

Review Article

The Role of Mutations on Genes RPS14, MIR145, MIR146A, in Myelodysplastic Syndrome

Shahin Asadi*

Division of Medical Genetics and Molecular Pathology Research, Harvard University, Boston Children's Hospital, Massachusetts, USA

Abstract

Myelodysplastic Syndrome (MDS) refers to a heterogeneous group of closely related clonal hematopoietic disorders commonly found in the aging population. All are characterized by one or more peripheral blood cytopenias. Bone marrow is usually hypercellular, but rarely, a hypocellular marrow mimicking aplastic anemia may be seen. Bone marrow cells display aberrant morphology and maturation (dysmyelopoiesis), resulting in ineffective blood cell production.

MDS affects hematopoiesis at the stem cell level, as indicated by cytogenetic abnormalities, molecular mutations, and morphologic and physiologic abnormalities in maturation and differentiation of one or more of the hematopoietic cell lines.

Keywords: Genetics mutations, MIR146A genes, MIR145, Myelodysplastic Syndrome (MDS), RPS14

Overview of Myelodysplastic Syndrome

Myelodysplastic syndrome, also known as minus 5q (-5q) syndrome, is a genetic disorder that affects the bone marrow. In myelodysplastic syndrome, the development of red blood cells is affected and results in the reduction of these cells (anemia) [1].

Clinical Signs and Symptoms of Myelodysplastic Syndrome

People with myelodysplastic syndrome are associated with decreased red blood cells (erythrocytes) and abnormal size of these cells (macrocytes). Most people with myelodysplastic syndrome have no symptoms of anemia, but some sufferers develop severe fatigue, weakness, and facial tiredness [1] (Figure 1).

*Corresponding author: Shahin Asadi, Division of Medical Genetics and Molecular Pathology Research, Harvard University, Boston Children's Hospital, Massachusetts, USA, Tel: +1 8576007921; E-mail: shahin.asadi1985@gmail.com

Citation: Asadi S (2020) The Role of Mutations on Genes RPS14, MIR145, MIR146A, in Myelodysplastic Syndrome. J Protein Res Bioinform 2: 004.

Received: February 25, 2020; **Accepted:** March 05, 2020; **Published:** March 13, 2020

Copyright: © 2020 Asadi S. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figure 1: Image of human hands with myelodysplastic syndrome with skin malformations.

People with myelodysplastic syndrome also suffer from abnormal bone marrow cells called megakaryocytes that produce platelets. In addition, some people with myelodysplastic syndrome have excessive platelets. Patients with myelodysplastic syndrome are also at risk for leukemia. This cancer can progress very quickly to Acute Myeloid Leukemia (AML). It is noteworthy that AML progression is less common in people with myelodysplastic syndrome [1,2] (Figure 2).

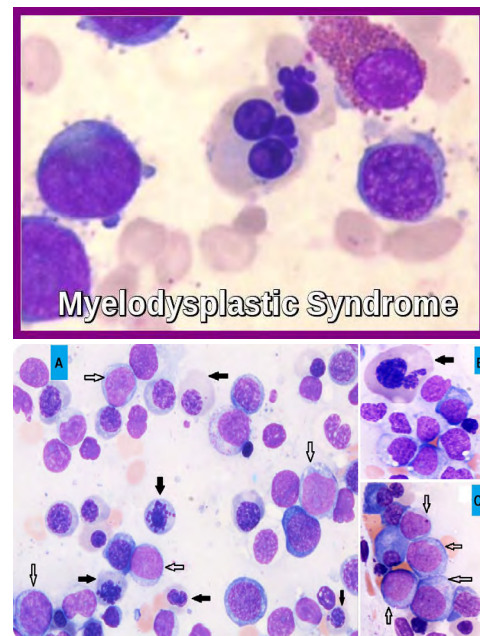
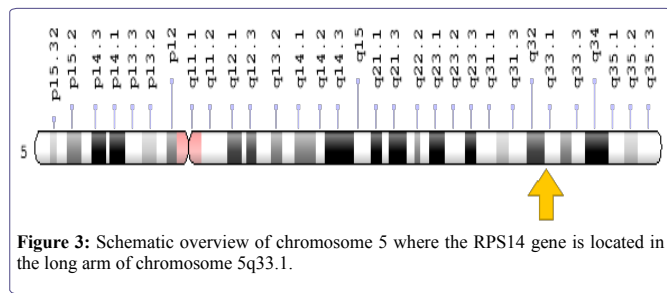


Figure 2: Microscopic image of peripheral blood flow associated with myelodysplastic syndrome.

