

Ribosomal Protein Genes *RPS10* and *RPS26* Are Commonly Mutated in Diamond-Blackfan Anemia

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Diamond-Blackfan anemia (DBA), an inherited bone marrow failure syndrome characterized by anemia that usually presents before the first birthday or in early childhood, is associated with birth defects and an increased risk of cancer. Although anemia is the most prominent feature of DBA, the disease is also characterized by growth retardation and congenital malformations, in particular craniofacial, upper limb, heart, and urinary system defects that are present in ~30%–50% of patients. DBA has been associated with mutations in seven ribosomal protein (RP) genes, *RPS19*, *RPS24*, *RPS17*, *RPL35A*, *RPL5*, *RPL11*, and *RPS7*, in about 43% of patients. To continue our large-scale screen of RP genes in a DBA population, we sequenced 35 ribosomal protein genes, *RPL15*, *RPL24*, *RPL29*, *RPL32*, *RPL34*, *RPL9*, *RPL37*, *RPS14*, *RPS23*, *RPL10A*, *RPS10*, *RPS12*, *RPS18*, *RPL30*, *RPS20*, *RPL12*, *RPL7A*, *RPS6*, *RPL27A*, *RPLP2*, *RPS25*, *RPS3*, *RPL41*, *RPL6*, *RPLP0*, *RPS26*, *RPL21*, *RPL36AL*, *RPS29*, *RPL4*, *RPLP1*, *RPL13*, *RPS15A*, *RPS2*, and *RPL38*, in our DBA patient cohort of 117 probands. We identified three distinct mutations of *RPS10* in five probands and nine distinct mutations of *RPS26* in 12 probands. Pre-rRNA analysis in lymphoblastoid cells from patients bearing mutations in *RPS10* and *RPS26* showed elevated levels of 18S-E pre-rRNA. This accumulation is consistent with the phenotype observed in HeLa cells after knockdown of *RPS10* or *RPS26* expression with siRNAs, which indicates that mutations in the *RPS10* and *RPS26* genes in DBA patients affect the function of the proteins in rRNA processing.

Diamond-Blackfan anemia (DBA) (MIM 105650) is an inherited bone marrow failure syndrome characterized by anemia that usually presents during infancy or early childhood.¹ Red cell aplasia is the most prominent feature of DBA; however, the disease is also characterized by growth retardation and congenital malformations, in particular craniofacial, upper limb, heart, and urinary system defects that are present in ~30%–50% of patients.^{2–4} In addition to anemia and birth defects, the disease is associated with predisposition to cancer, in particular acute myeloid leukemia (AML) and osteogenic sarcoma.^{5,6} DBA is a clinically heterogeneous disease: laboratory findings such as increased mean corpuscular volume (MCV), elevated erythrocyte adenosine deaminase activity (eADA), and hemoglobin F are observed in a majority but not in all DBA patients.^{7–9} Furthermore, within affected families, some individuals may exhibit mild or absent anemia with only subtle indications of erythroid abnormalities such as macrocytosis, elevated eADA, and/or hemoglobin F. The incidence of DBA is estimated to be between 1:100,000 and 1:200,000 live births⁹ or 5–7 per million live births,^{2,10,11} which remains consistent across ethnicities and equal in both genders.⁹ Approximately 45% of

patients are familial cases, with disease inherited in an autosomal-dominant pattern; the remaining 55% of patients are sporadic cases.³

DBA is genetically heterogeneous: heterozygous mutations in four small subunit ribosomal protein (RP) genes, *RPS19* (MIM 603474), *RPS24* (MIM 602412), *RPS17* (MIM 180472), and *RPS7* (MIM 612563), and in three large subunit ribosomal protein genes, *RPL35A* (MIM 180468), *RPL5* (MIM 612561), and *RPL11* (MIM 612562), have been reported in about 43% of DBA patients, indicating that DBA is a disorder of ribosomal biogenesis and/or function.^{12–16}

