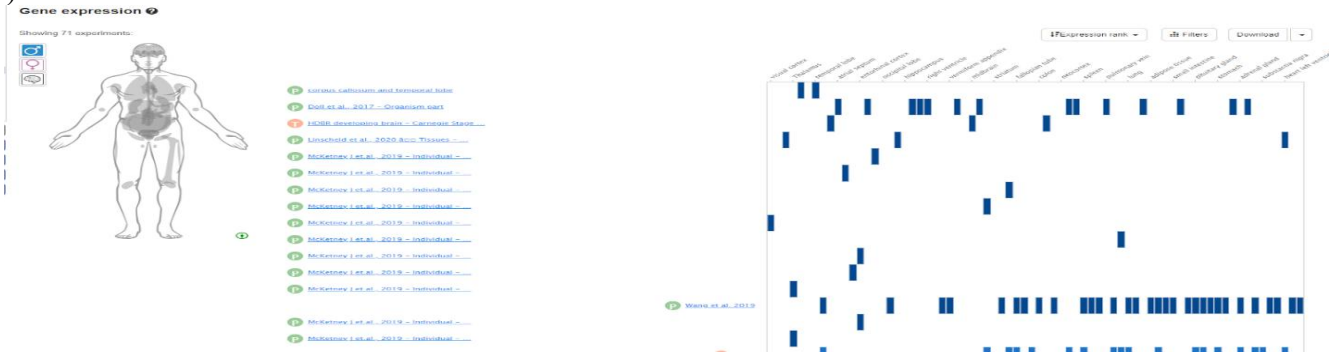

Figure 1: Tissue-specific expression of RPS14 protein across human tissues (RPS14 Gene Expression Ensembl).

Protein expression data from Ensembl show that RPS14 is expressed across multiple human tissues, with particularly high levels in the small intestine and the pulmonary artery. The small intestine is the primary site of dietary iron absorption (Camaschella, 2015), while systemic circulation supports oxygen transport. These findings indicate that RPS14 is active in tissues involved in nutrient handling and metabolic regulation.

3.3 Ribosomal Pathway Integration

KEGG pathway mapping localized RPS14 to the 40S small ribosomal subunit within the canonical human ribosome pathway (hsa03010) (Fig. 2). RPS14 functions as a structural ribosomal protein required for 40S maturation and translational initiation (Warner, 1999). Reduced RPS14 dosage impairs ribosome biogenesis and activates p53-dependent stress signaling, contributing to erythroid failure in 5q deletion syndrome (Ebert et al., 2008; Barlow et al., 2010). Because erythropoiesis requires sustained hemoglobin synthesis and rapid cellular proliferation, reduced translational capacity may increase vulnerability to metabolic or micronutrient limitation.

