Bone Marrow Failure Syndromes

Precision Panel

Overview

Bone Marrow Failure Syndromes (BMFS) are a group of disorders where the ability of the bone marrow to carry out effective haematopoiesis is impaired, result of intrinsic stem cell/progenitor defects. They are a rare yet clinically relevant cause of neonatal haematological and non-haematological manifestations with an increased risk of malignancy. Some BMFS may present with cytopenias in the neonatal period whereas others may present only with congenital physical abnormalities and progress to pancytopenia later in life. BMFS can be inherited or acquired. Morbidity and mortality from pancytopenia are caused by low levels of mature blood cells. Advancements in genetic analysis has provided a better understanding of normal hematopoiesis and how this is disrupted in patients with bone marrow failure.

The Igenomix Bone Marrow Failure Syndrome Precision Panel can be used to make an accurate and directed diagnosis as well as a differential diagnosis of pancytopenia ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved.

Indications

The Igenomix Bone Marrow Failure Syndrome Precision Panel is indicated for those patients with a clinical suspicion or diagnosis with or without the following manifestations:

- Weakness and fatigue
- Pallor
- Family history of BMFS
- Congestive heart failure
- Shortness of breath
- Bruising on the skin
- Gum bleeding
- Nosebleeds
- Fever, cellulitis, pneumonia or sepsis
- Physical developmental abnormalities

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular confirmation for an accurate clinical diagnosis of a symptomatic patient.
- Early initiation of treatment with a multidisciplinary team in the form of stem cell transplant, recurrent transfusions, medical treatment to prevent complications and surveillance for malignancy.
- Risk assessment and genetic counselling of asymptomatic family members according to the mode of inheritance.
- Improvement of delineation of genotype-phenotype correlation.

Genes & Diseases

Gene	OMIM Diseases	Inheritance*	% Gene Coverage (20x)	HGMD**
ABCB7	Anemia, Ataxia	X,XR,G	100	-
ACBD5	Retinal Dystrophy, Leukodystrophy	AR	100	3 of 3
ACD	Dyskeratosis Congenita, Melanoma, Hoyeraal-Hreidarsson Syndrome	AD,AR	99.89	14 of 14
ADA2	Polyarteritis Nodosa, Sneddon Syndrome, Blackfan-Diamond Anemia	AR	100	-
AK2	Reticular Dysgenesia	AR	100	21 of 21
ALAS2	Anemia, Protoporphyria	X,XR,XD,G	100	-
ANKRD26	Thrombocytopenia	AD	98.76	3 of 23
AP3B1	Hermansky-Pudlak Syndrome	AR	100	34 of 35
ATM	Ataxia-Telangiectasia, Breast Cancer, Mantle Cell Lymphoma	AD,AR	99.93	1608 of 1632
ATR	Cutaneous Telangiectasia And Cancer Syndrome, Seckel Syndrome	AD,AR	99.98	39 of 40
ATRX	Alpha-Thalassemia Myelodysplasia Syndrome, Carpenter-Waziri Syndrome, Chudley-Lowry-Hoar Syndrome, Holmes-Gang Syndrome, Juberg-Marsidi Syndrome, Neuroendocrine Tumor Of Stomach, Smith-Fineman-Myers Syndrome	X,XR,XD,G	98.5	-
BLM	Bloom Syndrome	AR	97.19	133 of 141
BRCA1	Breast Cancer, Fanconi Anemia, Pancreatic Carcinoma, Peritoneal Carcinoma	AD,AR,MU	98.97	2783 of 2894
BRCA2	Fanconi Anemia, Glioma Susceptibility, Medulloblastoma, Multiple Cancer Types, Wilms Tumor, Nephroblastoma	AD,AR,MU	98.51	3343 of 3451
BRIP1	Fanconi Anemia, Breast And Ovarian Cancer Syndrome	AD,AR	94.97	235 of 237
CARD11	B-Cell Expansion, Immunodeficiency	AD,AR	100	30 of 31
CBL	Leukemia, Noonan Syndrome, Mastocytosis	AD	100	46 of 47
CDAN1	Anemia	AR	99.59	68 of 68
CDIN1	Anemia	AR	-	-
CEBPA	Leukemia	AD	67.47	14 of 17
CHEK2	Li-Fraumeni Syndrome, Osteosarcoma, Prostate Cancer , Breast And Ovarian Cancer	AD	99.47	307 of 310
CLPB	3-Methylglutaconic Aciduria	AR	96	26 of 26
CSF3R	Neutropenia	AR	99.99	19 of 19
CTC1	Cerebroretinal Microangiopathy, Dyskeratosis Congenita	AR	99.73	43 of 44
CTLA4	Autoimmune Lymphoproliferative Syndrome, Hashimoto Thyroiditis, Lupus Erythematosus, Mycosis Fungoides, Granulomatosis, Sézary Syndrome	AD	99.97	60 of 60
CXCR4	Whim Syndrome	AD	100	19 of 19
DCLRE1B	Hoyeraal Hreidarsson Syndrome, Dyskeratosis, Spastic Paraplegia	-	99.77	1 of 1
DDX41	Myeloproliferative And Lymphoproliferative Neoplasms	AD	99.99	56 of 56
DKC1	Dyskeratosis Congenita, Hoyeraal-Hreidarsson Syndrome	X,XR,G	100	-