Several studies showed that *RPS19* protein plays an important role in 18S rRNA maturation in yeast and in human cells.^{17–20} Other studies demonstrated alterations of pre-rRNA processing and small or large ribosomal subunit synthesis in human cells with *RPS24*, *RPS7*, *RPL35A*, *RPL5*, and *RPL11* deficiency.^{15,16,21} These observations further indicate that DBA is a disorder of the ribosome. Increased apoptosis has been demonstrated by Perdahl²² and also in hematopoietic cell lines and in bone marrow cells with deficiency of *RPS19* and *RPL35A*,^{15,23} and imbalance of the p53 family proteins has been suggested as

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Table 1. One Hundred and Seventeen Probands Studied for Mutations in 35 Ribosomal Protein Genes

All Studied Probands	Sporadic Cases	Familial Cases	Probands Negative for Mutations in Ribosomal Protein (RP) Genes <i>S19</i> , <i>S24</i> , <i>L35A</i> , <i>S17</i> , <i>S7</i> , <i>L5</i> , <i>L11</i> , <i>S15</i> , <i>S27A</i> , and <i>L36</i>	Probands with Sequence Change in RP Genes <i>S19</i> , <i>S24</i> , <i>L5</i> , <i>L11</i> , <i>S15</i> , and <i>S27A</i>
117	103	14	103	14

a mechanism of abnormal embryogenesis and anemia in zebrafish upon perturbation of *RPS19* expression.²⁴ Furthermore, the DBA phenotype in the mouse is ameliorated by the knockdown of *p53*.²⁵

Here we report the results of a large-scale screen of 35 additional RP genes in a cohort of 117 DBA probands. Remarkably, we identified probable pathogenic mutations in two of these genes, *RPS10* (MIM 603632) and *RPS26* (MIM 603701). In addition, we found a possible missense mutation of *RPL9* (MIM 603686) in one family.

One hundred and seventeen DBA families participated in the study. The diagnosis of DBA in all probands and their family members was based on normochromic, often macrocytic, anemia; reticulocytopenia; a low number or lack of erythroid precursors in bone marrow; and, in some patients, congenital malformations and elevated eADA. Among these families, 14 were multiplex families and 103 comprised only one clinically affected individual. One hundred and three probands were negative for mutations in seven known DBA genes, *RPS19*, *RPS24*, *RPL35A*, *RPS17*, *RPS7*, *RPL5*, and *RPL11*, and did not have any sequence change in *RPS15*, *RPS27A*, and *RPL36*, previously described as variants of unknown significance.¹⁶ Twelve probands were mutated in one of the known genes, three with mutations in *RPS19*, one with *RPS24*, five with mutations in *RPL5*, and three with *RPS11* mutation. Two probands had sequence changes in *RPS15* and *RPS27A*, previously described as variants of unknown significance (Table 1).¹⁶ Informed consent was obtained from all patients and their family members participating in the study under a protocol at Children's Hospital Boston.

Genomic DNA was isolated from blood samples with nucleic acid isolation system QuickGene-610L (AutoGen) according to the manufacturer's instructions. To continue our large-scale screen of RP genes in a DBA population, we amplified genomic DNA samples from 96 unrelated DBA probands enrolled in the study by PCR and sequenced for mutations in 35 RP genes, *RPL15*, *RPL24*, *RPL29*, *RPL32*, *RPL34*, *RPL9*, *RPL37*, *RPS14*, *RPS23*, *RPL10A*, *RPS10*, *RPS12*, *RPS18*, *RPL30*, *RPS20*, *RPL12*, *RPL7A*, *RPS6*, *RPL27A*, *RPLP2*, *RPS25*, *RPS3*, *RPL41*, *RPL6*, *RPLP0*, *RPS26*, *RPL21*, *RPL36AL*, *RPS29*, *RPL4*, *RPLP1*, *RPL13*, *RPS15A*, *RPS2*, and *RPL38* (chromosomes 3, 4, 5, 6, 8, 9, 11, 12, 14, 15, 16, and 17), in our DBA patient cohort of 117 families (the majority of the patient cohort is the same as in previous studies).^{13,15,16} In total, we screened 64 RP genes, in addition to the 29 RP genes sequenced previously.^{13,15,16,26} Primers (see Table S1 available online) were designed with Primer3 software to amplify the coding exons and intron/exon boundaries of the above genes. PCR products,