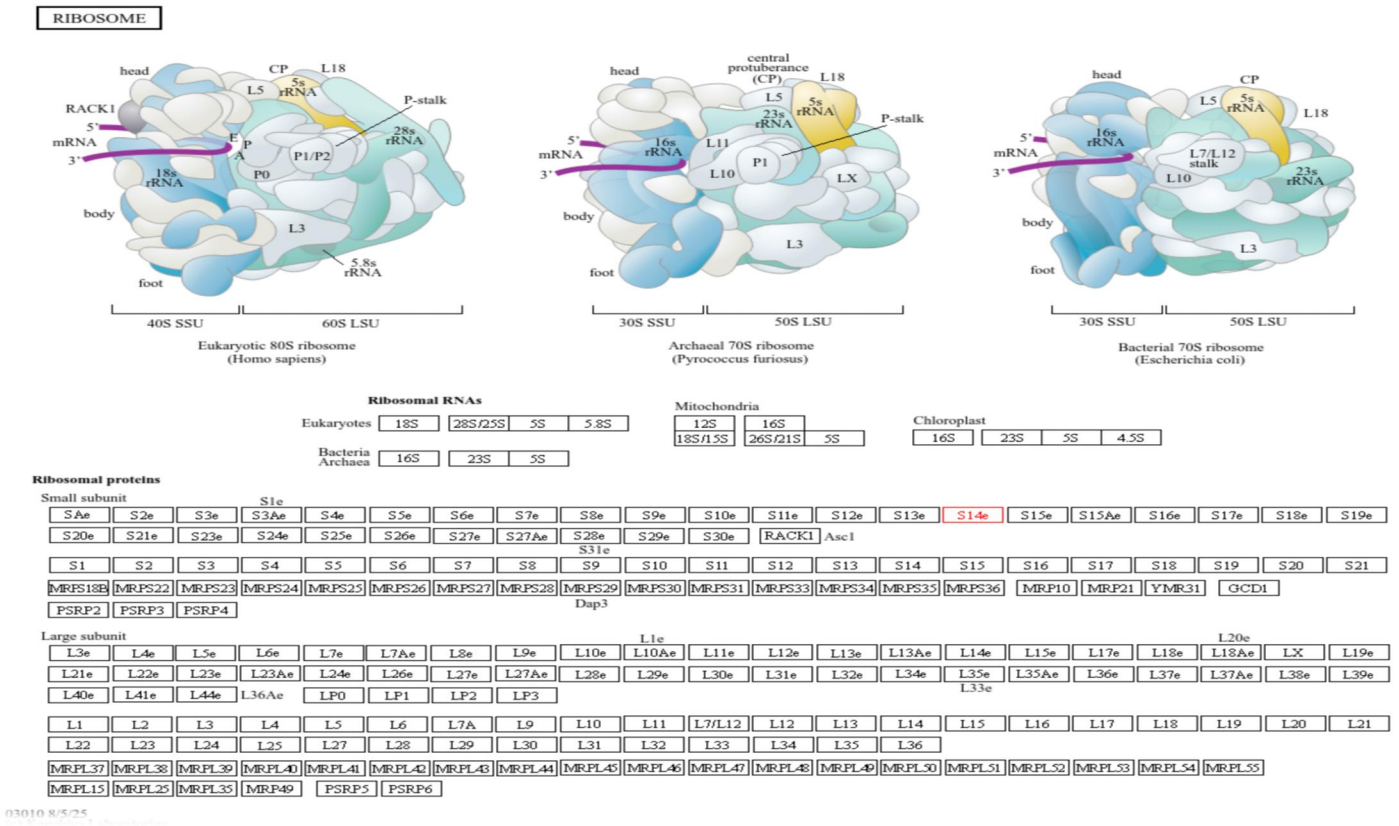

Figure 2: Localization of RPS14 within the human ribosome pathway (KEGG hsa03010).

KEGG pathway mapping identifies RPS14 as a structural component of the 40S small ribosomal subunit. RPS14 is required for ribosome assembly and translational initiation (Warner, 1999). Reduced expression impairs 40S maturation and activates p53-dependent stress signaling, contributing to erythroid defects in 5q deletion syndrome (Ebert et al., 2008; Barlow et al., 2010).

3.4 Differential Expression in Myelodysplastic Syndromes

Analysis of publicly available Gene Expression Omnibus datasets revealed differential RPS14 expression across myelodysplastic syndrome (MDS) subtypes compared with healthy bone marrow controls (Fig. 3).

RPS14 expression was elevated in refractory cytopenia with multilineage dysplasia (RCMD) bone marrow mesenchymal stromal cells compared with controls (mean ± SD: 11,536 ± 1,360 vs 8,642 ± 880; ~1.33-fold increase). In contrast, refractory anemia with excess blasts (RAEB) samples showed high inter-sample variability (9,068 ± 2,550) without a consistent directional change.

Group differences were assessed using the Kruskal–Wallis test, which did not reveal a significant overall effect ($H(2) = 3.81$, $p = 0.15$). Planned pairwise comparisons using two-tailed Mann–Whitney U testing revealed significantly increased RPS14 expression in RCMD samples relative to healthy controls ($U = 1$, $p = 0.03$). The effect size was large (rank-biserial correlation = 0.91). No significant difference was observed between RAEB samples and controls ($U = 13.5$, $p = 0.70$).

Ribosomal protein dysregulation is a recognized feature of 5q deletion–associated MDS and contributes to ineffective erythropoiesis by activating p53 (Ebert et al., 2008; Barlow et al., 2010). Because MDS is frequently accompanied by

altered iron handling and transfusion-associated iron overload, these findings support a model in which ribosomal dysfunction and nutrient imbalance may interact to influence erythropoietic outcomes.