Etiology of Myelodysplastic Syndrome

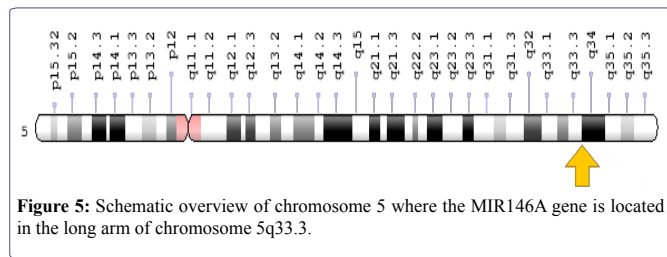
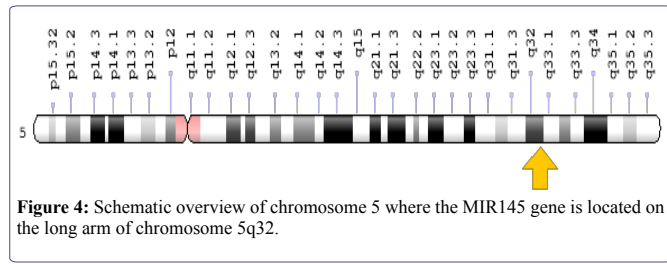
Myelodysplastic syndrome is caused by the deletion of a DNA region from the long arm (q) of chromosome 5. In this knockout mutation, about 1.5 million bp (1.5Mb) is removed from the building blocks of the DNA molecule. The magnitude of the knockout mutation in this syndrome varies among affected individuals. This deletion

mutation occurs in the immature blood cells of patients with myelodysplastic syndrome and affects one of two copies of chromosome 5 in each cell. The deletion region contains 40 genes, many of which play a critical role in the development of normal blood cells. Research shows that deleting multiple genes in the long arm of chromosome 5 contributes to the characteristics of myelodysplastic syndrome. Deletion of the RPS14 gene located on chromosome 5 arm 5q33.1 leads to impaired red blood cell development and deletion of the MIR145 gene located on chromosome 5 arm 5q32 or the MIR146A gene in the arm. The long chromosome 5 is located at 5q33.3, causing megakaryocyte and platelet abnormalities and may increase the immature cell growth. Researchers are trying to determine how deletion of numerous other genes from the long arm of chromosome 5 could be involved in the characterization of myelodysplastic syndrome. Myelodysplastic syndrome occurs as a result of new mutations in somatic cells and does not follow any inherited pattern [1,3] (Figure 3).



Frequency of Myelodysplastic Syndrome

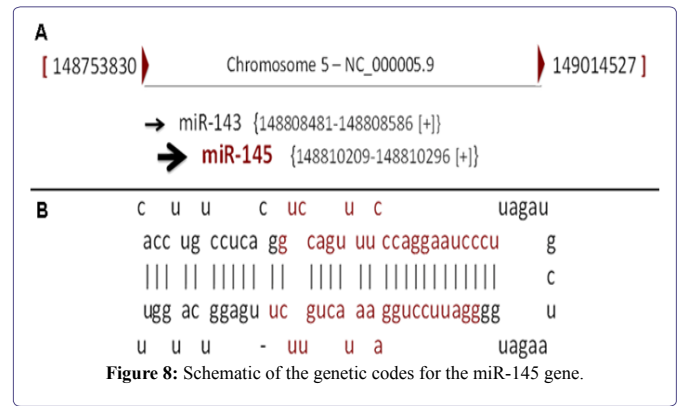
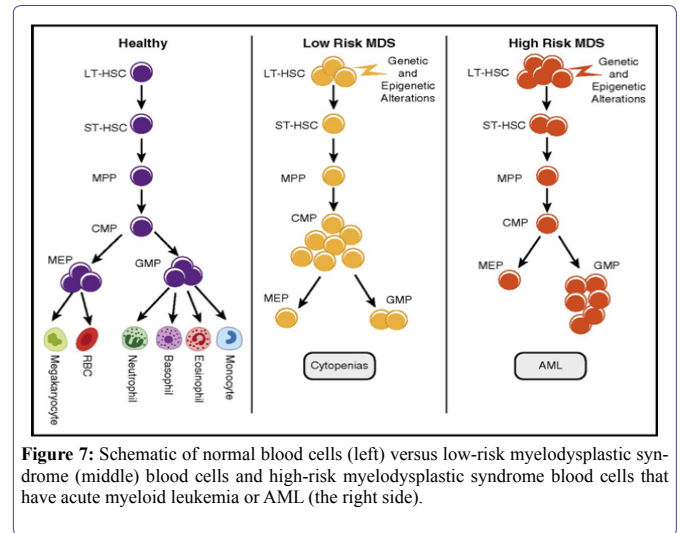
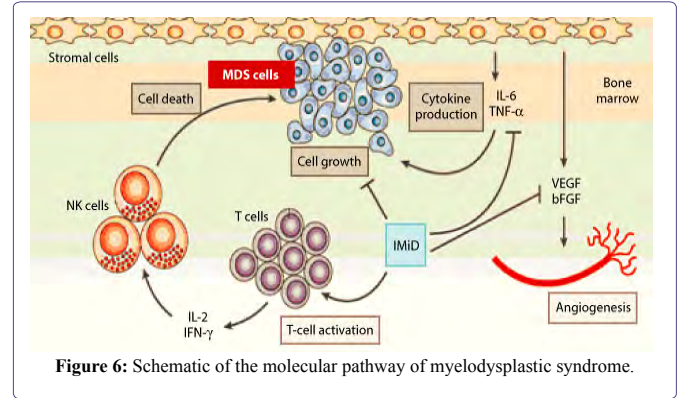
Myelodysplastic syndrome is a chromosomal disorder with a prevalence of 1 in 20,000 in the United States. Myelodysplastic syndrome is more common in men than in women [1,4] (Figures 4-6).