between 200 and 600 base pairs long, were robotically prepared with a Hamilton MicroLab STARplus (Hamilton Robotics), purified with ExoSAP enzyme (USB), and sequenced on both strands with an Applied Biosystems 3730 DNA Analyzer. The chromatograms were analyzed with Sequencher software version 4.7 (Gene Codes). When a sequence change was identified in a given gene, we sequenced an additional 21 samples (for a total of 117 samples) from unrelated probands for mutations in this gene. Duplicate, independent PCR products were sequenced to confirm the observed nucleotide changes in the probands. DNA samples from at least 260 control individuals, i.e., 520 chromosomes, were sequenced to determine whether the observed sequence variations were nonpathogenic variants. Subsequently, DNA samples from available family members were sequenced to determine whether the mutation cosegregated with the DBA phenotype within the pedigree.

Interestingly, we identified heterozygous sequence changes in *RPS10* in 5 of 117 probands. One sequence change is a missense mutation 3G>A that changes Met1lle and eliminates the start codon. The next downstream start codon is located at nucleotide position 61–63 (codon 21) and is predicted to start translation of a truncated protein of 144 amino acids. Another mutation is a c.260_261insC causing a frameshift at codon 87 and a stop at codon 97. Three other probands have a common nonsense mutation, c.337C>T, causing Arg113 stop (Table 2). Proband P3 has a de novo mutation, whereas SNP analysis of 14 polymorphisms spanning an ~20 kb region surrounding the *RPS10* gene demonstrated that probands P3 and P4 do not share the same background haplotype (data not shown) (Table 2). All of these changes are unique (i.e., not previously described in the literature or databases), and two of them were found in only a single kindred, whereas one was seen in three unrelated families.

We also identified nine distinct mutations in 12 probands in *RPS26* gene located on chromosome 12. Interestingly, we found mutation of the first codon, methionine change to leucine, valine, or arginine, in six probands and in two family members (Table 3), which suggests that the translation-initiation codon may be a hot spot in *RPS26*. These sequence changes eliminate a start codon; the next downstream start codon is located at nucleotide position 343–345. This is the last codon, codon 115, and the protein is predicted to not be translated. Probands P7–P10 share the same M1V mutation. Probands P7 and P8 have de novo mutations, whereas SNP analysis of 15 polymorphisms spanning an ~20 kb region surrounding the *RPS26* gene demonstrated that probands P9 and P10

Table 2. Sequence Changes in *RPS10* in DBA Patients

Proband's ID (Gender), Inheritance	Family Members	DNA Mutation	Exon or Intron	Predicted Amino Acid Change	Age at Diagnosis	Malformation Status	Response at First Steroid Therapy	Present Therapy
P1 (M), sporadic	-	c.3G>A	exon 1	Met1Ile	NA	NA	NA	NA
P2 (F), sporadic	f – normal sequence	c.260_261insC	exon 3	frameshift at codon 87; stop at 97	2 mo	none	responsive	steroid therapy
P3 (M), sporadic	-	c.337C>T	exon 4	Arg113stop	7 mo	none	responsive	RBC trx
P4 (F), sporadic	-	c.337C>T	exon 4	Arg113stop	12 yrs	none	responsive	steroid therapy
P5 (F), de novo	f, m – normal sequence	c.337C>T	exon 4	Arg113stop	birth	webbed neck	unresponsive	RBC trx

The following abbreviations are used: P, proband; f, father; m, mother; ins, insertion; NA, not available; RBC trx, red blood cell transfusion.

do not share the same background haplotype (data not shown) (Table 3). Other identified mutations are two missense mutations (c.97G>A changing Asp33Asn and c.334T>C resulting in Met115Thr), insertion G in exon 2 causing frameshift at codon 11 and stop at codon 25, and three donor splice-site mutations in introns 1 and 2. All of these changes are also unique, and eight of them were found in only a single kindred, whereas one was seen in four apparently unrelated families (Table 3). Parental DNA was available in two probands with *RPS10* mutations and in seven with *RPS26* mutations. De novo sequence changes of *RPS10* and *RPS26* were identified in one and five probands, respectively, with sporadic disease, further supporting our belief that these sequence changes are likely pathogenic mutations. In addition, six mutations in *RPS26* among 75 samples from DBA probands were identified by a separate ongoing RP gene resequencing project (unpublished data).