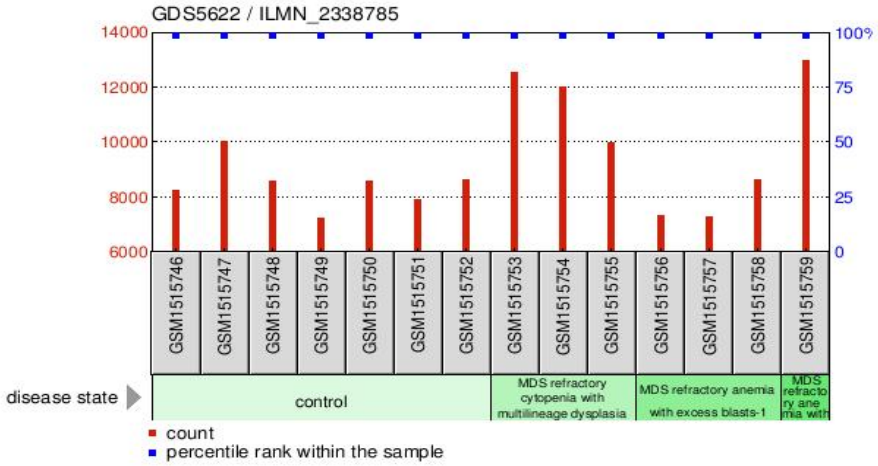

Figure 3: Differential RPS14 expression in bone marrow mesenchymal stromal cells from myelodysplastic syndrome (MDS) subtypes compared with healthy controls (MDS: Bone Marrow Mesenchymal Stromal Cells**).**

Normalized transcriptomic data obtained from publicly available Gene Expression Omnibus datasets demonstrate increased RPS14 expression in refractory cytopenia with multilineage dysplasia (RCMD; n = 3) relative to healthy controls (n = 7), with an approximate 1.3-fold elevation. Refractory anemia with excess blasts (RAEB; n = 4) exhibited greater inter-sample variability and no consistent directional change compared with controls. Statistical analysis was performed using Kruskal–Wallis testing followed by planned Mann–Whitney U comparisons. Exact p-values are reported. The effect size was calculated using rank-biserial correlation. These findings support subtype-specific alterations in ribosomal gene regulation within the bone marrow microenvironment. Ribosomal protein dysregulation is a recognized mechanism in 5q deletion–associated myelodysplastic syndromes and contributes to impaired erythropoiesis (Ebert et al., 2008; Barlow et al., 2010).

3.5 Population-Scale Expression in Hematopoietic Tissues

Analysis of GTEx RNA-sequencing data demonstrated robust RPS14 expression in hematopoietic-related tissues, including whole blood (n = 755), spleen (n = 241), and EBV-transformed lymphocytes (n = 174) (Fig. 4). Stable expression across large cohorts supports the fundamental and ubiquitous role of RPS14 in ribosomal biology and hematopoietic maintenance (Warner, 1999). Together, molecular validation, pathway localization, disease-associated dysregulation, and population-scale expression support a model in which RPS14 is broadly expressed but tightly regulated, and its perturbation may intersect with nutrient-dependent erythropoiesis.

