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Congenital Dyserythropoietic Anemia Type I

Hannah Tamary, MD[1] and Orly Dgany, PhD[2]

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Summary

Clinical characteristics

Congenital dyserythropoietic anemia type I (CDA I) is characterized by moderate-to-severe macrocytic anemia presenting occasionally in utero as severe anemia associated with hydrops fetalis but more commonly in neonates as hepatomegaly, early jaundice, and intrauterine growth restriction. Some individuals present in childhood or adulthood. After the neonatal period, most affected individuals have lifelong moderate anemia, usually accompanied by jaundice and splenomegaly. Secondary hemochromatosis develops with age as a result of increased iron absorption even in those who are not transfused. Distal limb anomalies occur in 4%-14% of affected individuals.

Diagnosis/testing

The diagnosis of CDA I is suspected based on hematologic findings and established with identification of biallelic pathogenic variants in *CDAN1* or *CDIN1*.

Management

Treatment of manifestations: Intramuscular or subcutaneous injections of interferon IFN-α2a or IFN-α2b are given two or three times a week or peginterferon-α2b once a week to increase hemoglobin and decrease iron overload. Allogeneic bone marrow transplantation should be considered only in transfusion-dependent persons who are resistant to IFN therapy. Treatment of iron overload using iron chelation as necessary; laparoscopic cholecystectomy for biliary stones; treatment of scoliosis per orthopedist; calcium and vitamin D supplementation for osteoporosis; treatment of extramedullary hematopoiesis including regular blood transfusions, surgical debulking, or low-dose radiation; treatment of vision issues per ophthalmologist.

Surveillance: Measurement of hemoglobin every three to six months and more frequently at the time of infections, measurement of bilirubin, iron, transferrin, and serum ferritin concentration every six to 12 months starting at age ten years to monitor anemia and iron overload; annual myocardial and liver T_2-weighted MRI

Author Affiliations: 1 Professor of Pediatrics Director, Hematology Diagnostic and Research Laboratory Schneider Children's Medical Center of Israel Petah Tiqva, Israel; Email: htamary@tauex.tau.ac.il. 2 Director, Pediatric Hematology Diagnostic Laboratory Felsenstein Medical Research Center Beilinson Campus Petah Tiqva, Israel.

starting at age ten years (if available). Annual abdominal ultrasound beginning at age five years; examination for scoliosis with orthopedist as needed; bone densitometry for osteoporosis as recommended by bone specialist; annual assessment of visual acuity and fundoscopic examination by ophthalmologist beginning at age 40 years or earlier if symptomatic.

Agents/circumstances to avoid: Any preparation containing iron.

Genetic counseling

CDA I is inherited in an autosomal recessive manner. If both parents are known to be heterozygous for a CDA I-causing pathogenic variant, each sib of an affected individual has at conception a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier. Once the pathogenic variants have been identified in an affected family member, carrier testing for at-risk relatives and prenatal and preimplantation genetic testing are possible.

Diagnosis

Suggestive Findings

Congenital dyserythropoietic anemia type I (CDA I) **should be suspected** in individuals with the following laboratory and clinical findings.

Laboratory features

- Moderate-to-severe macrocytic anemia with mean corpuscular volume (MCV) >90 fL in the presence of normal folic acid and serum vitamin B_{12} levels
- Inappropriately low number of reticulocytes for the degree of anemia compared to other hemolytic anemias (secondary to ineffective erythropoiesis)
- On peripheral blood smear: macrocytosis, elliptocytes, basophilic stippling, and occasional mature nucleated erythrocytes
- In bone marrow aspirate:
  - On light microscopy, erythroid hyperplasia, few double-nucleated erythroblasts, and interchromatin bridges between erythroblasts (in 0.6%-2.8% of erythroblasts)
  - On electron microscopy, erythroid precursors with spongy appearance of heterochromatin (in ≤60% of erythroblasts) and invaginations of the nuclear membrane

Clinical features

- Jaundice
- Splenomegaly resulting from marrow expansion secondary to ineffective erythropoiesis
- Distal limb anomalies including hypoplastic nails and syndactyly

Establishing the Diagnosis

The diagnosis of CDA I **is established** in a proband with suggestive findings and biallelic pathogenic variants in *CDAN1* or *CDIN1* identified on molecular genetic testing.

Molecular genetic testing approaches can include a combination of **gene-targeted testing** (single-gene testing, multigene panel) and **comprehensive genomic testing** (exome sequencing, genome sequencing) depending on the phenotype.

Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Individuals with the distinctive findings described in Suggestive Findings are likely to be

diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from many other inherited disorders with anemia are more likely to be diagnosed using genomic testing (see Option 2).

Option 1

Single-gene testing. Targeted analysis for the c.3124C>T pathogenic variant in *CDAN1* can be performed first in individuals of Bedouin ancestry.

A multigene panel that includes *CDAN1*, *CDIN1*, and other genes of interest (see Differential Diagnosis) is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Option 2

Comprehensive genomic testing does not require the clinician to determine which gene(s) are likely involved. **Exome sequencing** is most commonly used; **genome sequencing** is also possible.

For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

Table 1. Molecular Genetic Testing Used in Congenital Dyserythropoietic Anemia Type I (CDA I)

Gene [1]	Proportion of CDA I Attributed to Pathogenic Variants in Gene	Proportion of Pathogenic Variants [2] Detectable by Method	
		Sequence analysis [3]	Gene-targeted deletion/duplication analysis [4]
CDAN1	85% [5]	100%	Unknown [6]
CDIN1	~5% [7]	100%	Unknown [6]
Unknown [8]	~10%	NA	

1. See Table A. Genes and Databases for chromosome locus and protein.
2. See Molecular Genetics for information on variants detected in this gene.
3. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
4. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.
5. In 60% of affected individuals two pathogenic variants were identified by sequence analysis, in 28% only one pathogenic variant was identified, and in 11% no pathogenic variant was identified (Note: Testing to detect splice site variants and large deletions was not performed) [Authors and other labs, combined data, unpublished].
6. No data on detection rate of gene-targeted deletion/duplication analysis are available.
7. Author, personal observation
8. The existence of at least one additional locus is suggested by the absence of pathogenic variants in *CDAN1* or *CDIN1* in seven families with CDA I [Babbs et al 2013].

Clinical Characteristics

Clinical Description

Prenatal findings. Rarely, congenital dyserythropoietic anemia type I (CDA I) presents as severe in utero anemia that may be associated with hydrops fetalis, requiring intrauterine red blood cell (RBC) transfusion. Prenatal management of pregnancies at risk for complications of CDA I involves monitoring of fetal hemoglobin by Doppler ultrasonography and fetal transfusions to prevent hydrops fetalis if severe fetal anemia is detected.

Neonatal presentation. Of 70 Bedouin neonates with CDA I, 45 (64%) were symptomatic [Shalev et al 2004]. Of those with symptoms, 65% had hepatomegaly, 53% had early jaundice, and 27% were small for gestational age. A few had persistent pulmonary hypertension, direct hyperbilirubinemia, and transient thrombocytopenia. The majority of affected infants required at least one blood transfusion during the neonatal period.

Childhood and later

- **Anemia.** Most affected individuals have lifelong moderate anemia (mean hemoglobin levels 85±6 g/L). Anemia is usually accompanied by jaundice and splenomegaly, which was present in 17 of 21 (80%) individuals [Heimpel et al 2006]. Few are transfusion dependent; Heimpel et al [2006] found that only two of 21 individuals followed for up to 37 years were dependent on transfusion.
- **Iron overload.** Even in those with CDA I who are not transfused, secondary hemochromatosis develops with age as a result of increased iron absorption. Free iron precipitating in parenchymal organs and especially in the heart can cause congestive heart failure and arrhythmias. Low hepcidin levels have been documented in individuals with CDA I.
- **Splenomegaly** may be absent in infants or young children but develop later with age.
- **Gallstones** were detected in four of 21 individuals before age 30 years.
- **Skeletal findings.** Distal limb anomalies including syndactyly, hypoplastic nails, and duplication of the fourth metatarsal bone were described in 4%-14% of affected individuals. Lumbar scoliosis resulting from a partly duplicated L3 vertebra was also described.

  Osteoporosis was found in the majority of individuals [Shalev et al 2017]. Progression should be monitored with bone densitometry. Treatment includes calcium and vitamin D supplementation.
- **Extramedullary hematopoiesis** (EMH) is a known complication of CDA I although the prevalence is unclear. Treatment is as in non-transfusion-dependent thalassemia, including regular blood transfusions to suppress EMH, surgical debulking, or low-dose radiation [Taher et al 2017].
- **Pregnancy complications.** A high rate of pregnancy complications was described among 28 women with CDA I, including one stillbirth, one first-trimester spontaneous abortion, and low birth weight in 42% of infants [Shalev et al 2008]. The incidence of cæsarean section was high compared to the control group. Follow up in a high-risk pregnancy unit is therefore recommended.
- **Ophthalmic concerns.** Retinal angioid streaks with deterioration of vision have been reported as a rare complication in four adults aged 45-57 years [Roberts et al 2006, Tamary et al 2008, Frimmel & Kniestedt 2016].