We also found a heterozygous missense mutation, c.375G>C, resulting in Arg125Ser substitution in *RPL9* in one proband and his affected mother. None of the identified sequence changes were found on the NCBI SNP lists, and none were identified in at least 520 control chromosomes from a control population of similar, largely European origin.

Review of medical records of DBA probands and data from the DBA Registry of North America (DBAR)^{4,6} revealed that among four patients with *RPS10* mutations and available medical data, one had a physical malformation of a webbed neck and three patients were without malformations, whereas among 11 *RPS26* mutated patients whose clinical data were available, only three patients had malformations. These physical abnormalities were similar to those observed in other RP gene mutations (Table 2; Table 3). One patient with *RPS26* mutation has cleft lip and cleft palate. Interestingly, to date this malformation has only been found in DBA patients with *RPL5* and *RPL11* mutations.^{16,27} Thus, the *RPL26* gene is the third DBA gene whose mutation is associated with clefting in DBA. In general, physical malformations are present in about 30%–50% of patients in the overall study cohort.^{2–4}

Although the sample size is small, physical malformations seem to be rare events in patients with *RPS26* mutations.

Interestingly, 5 of 11 patients with *RPS26* mutations whose treatment data were available responded well to the steroid treatment and six were unresponsive. Among four patients with *RPS10* mutations and available medical data, three patients were responsive and one unresponsive to steroid treatment. According to data from DBAR, 79% of DBA patients have been initially responsive to steroids, 17% unresponsive, and 4% were never treated with steroids.⁴ At present, four *RPS26*-mutated patients are dependent on red blood transfusions, three are steroid dependent, two do not need any treatment, and two are deceased (Table 3). Two *RPS10*-mutated patients are red-blood-cell-transfusion dependent and two are dependent on steroid treatment (Table 2).

The role of *RPS10* and *RPS26* in pre-rRNA processing was assessed by knocking down expression of these proteins with siRNAs in HeLa cells. Pre-rRNA processing analysis was performed as previously described.²¹ Depletion of both proteins led to decreased levels of 18S rRNA, indicating that they are necessary for production of the small subunit. Accordingly, RNA blot analysis of the pre-rRNAs revealed that these proteins are both required for proper processing of the pre-rRNA (Figure 1A). Depletion of *RPS26* led to the accumulation of 43S, 26S, and 18S-E pre-rRNAs, which indicates defects in cleavages at both ends of the 18S rRNA. Interestingly, knockdown of *RPS10* expression yielded a very similar phenotype. This phenotype differed from what we observed previously upon depletion of *RPS19*, *RPS24*, or *RPS7*, three other RPS proteins mutated in DBA²¹ for which the processing was blocked upstream of 18S-E pre-rRNA formation. Pre-rRNAs were next detected by RNA blot analysis in RNAs extracted from lymphoblastoid cells derived from patients with mutations in *RPS10* and *RPS26* (Figure 1B). In the case of the *RPS26*^{+/-mut} patients, we compared their profiles to those of unaffected relatives. Quantitative analysis by phosphorimager indicated that four out of five patients had elevated levels of 18S-E RNA when compared to their relatives (Figures 1B and 1C). The remaining *RPS26*^{+/-mut}