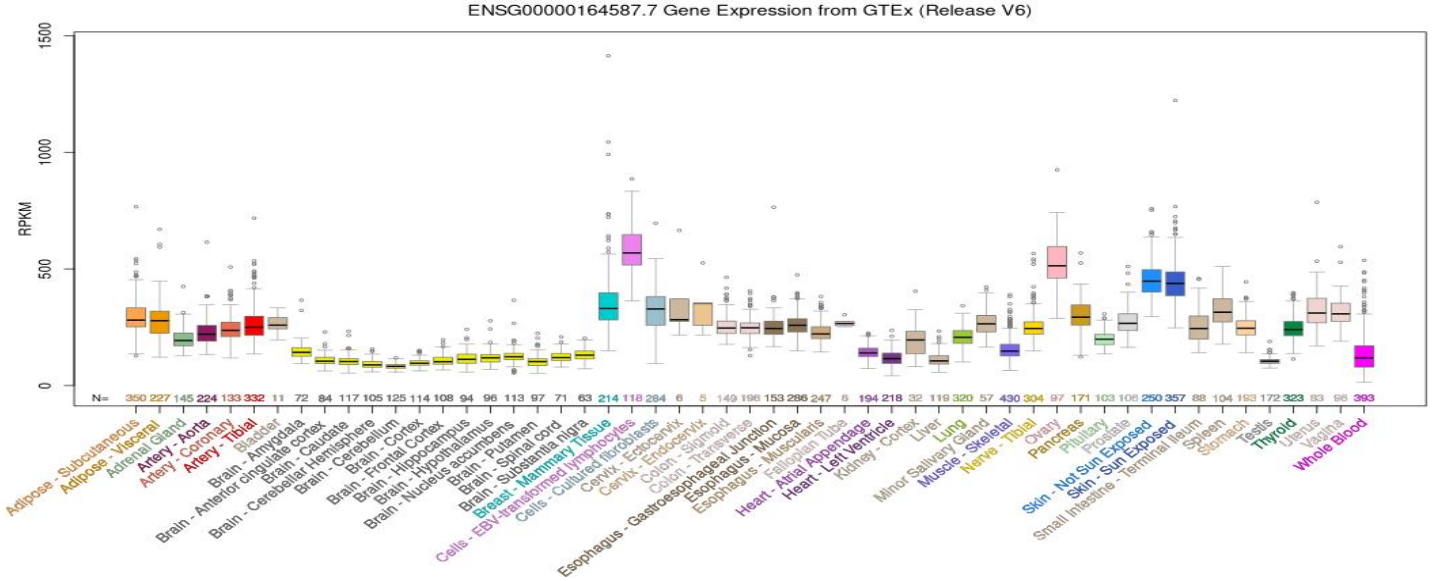

Figure 4: RPS14 RNA expression across hematopoietic-related tissues 9 (RNA-Seq Expression Data from GTEx**)**

GTEx RNA-sequencing data show robust RPS14 expression in whole blood (n = 755), spleen (n = 241), and EBV-transformed lymphocytes (n = 174). Consistent expression across large populations supports the fundamental role of RPS14 in ribosomal function and hematopoietic maintenance (Warner, 1999).

RPS14 impairs 40S ribosomal subunit maturation, leading to decreased translational capacity and activation of p53-dependent stress pathways (Fig.5). Erythroid progenitors, which require sustained ribosome biogenesis and iron-dependent hemoglobin synthesis, are particularly sensitive to such translational stress. Concurrent micronutrient limitation, including iron deficiency (Camaschella, 2015), may further exacerbate erythropoietic failure. Together, ribosomal insufficiency and metabolic constraint converge to promote ineffective erythropoiesis and anemia in myelodysplastic syndromes.

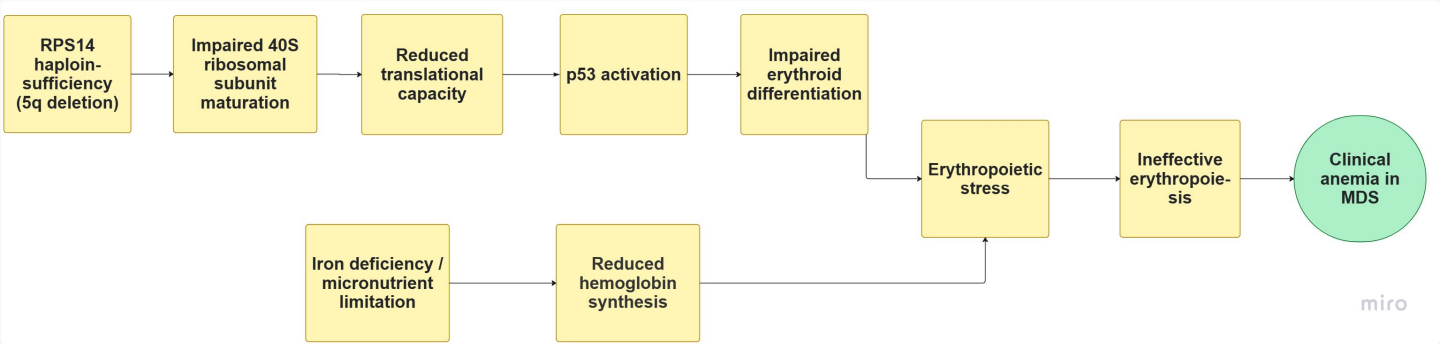

Figure 5: Proposed mechanistic model linking RPS14 haploinsufficiency to nutrient-sensitive erythropoietic vulnerability.