DNAJC21	Bone Marrow Failure Syndrome, Shwachman-Diamond Syndrome	AR	99.83	12 of 12
DNMT3A	Heyn-Sproul-Jackson Syndrome, Leukemia, Tatton-Brown-Rahman Syndrome, Pheochromocytoma, Paraganglioma	AD	99.95	67 of 68
DUT	Cysticercosis	-	99.5	1 of 1
EFL1	Shwachman-Diamond Syndrome	AR	99.94	-
ELANE	Cyclic Hematopoiesis, Neutropenia	AD	100	227 of 227
EPCAM	Colorectal Cancer, Diarrhea, Lynch Syndrome	AR	99.94	52 of 70
EPO	Diamond-Blackfan Anemia, Erythrocytosis	AD,AR	99.89	3 of 4
ERCC4	Fanconi Anemia, Xeroderma Pigmentosum, Xfe Progeroid Syndrome, Cockayne Syndrome	AR	99.68	69 of 72
ERCC6L2	Bone Marrow Failure Syndrome	AR	97.82	13 of 14
ETV6	Leukemia, Thrombocytopenia	AD	100	41 of 41
FANCA	Fanconi Anemia	AR	95.17	497 of 502
FANCB	Fanconi Anemia, Vacterl, Hydrocephalus	X,XR,G	95.53	-
FANCC	Fanconi Anemia	AR	100	75 of 75
FANCD2	Fanconi Anemia	AR	100	62 of 63
FANCE	Fanconi Anemia	AR	97	17 of 18
FANCF	Fanconi Anemia	AR	99.31	17 of 18
FANCG	Fanconi Anemia	-	100	94 of 94
FANCI	Fanconi Anemia	AR	100	53 of 54
FANCL	Fanconi Anemia	AR	100	25 of 26
FANCM	Ovarian And Spermatogenic Failure, Fanconi Anemia, Male Infertility With Azoospermia Or Oligozoospermia	AR	99.73	59 of 61
FAS	Autoimmune Lymphoproliferative Syndrome, Behçet Disease, Vogt-Koyanagi-Harada Disea	AD	100	135 of 135
G6PC3	Neutropenia	AR	100	45 of 45
GATA1	Anemia, Down Syndrome, Thrombocytopenia, Hemolysis, Beta-Thalassemia, Blackfan-Diamond Anemia, Congenital Erythropoietic Porphyria	X,XR,G	99.93	-
GATA2	Dendritic Cell, Monocyte, B Lymphocyte, And Natural Killer Lymphocyte Deficiency, Leukemia, Lymphedema, Myelodysplastic Syndrome, Deafness	AD	100	137 of 142
GFI1	Neutropenia	AD	98.77	4 of 4
GLRX5	Anemia, Spasticity With Hyperglycinemia	AR	97.17	7 of 8
GMPS	Pallister-Killian Syndrome	-	99.91	-
GNE	Nonaka Myopathy, Sialuria	AD,AR	99.97	248 of 253
GP1BA	Bernard-Soulier Syndrome, Neuropathy, Von Willebrand Disease, Thrombocytopenia	AD,AR	99.98	73 of 73
HAX1	Neutropenia	AR	100	22 of 23
HOXA11	Radioulnar Synostosis, Amegakaryocytic Thrombocytopenia	AD	99.92	3 of 3
IKZF1	Immunodeficiency, Stevens-Johnson Syndrome	AD	99.98	43 of 43
ITGA2B	Glanzmann Thrombasthenia, Thrombocytopenia	AD,AR	100	237 of 239
ITK	Lymphoproliferative Syndrome	AR	100	19 of 19
JAGN1	Neutropenia	AR	99.95	10 of 10
JAK2	Budd-Chiari Syndrome, Erythrocytosis, Leukemia, Myelofibrosis, Polycythemia Vera, Thrombocythemia, Thrombocytosis	AD,AR	99.63	25 of 27
KDM1A	Cleft Palate, Developmental Delay	AD	98.18	16 of 16
KIF23	Dyserythropoietic Anemia	-	99.63	3 of 3
KIT	Gastrointestinal Stromal Tumor, Leukemia, Mast Cell Disease, Piebald Trait, Testicular Tumor, Piebaldism, Mastocytosis, Hematologic Neoplasm	AD	100	112 of 112