Table 3. Sequence Changes in *RPS26* in DBA Patients

Mutation Type	Proband's ID (Gender), Inheritance	Family Members	DNA Mutation	Exon or Intron	Predicted Amino Acid Change	Age at Diagnosis	Malformation Status	Response at First Steroid Therapy	Present Therapy
Missense mutation	P6 (M), de novo	f, m, s – normal sequence	c.1A>T	exon 1	Met1Leu	NA	none	unresponsive	RBC trx
-	P7 (M), familial	f, m – normal sequence	c.1A>G	exon 1	Met1Val	2 mo	none	responsive	steroid therapy
-		d of P7	c.1A>G	exon 1	Met1Val	6 wks	none	unresponsive	RBC trx
-	P8 (M), de novo	f, m – normal sequence	c.1A>G	exon 1	Met1Val	NA	none	unresponsive	RBC trx
-	P9 (M), familial	-	c.1A>G	exon 1	Met1Val	NA	none	responsive	steroid therapy
-		d of P9	c.1A>G	exon 1	Met1Val	NA	none	responsive	no therapy
-	P10 (M), sporadic	-	c.1A>G	exon 1	Met1Val	7 wks	duplicated pelvocalicon on right kidney	unresponsive	RBC trx
-	P11 (M), familial	d – normal sequence	c.1T>G	exon 1	Met1Arg	NA	NA	NA	NA
-	P12 (M), de novo	f, m, s – normal sequence	c.97G>A	exon 2	Asp33Asn	8 mo	inguinal hernia, missing vas deferens (unilateral), slightly abnormal epidymis, pronounced boney prominence of a cervical spinous process	unresponsive	RBC trx
-	P13 (M), de novo	f, m, s – normal sequence	c.344T > C	exon 4	Met115Thr	8 mo	none	responsive	no therapy
Insertion	P14 (F), sporadic	-	c.31_32insG	exon 2	frameshift at codon 11; stop at 25	NA	none	unresponsive	deceased
Splice-site mutations	P15 (M), sporadic	s – normal sequence	donor splice site IVS1+1g>c	intron 1	-	NA	NA	NA	NA
-	P16 (M)	f, m, s, b – normal sequence	donor splice site IVS1+1g>a	intron 1	-	NA	none	unresponsive	RBC trx
-	P17 (F), de novo	f, m – normal sequence	donor splice site IVS1+t>g	intron 2	-	NA	NA	NA	NA

The following abbreviations are used: P, proband; f, father; m, mother; d, daughter; s, sister; b, brother; ins, insertion; NA, not available; RBC trx, red blood cell transfusion.

patient instead showed a higher amount of 21S RNA, a species just upstream the 18S-E RNA in the pre-rRNA maturation pathway (Figures 1B and 1C, patient D). Higher levels of 18S-E pre-rRNA were also detected in *RPS10*^{+ /mut} patients when compared to cells from unaffected individuals (Figure 1B). Interestingly, this phenotype was not detected in an individual bearing a missense

mutation in *RPS10* (Figure 1B, last lane). Higher levels of 18S-E pre-rRNA in *RPS26*^{+ /mut} and *RPS10*^{+ /mut} DBA patients translated into high 18S-E/30S or 18S-E/21S pre-rRNA ratios (Figure 1D), whereas the 21S/30S ratio remained in the same range as in controls, unlike in *RPS19*^{+ /mut} patient cells. The similarity of the pre-rRNA pattern modifications in patient cells and in cells depleted