Loss or reduced dosage of RPS14 impairs 40S ribosomal subunit maturation, leading to decreased translational capacity and activation of p53-dependent stress pathways. Erythroid progenitors, which require sustained ribosome biogenesis and iron-dependent hemoglobin synthesis, are particularly sensitive to such translational stress. Concurrent micronutrient limitation, including iron deficiency (Camaschella, 2015), may further exacerbate erythropoietic failure. Together, ribosomal insufficiency and metabolic constraint converge to promote ineffective erythropoiesis and anemia in myelodysplastic syndromes. This study combines molecular validation, tissue-level expression profiling, pathway mapping, and disease-associated transcriptomic data (Figures 1–5) to show that RPS14 plays a central role at the intersection of ribosomal biology and nutrient-dependent erythropoiesis. Instead of viewing 5q deletion syndrome only as a cytogenetic abnormality, this analysis places RPS14 insufficiency within a broader metabolic context.

PCR-based analysis of the RPS14 locus created a reproducible molecular framework for studying ribosomal genes. Although conventional PCR cannot measure gene dosage or directly detect chromosomal deletions, it provides a strong foundation for future quantitative approaches, including copy-number analysis and gene expression profiling under different nutritional conditions. This groundwork is important because even partial reductions in RPS14 expression have been shown to impair 40S ribosomal subunit maturation and activate p53-mediated erythroid failure (Ebert et al., 2008; Barlow et al., 2010).

Tissue-level expression data further support the systemic importance of RPS14 (Figure 1). Elevated protein expression in the spleen highlights its role in erythrocyte turnover and iron recycling. The spleen is a major site of red blood cell filtration and iron reclamation, both of which are closely linked to efficient erythropoiesis. RPS14 expression in the small intestine (Moustarah & Daley, 2024), the principal site of dietary iron absorption, indicates activity in metabolically demanding tissues involved in nutrient handling. Together, these findings show that RPS14 functions in tissues that are central to iron homeostasis and metabolic regulation. KEGG pathway analysis confirmed that RPS14 is a structural component of the 40S ribosomal subunit (Figure 2). Ribosome biogenesis is one of the most energetically demanding cellular processes, requiring coordinated synthesis of ribosomal RNA and proteins as well as adequate metabolic substrates (Warner, 1999). When ribosomal protein dosage is disrupted, cells experience translational stress, especially highly proliferative populations such as erythroid progenitors. Because erythropoiesis requires continuous hemoglobin synthesis, an iron-dependent process, ribosomal insufficiency may increase vulnerability to micronutrient limitations.

Transcriptomic analysis of myelodysplastic syndrome (MDS) subtypes showed altered RPS14 expression compared with healthy bone marrow controls (Figure 3). This supports dysregulation of ribosomal gene networks in pathologic hematopoiesis. MDS is often associated with disrupted iron handling, chronic transfusion-related iron overload, and ineffective erythropoiesis (An et al., 2023). The combination of ribosomal imbalance and altered iron metabolism suggests a biologically plausible link between genetic ribosomal defects and nutrient-dependent hematopoietic stress. Although these data derive from mesenchymal stromal cells rather than erythroid progenitors, altered ribosomal gene expression within the marrow microenvironment may influence hematopoietic support and contribute to dysplastic erythropoiesis.

Population-scale data from the GTEx dataset showed strong, consistent RPS14 expression in whole blood, spleen, and lymphoid tissues across large sample sizes (Figure 4). This stability across many individuals supports the fundamental and widespread role of RPS14 in human biology. However, erythroid cells appear especially sensitive to ribosomal perturbations, meaning tissue-specific effects can occur despite broad overall expression.

Overall, these findings support a model in which RPS14 haploinsufficiency reduces translational capacity in metabolically demanding hematopoietic cells (Figure 5). This lowers the threshold at which micronutrient insufficiency disrupts erythropoiesis. Rather than acting only in hematopoietic cells, RPS14 is broadly expressed, but its disruption has the greatest impact in nutrient-sensitive lineages.

Although this study relies on secondary transcriptomic datasets and does not include direct quantitative deletion analysis or functional nutrient manipulation experiments, it provides a clear framework linking ribosomal haploinsufficiency to metabolic vulnerability in erythropoiesis. Future studies should include copy-number analysis in del(5q) patient samples, precise measurement of RPS14 dosage, and controlled micronutrient modulation experiments in erythroid progenitor systems. These approaches will be necessary to directly test the proposed ribosomal–nutrient interaction model and determine whether nutritional optimization can help reduce ribosomal stress–associated hematopoietic dysfunction.

