Hereditary MDS/Leukemia Panel

Features of Hereditary Myelodysplastic Syndrome (MDS)/Leukemia

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

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

Current Lifetime Cancer and/or Tumor Risks

	Gene	Lifetime Cancer and/or Tumor Risk*
High-Risk Genes	*TERC*	Acute myeloid leukemia, Myelodysplastic syndrome, Bone marrow failure, Squamous cell carcinoma-head and neck, Anogenital cancers
	TERT	Acute myeloid leukemia, Myelodysplastic syndrome, Bone marrow failure, Squamous cell carcinoma-head and neck, Anogenital cancers
	TP53	Female breast (85%), Sarcoma-bone and soft tissue, Brain, Hematologic malignancies-Acute leukemias among others, Adrenocortical carcinoma, among others. Overall risk for cancer: up to 95% in females, 88% in males
Newer-Risk Genes	*ANKRD26*	Thrombocytopenia, Acute myeloid leukemia among others, Myelodysplastic syndrome, Chronic myeloid leukemia
	CEBPA	Acute myeloid leukemia
	DDX41	Acute myeloid leukemia, Myelodysplastic syndrome
	ETV6	Thrombocytopenia, Acute lymphocytic leukemia, Acute myeloid leukemia, Myelodysplastic syndrome
	GATA2	Myelodysplastic syndrome, Acute myeloid leukemia
	RUNX1	Myelodysplastic syndrome, Acute myeloid leukemia among others, Platelet disorder
	SAMD9	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML)
	SAMD9L	Myelodysplastic syndrome (MDS), Acute myeloid leukemia (AML)
	SRP72	Myelodysplastic syndrome, 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 for additional information on sample types.

We strongly encourage you to call us at 1-888-729-1206 or email us at zebras@genedx.com before submitting a specimen if your patient has a history of a hematologic disorder or if there are questions about the patient's specific diagnosis or sample collection.

Possible Outcomes of Genetic Testing:

There are four possible outcomes of genetic testing: positive (pathogenic variant), likely pathogenic variant, variant of uncertain significance (VUS), and negative. Genetic counseling is recommended prior to genetic testing to understand the benefits and limitations of testing.

A **positive** result indicates a genetic variant (change) was identified in a specific gene and that variant is pathogenic (harmful). With a **positive** test result, the risk to develop a particular disease (in this case, cancer and/or tumors) is increased.

A **likely pathogenic variant** result indicates that there is a variant in a specific gene for which there is significant, but not conclusive, evidence of an increased risk to develop a particular disease (in this case, cancer and/or tumors).

A **variant of uncertain significance (VUS)** result means that a change in a specific gene was identified, however the effect of the variant cannot be clearly established. There may be conflicting or incomplete information in the medical literature about this variant and its association with an increased risk of cancers and/or tumors is unknown. In other words, it cannot be determined yet whether this variant is associated with an increased risk of cancer and/or tumors or it is a harmless (normal) variant.

A **negative** result means that no reportable changes were identified.

Medical Management Based on Genetic Test Results

Clinical guidelines may be available which provide options and recommendations for patients who have a **positive** (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

If you or your child has a **positive** or a **likely pathogenic variant** result, the test report will include additional information regarding available medical management options.

If you or your child has a **negative** or a **variant of uncertain significance (VUS)** test result, medical management should be based upon your personal and/or family history of cancer and/or tumors.

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.

Regardless of the test results, consider sharing them with family members so that they may discuss the results with their healthcare providers. If you or your child has a **positive** or a **likely pathogenic variant** result, family members are at risk to have the same variant and should consider genetic testing to best understand their chance of developing cancer and/or tumors.

Resources

General

American Cancer Society
www.cancer.org/cancer/cancerinchildren

GeneDx
www.genedx.com/oncology

National Cancer Institute
www.cancer.gov

Hematologic Malignancy Resources

American Society of Hematology
www.hematology.org

Aplastic Anemia and MDS International Foundation
www.aamds.org

MDS Foundation
www.mds-foundation.org

Leukemia & Lymphoma Society (LLS)
www.lls.org

Find a Genetic Counselor

Canadian Association of Genetic Counsellors
www.cagc-accg.ca

National Society of Genetic Counselors
www.nsgc.org

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