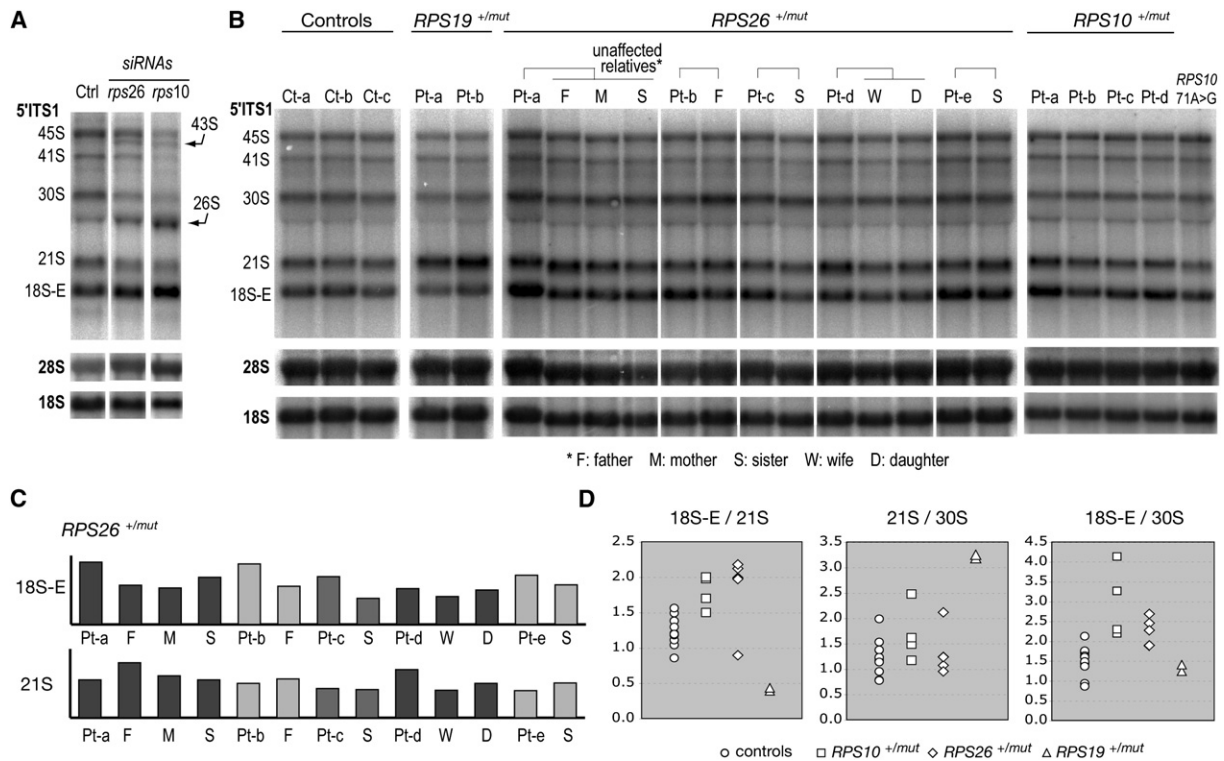


Figure 1. RNA Blot Analysis of the Effects of *RPS10* and *RPS26* Mutation on Pre-rRNA Processing

(A) HeLa cells were transfected with siRNAs to knock down *RPS10* and *RPS26* expression. RNAs extracted 48 hr posttransfection were probed with oligonucleotides complementary to the 5' end of the ITS1 (5' ITS1), which detects the precursors to the 18S rRNA or to the mature 18S and 28S rRNAs. Transfected cells show similar phenotypes with high levels of 43S, 26S, and 18S-E RNA, together with low levels of 18S rRNA. Similar results were obtained with two independent siRNAs for each gene.

(B) Total RNAs from lymphoblastoid cells derived from DBA patients (Pt) and unaffected relatives were analyzed as in (A). Controls (Ct) correspond to cells from unaffected individuals unrelated to patients. RNAs from patients mutated in *RPS19* are also shown for comparison. The last lane on the right corresponds to an individual bearing a missense change in *RPS10*, most likely a rare normal variant.

(C) Phosphorimager analysis of the 18S-E and 21S pre-rRNA levels in *RPS26*^{+/mut} patients shows that four out of five patients have elevated levels of 18S-E rRNA when compared to their unaffected relatives. In each lane, measurements were normalized to the amount of 28S rRNA and divided by the mean of the corresponding value in the three controls.

(D) Relative abundance of the 18S RNA precursors was quantified by phosphorimaging in DBA patients mutated in *RPS10*, *RPS26*, and *RPS19*. Controls in this panel correspond to all the unaffected individuals shown in (B), both patient relatives and unrelated persons.

of the corresponding ribosomal proteins strongly suggests that the mutations in *RPS10* and *RPS26* identified in DBA patients alter the function of ribosomal proteins in ribosome biogenesis, as shown before for other ribosomal protein genes affected in DBA.

In summary, we found that mutations in *RPS10* and *RPS26* are present in about 4.8% and 11.6% of our DBA proband cohort, respectively. After correcting for the fact that our study population was prescreened for *RPS19*, *RPS24*, *RPL35A*, *RPS17*, *RPL5*, *RPL11*, and *RPS7* mutations, we estimate that *RPS10* and *RPS26* mutations are present in about 2.6% and 6.4% of the overall DBA population. The *RPS10* gene is located on chromosome 6 and contains six exons, with the start codon in exon 2. *RPS10* encodes a 165-amino-acid-long RPS10 protein, a component of the 40S ribosomal subunit. In the present work, we identified three sequence changes in *RPS10* in five DBA probands. In addition, we found one missense change, c.71A>G, resulting in Lys24Arg in the patient with transfusion-dependent anemia and in her unaffected brother.