Conclusion

This study shows RPS14 as a critical mediator at the interface of ribosomal genetics and nutritional physiology. Molecular analysis, tissue-specific expression profiling, pathway mapping, and disease transcriptomic data support a ribosome–nutrition interaction model explaining erythroid vulnerability in 5q deletion syndrome and related hematologic disorders. Reduced RPS14 dosage decreases translational capacity and increases sensitivity to micronutrient imbalance, particularly during iron-dependent erythropoiesis. Future studies should integrate quantitative gene dosage and micronutrient measurements to determine the combined effects of ribosomal insufficiency and nutritional status on hematopoiesis. Recognizing ribosomal proteins such as RPS14 as metabolically sensitive regulators of translation expands the conceptual understanding of ribosomopathies and highlights the importance of integrating genomic and nutritional perspectives in hematologic disease research.

Acknowledgment

The authors are thankful to the Department of Biological Sciences laboratory, where all work was conducted.

Conflict of Interest

Authors declare no conflict of interest.

Funding Resource

Institutional resources from the Department of Biological Sciences at California State University, Long Beach, supported this work.

References

An, W., Feola, M., Levy, M., Aluri, S., Ruiz-Martinez, M., Sridharan, A., Fibach, E., Zhu, X., Verma, A., & Ginzburg, Y. (2023, December 28). Iron chelation improves ineffective erythropoiesis and iron overload in myelodysplastic syndrome mice. eLife, 12, e83103. https://doi.org/10.7554/eLife.83103

Barlow, J. L., Drynan, L. F., Hewett, D. R., Holmes, L. R., Lorenzo-Abalde, S., Lane, A. L., Jolin, H. E., Pannell, R., Middleton, A. J., Wong, S. H., Warren, A. J., Wainscoat, J. S., Boultwood, J., & McKenzie, A. N. J. (2010). A p53 dependent mechanism underlies macrocytic anemia in a mouse model of 5q− syndrome. Nature Medicine, 16(1), 59–66. https://doi.org/10.1038/nm.2063.

Camaschella, C. (2015). Iron-deficiency anemia. *The New England Journal of Medicine, 372*(19), 1832–1843. https://doi.org/10.1056/NEJMra1401038

Ebert, B. L., Pretz, J., Bosco, J., Chang, C. Y., Tamayo, P., Galili, N., Raza, A., Root, D. E., Attar, E., Ellis, S. R., & Golub, T. R. (2008). Identification of RPS14 as a 5q− syndrome gene by RNA interference screen. *Nature, 451*(7176), 335-339. https://doi.org/10.1038/nature06494

Ensembl. (2024, February 9). *Homo sapiens RPS14 gene*. https://useast.ensembl.org/Homo_sapiens/Gene/ExpressionAtlas?db=core;g=ENSG00000164587;r=5:150426351504 49739;t=ENST00000407193

Ganz, T., & Nemeth, E. (2012). Hepcidin and iron homeostasis. Biochimica et Biophysica Acta (BBA) – Molecular Cell Research, 1823(9), 1434–1443. https://doi.org/10.1016/j.bbamcr.2012.01.014

GTEx Consortium. (2024, March 9). *RPS14 gene expression across tissues*. https://genome.ucsc.edu/cgibin/hgGene?db=hg38&hgg_gene=ENST00000407193.7

KEGG. (2024, March 9). *Ribosome – Reference pathway*. https://www.genome.jp/dbgetbin/www_bget?pathway:hsa03010

Moustarah, F., & Daley, S. F. (2024, January 8). Dietary iron. In StatPearls. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK540969/

Mullis, K. B., & Faloona, F. A. (1987). Specific synthesis of DNA in vitro via a polymerase-catalyzed chain reaction. Methods in Enzymology, 155, 335–350. https://doi.org/10.1016/0076-6879(87)55023-6

Narla, A., & Ebert, B. L. (2010). Ribosomopathies: Human disorders of ribosome dysfunction. Blood, 115(16), 3196-3205. https://doi.org/10.1182/blood-2009-10-178129

NCBI Gene Expression Omnibus. (2024, March 29). *Myelodysplastic syndrome disorder*. https://www.ncbi.nlm.nih.gov/geo/tools/profileGraph.cgi?ID=GDS5622:ILMN_2338785

O'Leary, F., & Samman, S. (2010). Vitamin B12 in health and disease. *Nutriets, 2*(3), 299–316. https://doi.org/10.3390/nu2030299

Warner, J. R. (1999). The economics of ribosome biosynthesis in yeast. *Trends in Biochemical Sciences, 24*(11), 437-440. https://doi.org/10.1016/S0968-0004(99)01460-7

Received: January 28, 2026 **Accepted: February 24, 2026**