Diagnosis of Myelodysplastic Syndrome

Myelodysplastic syndrome is diagnosed based on the clinical and physical findings of the patients and some pathological tests. The best way to diagnose this syndrome is by molecular cytogenetic testing, such as in situ fluorescence hybridization (FISH) technique, to

investigate the presence of a deletion mutation in chromosome number 5 arm. Prenatal diagnosis is also possible using PGD and amniocentric fluid or sampling of fetal placenta chorionic villi [1,5] (Figures 7 & 8).



Therapeutic pathways of Myelodysplastic Syndrome

The strategy of treatment and management of myelodysplastic syndrome is symptomatic and supportive. Treatment may be done with the efforts of a team of specialists including pediatricians,

hematologists, oncologists and other health care professionals. There is little effective treatment for this syndrome and all clinical measures are to reduce the suffering of patients. Genetic counseling is also important for all parents who want a healthy baby [1,6] (Figure 9).

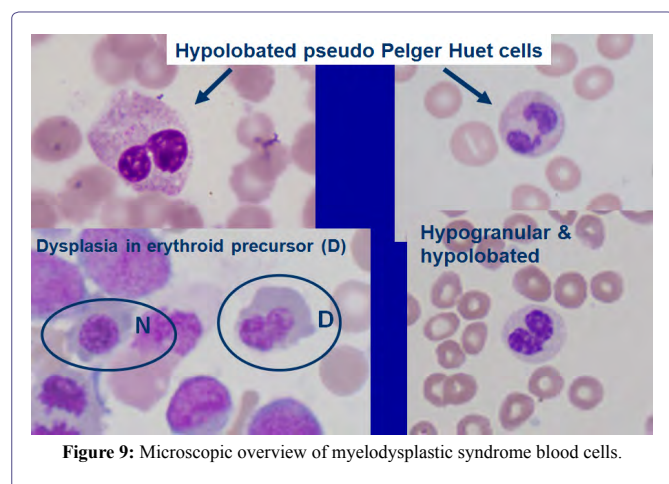


Figure 9: Microscopic overview of myelodysplastic syndrome blood cells.

Discussion and Conclusion

In a patient with a myelodysplastic syndrome, the blood stem cells (immature cells) do not become mature red blood cells, white blood cells, or platelets in the bone marrow. These immature blood cells, called blasts, do not work the way they should and either die in the bone marrow or soon after they go into the blood. This leaves less room for healthy white blood cells, red blood cells, and platelets to form in the bone marrow. When there are fewer healthy blood cells, infection, anemia, or easy bleeding may occur. Different types of treatment are available for patients with myelodysplastic syndromes. Some treatments are standard (the currently used treatment), and some are being tested in clinical trials. A treatment clinical trial is a research study meant to help improve current treatments or obtain information on new treatments for patients with cancer. When clinical trials show that a new treatment is better than the standard treatment, the new treatment may become the standard treatment. Patients may want to think about taking part in a clinical trial. Some clinical trials are open only to patients who have not started treatment. Patients with a myelodysplastic syndrome who have symptoms caused by low

