

## Hereditary Myelodysplastic Syndrome (MDS)/Leukemia

Genetic testing with the Hereditary MDS/Leukemia Panel may be appropriate if you or your child's personal and/or family history is suggestive of a hereditary predisposition to cancer and/or tumors. **This includes:**

- A personal history of myelodysplastic syndrome diagnosed under age 50
- A personal history of leukemia or myelodysplastic syndrome and a family history of acute leukemia, myelodysplastic syndrome, thrombocytopenia, aplastic anemia, and/or pancytopenia
- A personal history of leukemia or myelodysplastic syndrome and other health problems including pulmonary fibrosis, early onset breast cancer, sarcoma, or squamous cell carcinoma of the head and neck or anogenital region
- Multiple relatives on the same side of the family diagnosed with leukemia, myelodysplastic syndrome and/or other related features (see table below) on the same side of the family and spanning multiple generations

Your healthcare provider will determine if genetic testing is medically necessary for you.

## Genes Included on the Hereditary MDS/Leukemia Panel are Listed in the Table Below

**High-Risk Genes** Well-studied • Greater than 4-fold risk of developing one or more cancers • Can cause a moderate risk for other cancers • National or expert opinion guidelines for screening and prevention are established

**Newer Genes** Not as well-studied • Precise lifetime risks and tumor spectrum not yet determined • Guidelines for screening and prevention are limited or not available

	Gene	Lifetime Cancer and/or Tumor Risks*
High-Risk Genes	<i>TERC</i>	Acute myeloid leukemia (AML), Myelodysplastic syndrome (MDS), Bone marrow failure, Squamous cell carcinoma-head and neck, Anogenital cancers
	<i>TERT</i>	Acute myeloid leukemia (AML), Myelodysplastic syndrome (MDS), Bone marrow failure, Squamous cell carcinoma-head and neck, Anogenital cancers
	<i>TP53</i>	Female breast (85%), Soft tissue sarcoma, Osteosarcoma, Brain, Hematologic malignancies-Acute leukemias among others, Adrenocortical carcinoma, among others. Overall risk for cancer: up to 95% in females, 88% in males
Newer Genes	<i>ANKRD26</i>	Thrombocytopenia, Acute myeloid leukemia (AML) among others, Myelodysplastic syndrome (MDS), Chronic myeloid leukemia (CML)
	<i>CEBPA</i>	Acute myeloid leukemia (AML)
	<i>DDX41</i>	Acute myeloid leukemia (AML), Myelodysplastic syndrome (MDS)
	<i>ETV6</i>	Thrombocytopenia, Acute lymphocytic leukemia (ALL), Acute myeloid leukemia (AML), Myelodysplastic syndrome (MDS)
	<i>GATA2</i>	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML)
	<i>RUNX1</i>	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML) among others, Platelet disorder
	<i>SAMD9</i>	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML)
	<i>SAMD9L</i>	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML)
<i>SRP72</i>	Myelodysplastic syndrome (MDS), Aplastic anemia, Pancytopenia	

\* Most commonly associated cancer/tumors listed; lifetime risks provided when available. Risks relate to carriers of a single pathogenic variant.

## Specimen Considerations for Individuals with Hematologic Disease:

Cultured skin fibroblasts are recommended for individuals diagnosed with certain hematologic disease or those that had an allogenic bone marrow/stem cell transplant. If fibroblasts are indicated, GeneDx can culture fibroblasts from a skin biopsy. Punch biopsy specimen collection kits are available upon request and contain detailed instructions on collection, specimen handling and shipping. Please visit [www.genedx.com/specimen-requirements](http://www.genedx.com/specimen-requirements) for additional information on sample types.

**If your patient has a history of a hematologic disorder or if there are questions about the patient's specific diagnosis or preferred sample type, please reach out to us at 1-888-729-1206 or email us at [zebras@genedx.com](mailto:zebras@genedx.com) to discuss. In some cases, fibroblasts may be recommended or required.**

## Possible Outcomes of Genetic Testing



### Positive

- Pathogenic or likely pathogenic variant identified
- Medical management recommendations may be available
- Family member testing may be recommended



### Negative

- No significant genetic changes identified
- Medical management based on personal and/or family history



### Variant of Uncertain Significance (VUS)

- A genetic change identified, but its association with disease is unclear
- Medical management based on personal and/or family history

## Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a **positive** (pathogenic or likely pathogenic variant) test result indicating an increased risk for cancer and/or tumors. Guidelines and recommendations for early detection and/or risk reduction are specific to the gene in which the pathogenic variant was found.

### Recommendations may include:

- Blood analysis
- Bone marrow biopsy
- Clinical exams

In some cases, guidelines for screening and prevention are limited or not available for a positive result. Once your test results are available, a discussion with your healthcare provider is recommended to determine the most appropriate medical management options for you and your family.

### Resources

#### General

American Cancer Society  
[www.cancer.org](http://www.cancer.org)

GeneDx  
[www.genedx.com/oncology](http://www.genedx.com/oncology)

National Cancer Institute  
[www.cancer.gov](http://www.cancer.gov)

#### Hematologic Malignancy Resources

American Society of Hematology  
[www.hematology.org](http://www.hematology.org)

Aplastic Anemia and MDS International Foundation  
[www.aamds.org](http://www.aamds.org)

MDS Foundation  
[www.mds-foundation.org](http://www.mds-foundation.org)

Leukemia & Lymphoma Society (LLS)  
[www.lls.org](http://www.lls.org)

#### Find a Genetic Counselor

Canadian Association of Genetic Counsellors  
[www.cagc-accg.ca](http://www.cagc-accg.ca)

National Society of Genetic Counselors  
[www.nsgc.org](http://www.nsgc.org)