Life span. Five (23%) of 21 adults described by Heimpel et al [2006] died, mainly as a result of iron overload. According to the authors' published follow-up data, 9% (3/32) of adults died at age 46-59 years. Causes of death included sepsis and severe arterial pulmonary hypertension [Shalev et al 2017]. It should be noted that all deceased individuals previously underwent splenectomy.

Phenotype Correlations by Gene

The phenotype does not differ based on associated gene.

Genotype-Phenotype Correlations

No phenotype-genotype correlations are known. Marked clinical variability is observed even among individuals with the same pathogenic variants.

Nomenclature

CDAN1-related CDA I is also referred to as CDA type Ia. *CDIN1*-related CDA I is also referred to as CDA type Ib.

Prevalence

About 100 simplex cases (i.e., single occurrences in a family) – mainly from Europe – and about 70 consanguineous Israeli Bedouin families have been described in the literature. Six *CDIN1* variants have been described so far in 15 individuals [Babbs et al 2013, Palmblad et al 2018, Rathe et al 2018, Russo et al 2018, Wang et al 2018, Russo et al 2019.]

Genetically Related (Allelic) Disorders

No phenotypes other than those discussed in this *GeneReview* are known to be associated with germline pathogenic variants in *CDAN1* or *CDIN1*.

Differential Diagnosis

Congenital anemias in the differential diagnosis of congenital dyserythropoietic anemia type I (CDA I) are summarized in Table 2.

Table 2. Congenital Anemias of Interest in the Differential Diagnosis of Congenital Dyserythropoietic Anemia Type I

Gene	DiffDx Disorder	MOI	Clinical Features of DiffDx Disorder	Comment/Distinguishing Features
KIF23 [1]	CDA III	AD	Rarest CDA. The most marked anomaly in bone marrow is the presence of giant multinucleated erythroblasts w/≤12 nuclei per cell. Addl findings incl retinal angioid streaks, macular degeneration, & monoclonal gammopathy ± multiple myeloma.	The clinical presentation is similar to that of CDA I & CDA II; however, in the reported Swedish family, the anemia is not severe & transfusions are not required.
KLF1	CDA IV (OMIM 613673)	AD	Anemia of variable severity (intrauterine anemia & transfusion dependency to mild anemia). Splenomegaly is common. Peripheral blood w/↑ nucleated RBCs & bi-nucleated RBCs. MCV is usually nl. Reticulocytes usually lower compared to degree of anemia. HbF can be very high (≤40%), RBC CD44 is low.	CDA IV has numerous nucleated RBCs on blood smear, MCV is not ↑, HbF is very high, BM EM shows erythroblasts w/cytoplasmic inclusions.

Table 2. continued from previous page.

Gene	DiffDx Disorder	MOI	Clinical Features of DiffDx Disorder	Comment/Distinguishing Features
SEC23B	CDA II (HEMPAS) (OMIM 224100) [2]	AR	Most common CDA, characterized by mild-to-severe anemia, jaundice, & (in 50%-60% of affected persons) splenomegaly. ≤15% are transfusion dependent. [3] After age 20 yrs most develop iron overload.	The diagnosis of CDA II requires evidence of congenital anemia, ineffective erythropoiesis, & typical bone marrow findings w/binuclearity in 10%-50% of erythroblasts.

AD = autosomal dominant; AR = autosomal recessive; BM = bone marrow; CDA = congenital dyserythropoietic anemia; DiffDx = differential diagnosis; EM = electron microscopy; HbF = fetal hemoglobin; MCV = mean corpuscular volume; MOI = mode of inheritance; RBC = red blood cell

1. Liljeholm et al [2013], Méndez et al [2021]

2. CDA II is also known as HEMPAS (*h*ereditary *e*rythroblastic *m*ultinuclearity with *p*ositive *a*cidified *s*erum lysis test) because the RBCs of affected individuals are lysed by acidified sera of 40%-60% of healthy adults due to the presence of natural cold-reacting IgM antibody.

3. Heimpel et al [2003], Wickramasinghe & Wood [2005]

Other. The diagnosis of CDA I should be considered following exclusion of other causes of macrocytosis (mainly B_{12} deficiency and folic acid deficiency) and dyserythropoiesis, including thalassemia syndromes and hereditary sideroblastic anemia. However, the latter two are associated with microcytic anemia.

Management

No clinical practice guidelines for congenital dyserythropoietic anemia type I (CDA I), have been published.