blood counts are given supportive care to relieve symptoms and improve quality of life. Drug therapy may be used to slow progression of the disease. Certain patients can be cured with aggressive treatment with chemotherapy followed by stem cell transplant using stem cells from a donor [1,7]. Research shows that deleting multiple genes in the long arm of chromosome 5 contributes to the characteristics of myelodysplastic syndrome. Deletion of the RPS14 gene located on chromosome 5 arm 5q33.1 leads to impaired red blood cell development and deletion of the MIR145 gene located on chromosome 5 arm 5q32 or the MIR146A gene in the arm. The long chromosome 5 is located at 5q33.3, causing megakaryocyte and platelet abnormalities and may increase the immature cell growth. Researchers are trying to determine how deletion of numerous other genes from the long arm of chromosome 5 could be involved in the characterization of myelodysplastic syndrome. Based on the findings of this study, it can be concluded that mutations in each of these three genes lead to separate abnormalities, all of which are associated with blood cells [1,7].

References

1. Asadi S (2018) Pathology in Medical Genetics Book. Amidi Publications. Vol 6.
2. Ebert BL, Pretz J, Bosco J, Chang CY, Tamayo P, et al. (2008) Identification of RPS14 as a 5q- syndrome gene by RNA interference screen. *Nature* 451: 335-339.
3. Gaballa MR, Besa EC (2014) Myelodysplastic syndromes with 5q deletion: pathophysiology and role of lenalidomide. *Ann Hematol* 93: 723-733.
4. Giagounidis A, Mufti GJ, Fenaux P, Germing U, List A, et al. (2014) Lenalidomide as a disease-modifying agent in patients with del(5q) myelodysplastic syndromes: linking mechanism of action to clinical outcomes. *Ann Hematol* 93: 1-11.
5. Komrokji RS, Padron E, Ebert BL, List AF (2013) Deletion 5q MDS: molecular and therapeutic implications. *Best Pract Res Clin Haematol* 26: 365-375.
6. Kumar MS, Narla A, Nonami A, Mullally A, Dimitrova N, et al. (2011) Coordinate loss of a microRNA and protein-coding gene cooperate in the pathogenesis of 5q- syndrome. *Blood* 118: 4666-4673.
7. Starczynowski DT, Kuchenbauer F, Argiropoulos B, Sung S, Morin R, et al. (2010) Identification of miR-145 and miR-146a as mediators of the 5q- syndrome phenotype. *Nat Med* 16: 49-58.



- Advances In Industrial Biotechnology | ISSN: 2639-5665
- Advances In Microbiology Research | ISSN: 2689-694X
- Archives Of Surgery And Surgical Education | ISSN: 2689-3126
- Archives Of Urology
- Archives Of Zoological Studies | ISSN: 2640-7779
- Current Trends Medical And Biological Engineering
- International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X
- Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276
- Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292
- Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370
- Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594
- Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X
- Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562
- Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608
- Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879
- Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397
- Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751
- Journal Of Aquaculture & Fisheries | ISSN: 2576-5523
- Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780
- Journal Of Biotech Research & Biochemistry
- Journal Of Brain & Neuroscience Research
- Journal Of Cancer Biology & Treatment | ISSN: 2470-7546
- Journal Of Cardiology Study & Research | ISSN: 2640-768X
- Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943
- Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771
- Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844
- Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801
- Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978
- Journal Of Cytology & Tissue Biology | ISSN: 2378-9107
- Journal Of Dairy Research & Technology | ISSN: 2688-9315
- Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783
- Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X
- Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798
- Journal Of Environmental Science Current Research | ISSN: 2643-5020
- Journal Of Food Science & Nutrition | ISSN: 2470-1076
- Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X
- Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566
- Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485
- Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662
- Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999
- Journal Of Hospice & Palliative Medical Care
- Journal Of Human Endocrinology | ISSN: 2572-9640
- Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654
- Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493
- Journal Of Light & Laser Current Trends
- Journal Of Medicine Study & Research | ISSN: 2639-5657
- Journal Of Modern Chemical Sciences
- Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044
- Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X
- Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313
- Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400
- Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419
- Journal Of Obesity & Weight Loss | ISSN: 2473-7372
- Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887
- Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052
- Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X
- Journal Of Pathology Clinical & Medical Research
- Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649
- Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670
- Journal Of Plant Science Current Research | ISSN: 2639-3743
- Journal Of Practical & Professional Nursing | ISSN: 2639-5681
- Journal Of Protein Research & Bioinformatics
- Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150
- Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177
- Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574
- Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060
- Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284
- Journal Of Toxicology Current Research | ISSN: 2639-3735
- Journal Of Translational Science And Research
- Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193
- Journal Of Virology & Antivirals
- Sports Medicine And Injury Care Journal | ISSN: 2689-8829
- Trends In Anatomy & Physiology | ISSN: 2640-7752

Submit Your Manuscript: <https://www.heraldopenaccess.us/submit-manuscript>