Although this sequence change was not found in 285 control individuals, we strongly suspect that it may be a rare normal variant because there is no phenotype in the pre-rRNA maturation assay in the sample of the brother carrying the sequence change (Figure 1B, last lane). Because the substituted amino acid is also basic, we hypothesize that this change affects only mildly the overall *RPS10* conformation and/or function.

We also identified nine distinct mutations in the *RPS26* gene in 12 patients. The *RPS26* gene is located on chromosome 12 and contains four exons, with the start codon in exon 1. This gene encodes a 115-amino-acid-long RPS26 protein, which is also a component of the 40S ribosomal subunit. The translation-initiation codon may be a hot spot for mutation in *RPS26*, because we found mutation of the first codon, methionine change to leucine, valine, or arginine, in six probands and in two affected family members (Table 3). One missense sequence change, c.344T>C, resulting in substitution of methionine by threonine at the last codon 115, may be a rare or private

nonpathogenic genetic variant; therefore, the DNA sample carrying this sequence change is currently being screened for mutations in the remaining 15 RP genes.

The *RPL9* gene is located on chromosome 4 and comprises two isoforms, which contain seven and eight exons, respectively. In the seven-exon-long isoform the start codon is located in exon 1, and in the eight-exon-long isoform the start codon is located in exon 2. Both isoforms encode a 192-amino-acid-long RPL9 protein, a component of the large ribosomal subunit. The only *RPL9* missense change, c.375G>C, causing Arg125Ser, was found in one of the probands and his affected mother. Unlike for mutations *RPS10* and *RPS26*, lymphoblastoid cells established from these persons do not display a pre-rRNA processing defect similar to that observed upon knockdown of RPL9 with siRNAs (data not shown). Our data do not allow definitive determination of pathogenicity for this mutation. Therefore, we consider this change to be a rare variant of unknown significance, and DNA samples carrying these sequence changes are currently being screened for mutations in the remaining 15 RP genes.

Thus, this report brings the total number of known DBA-associated genes to nine and includes *RPS19* (~25%), *RPS24* (~2%), *RPS17* (~1%), *RPL35A* (~3.5%), *RPL5* (~6.6%), *RPL11* (~4.8%), *RPS7* (~1%), *RPS10* (~6.4%), and *RPS26* (~2.6%), in total accounting for approximately ~52.9% of patients with DBA. In addition, there were four rare variants of unknown significance identified in *RPS15*, *RPS27A*, *RPL36*, and *RPL9*.^{12–16}

Our data indicate that *RPS10* and *RPS26* contribute differently to pre-rRNA processing when compared to other RPS proteins involved in DBA, like *RPS19* and *RPS24*.^{18,21} It remains to be understood how mutations in proteins having different functions in ribosome biogenesis all lead to the same disease. The most direct consequence of these mutations is a defect in ribosome synthesis. This may elicit a ribosomal stress response, to which erythrocytic progenitors would be especially sensitive at some stage of their differentiation. A defect of ribosome biogenesis may also alter regulation and efficacy of translation by affecting the rate of ribosome production and ribosome quality. Such translation disorders could disturb the synthesis timing of important regulators in the erythrocyte differentiation pathway or impede high-rate synthesis of globin. The effects of ribosomal protein gene mutations could be further exacerbated in erythrocytic progenitors when compared to other cell lineages because of the dramatic changes in gene expression that result from the massive chromatin condensation preceding nuclear extrusion. Generation of animal models reproducing the mutations in *RPS10* and *RPS26* described here could help to answer these questions.

Supplemental Data

Supplemental Data include one table and can be found with this article online at <http://www.ajhg.org>.

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Web Resources

The URLs for data presented herein are as follows:

Online Mendelian Inheritance in Man (OMIM), <http://www.ncbi.nlm.nih.gov/Omim/>
Primer 3, <http://frodo.wi.mit.edu/primer3/>
UCSC Genome Browser, <http://genome.ucsc.edu/>
Entrez Gene, <http://www.ncbi.nlm.nih.gov/gene>
Single Nucleotide Polymorphism, <http://www.ncbi.nlm.nih.gov/SNP/>

Accession Numbers

The GenBank accession numbers for human *RPS10*, *RPS26*, and *RPL9* are NM_001014; NM_001029; and NM_000661 and NM_001024921, respectively.

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