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with CDA I, the evaluations summarized in Table 3 (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Table 3. Recommended Evaluations Following Initial Diagnosis in Individuals with Congenital Dyserythropoietic Anemia Type I

System/Concern	Evaluation	Comment
Anemia	• Hemoglobin concentration • Serum bilirubin concentration	At diagnosis
Iron overload	Serum ferritin concentration	In persons who are not transfusion dependent beginning at age 10 yrs
	Liver & myocardial T_2-weighted MRI	
Biliary stones	Abdominal ultrasound exam	Beginning at age 5 yrs
Skeletal anomalies	Clinical exam for scoliosis by orthopedic surgeon	Beginning at age 5-6 yrs
	Eval of osteoporosis by bone specialist	Beginning at age 15 yrs
Ophthalmic manifestations	Ophthalmology exam incl vision assessment	Beginning at age 40 yrs
Genetic counseling	By genetics professionals [1]	To inform patients & families re nature, MOI, & implications of CDA I in order to facilitate medical & personal decision making

CDA = congenital dyserythropoietic anemia; MOI = mode of inheritance

1. Medical geneticist, certified genetic counselor, certified advanced genetic nurse

Treatment of Manifestations

Table 4. Treatment of Manifestations in Individuals with Congenital Dyserythropoietic Anemia Type I

Manifestation/ Concern	Treatment	Considerations/Other
Anemia	• Intramuscular or subcutaneous injections of IFN- α_{2a} or IFN- α_{2b} given 2-3x/wk or peginterferon-α_{2b} 1x/wk [Abu-Quider et al 2020] • Treatment should be given by a physician experienced in IFN administration.	Treatment ↑ hemoglobin & ↓ iron overload in majority of those treated [Lavabre-Bertrand et al 2004]. The mechanism behind this response is unknown. To date, a limited number of persons, incl infants, have been treated.
	Allogeneic bone marrow transplantation in transfusion-dependent persons who are resistant to IFN therapy.	Successful transplantation described in 11 of 13 children [Ayas et al 2002, Miano et al 2019]
	Splenectomy should be cautiously considered as is recommended for non-transfusion-dependent thalassemia [Taher et al 2013].	• Splenectomy is of unproven value & has not been studied systematically; it failed to ↑ hemoglobin levels & also may → thromboembolic complications. • Expert opinion by European Haematology Assoc suggested reserving splenectomy for painful splenomegaly, symptomatic thrombocytopenia, or leukopenia [Iolascon et al 2017].
Iron overload	Iron chelators as necessary	Iron overload therapy should follow guidelines used for non-transfusion-dependent thalassemia [Taher et al 2017].
Biliary stones	Laparoscopic cholecystectomy	
Scoliosis	Treatment per orthopedist	
Osteoporosis	Calcium & vitamin D supplementation	
Extramedullary hematopoiesis (EMH)	Regular blood transfusions to suppress EMH, surgical debulking, or low-dose radiation	Treatment as recommended in non-transfusion-dependent thalassemia [Taher et al 2017]
Vision issues	Treatment per ophthalmologist	

IFN = interferon

Surveillance

Table 5. Recommended Surveillance for Individuals with Congenital Dyserythropoietic Anemia Type I

System/Concern	Evaluation	Frequency
Anemia	Hemoglobin	Every 3-6 mos, more frequent at time of infections
Iron overload	Bilirubin, iron, transferrin & serum ferritin concentration	Every 6-12 mos beginning at age 10 yrs
	Liver & myocardial T_2-weighted MRI	Annually beginning at age 10 yrs (if available)
Biliary stones	Abdominal ultrasound	Annually beginning at age 5 yrs
Scoliosis	Exam w/orthopedist	As needed
Osteoporosis	Bone densitometry	As recommended by bone specialist
Vision issues	Visual acuity, fundoscopic exam	Annually beginning at age 40 yrs, earlier if symptomatic

Agents/Circumstances to Avoid

Avoid any preparation containing iron.

Evaluation of Relatives at Risk

Evaluation of the younger sibs of a proband for early manifestations of CDA I is recommended so that monitoring of hemoglobin and ferritin levels and treatment can begin as soon as necessary in those who are affected.

- Evaluation of at-risk family members should include CBC to identify macrocytic anemia as well as typical findings on blood smear including macrocytosis, elliptocytes, and basophilic stippling.
- The diagnosis can be confirmed by molecular genetic testing if the pathogenic variants in the family have been identified.

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Pregnancy Management

Anemia places pregnancies of affected women at high risk for delivery-related and outcome complications [Shalev et al 2008]. Management by a high-risk obstetrics team is recommended.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Congenital dyserythropoietic anemia type I (CDA I) is inherited in an autosomal recessive manner.

Risk to Family Members

Parents of a proband

- The parents of an affected child are obligate heterozygotes (i.e., presumed to be carriers of one CDA I-causing pathogenic variant based on family history).
- If a molecular diagnosis has been established in the proband, molecular genetic testing is recommended for the parents of a proband to confirm that both parents are heterozygous for a *CDAN1* or *CDIN1* pathogenic variant and to allow reliable recurrence risk assessment. If a pathogenic variant is detected in only one parent and parental identity testing has confirmed biological maternity and paternity, the following possibilities should be considered:
  - One of the pathogenic variants identified in the proband occurred as a *de novo* event in the proband or as a postzygotic *de novo* event in a mosaic parent [Jónsson et al 2017].
  - Uniparental isodisomy for the parental chromosome with the pathogenic variant resulted in homozygosity for the pathogenic variant in the proband.
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Sibs of a proband

- If both parents are known to be heterozygous for a CDA I-causing pathogenic variant, each sib of an affected individual has at conception a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.
- Heterozygotes (carriers) are asymptomatic and are not at risk of developing the disorder.

Offspring of a proband

- Unless an individual with CDA I has children with an affected individual or a carrier, his/her offspring will be obligate heterozygotes (carriers) for a CDA I-causing pathogenic variant.
- In populations with a high carrier rate and/or a high rate of consanguinity, it is possible that the reproductive partner of the proband is affected or is a carrier. Thus, the risk to offspring is most accurately determined after molecular genetic testing of the proband's reproductive partner (see Prevalence).

Other family members. Each sib of the proband's parents is at a 50% risk of being a carrier of a CDA I-causing pathogenic variant.

Carrier Detection

Carrier testing for at-risk relatives requires prior identification of the CDA I-causing pathogenic variants in the family.

Related Genetic Counseling Issues

See Management, Evaluation of Relatives at Risk for information on evaluating at-risk relatives for the purpose of early diagnosis and treatment.

Family planning

- The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to young adults who are affected, are carriers, or are at risk of being carriers.

DNA banking. Because it is likely that testing methodology and our understanding of genes, allelic variants, and diseases will improve in the future, consideration should be given to banking DNA from probands in whom a molecular diagnosis has not been confirmed (i.e., the causative genetic alteration/s are unknown).

Prenatal Testing and Preimplantation Genetic Testing

If the CDA I-causing pathogenic variants have been identified in an affected family member, prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **MedlinePlus**
  Congenital dyserythropoietic anemia

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Congenital Dyserythropoietic Anemia Type I: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
CDAN1	15q15.2	Codanin-1	CDAN1 database	CDAN1	CDAN1
CDIN1	15q14	CDAN1-interacting nuclease 1		CDIN1	CDIN1

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Congenital Dyserythropoietic Anemia Type I (View All in OMIM)

224120	ANEMIA, CONGENITAL DYSERYTHROPOIETIC, TYPE Ia; CDAN1A
607465	CODANIN 1; CDAN1
615626	CDAN1-INTERACTING NUCLEASE 1; CDIN1
615631	ANEMIA, CONGENITAL DYSERYTHROPOIETIC, TYPE Ib; CDAN1B

Molecular Pathogenesis

The mechanism by which pathogenic variants in *CDAN1* and *CDIN1* cause CDA type I is not completely understood. It has been shown that codanin-1 binds ASF1 histone chaperone and acts as a negative regulator of ASF1 function in chromatin assembly [Ask et al 2012]. CDIN1 binds to codanin-1 and stabilizes its structure [Swickley et al 2020]. It has recently also been shown that codanin-1 is essential for embryonal erythropoiesis [Noy-Lotan et al 2021]; however, whether CDA I is directly due to abnormal chromatin assembly remains to be discovered.

Mechanism of disease causation. Predicted loss of function

Table 6. Congenital Dyserythropoietic Anemia Type I: Notable *CDAN1* Pathogenic Variants

Reference Sequences	DNA Nucleotide Change	Predicted Protein Change	Comment [Reference]
NM_138477.4 NP_612486.2	c.3124C>T	p.Arg1042Trp	Founder variant in Bedouin population [Dgany et al 2002]

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.

Chapter Notes

Revision History

- 29 July 2021 (sw) Comprehensive update posted live
- 25 August 2016 (ha) Comprehensive update posted live
- 20 February 2014 (me) Comprehensive update posted live

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