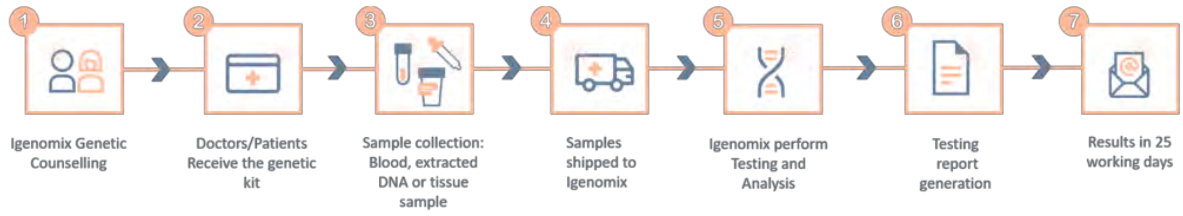
KLF1	Anemia, Beta-Thalassemia	AD	99.76	48 of 50
KRAS	Aplasia Cutis Congenita, Cardiofaciocutaneous Syndrome, Leukemia, Noonan Syndrome, Autoimmune Lymphoproliferative Syndrome, Schimmelpenning-Feuerstein-Mims Syndrome, Encephalocraniocutaneous Lipomatosis, Linear Nevus Sebaceus Syndrome, Lynch Syndrome, Toriello-Lacassie-Droste Syndrome	AD	100	38 of 38
LAMTOR2	Primary Immunodeficiency Syndrome	AR	100	1 of 1
LIG4	Lig4 Syndrome, Myeloma, Dubowitz Syndrome, Omenn Syndrome	AR	99.48	46 of 46
LYST	Chediak-Higashi Syndrome	AR	99.98	117 of 117
MAD2L2	Fanconi Anemia	AR	99.91	1 of 1
MASTL	Thrombocytopenia, Gray Platelet Syndrome	-	99.95	5 of 5
MBD4	Rett Syndrome, Angelman Syndrome	-	100	14 of 14
MECOM	Radioulnar Synostosis, Thrombocytopenia	AD	99.97	26 of 27
MLH1	Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome, Lynch Syndrome	AD,AR	99.94	1079 of 1118
MPIG6B	Thrombocytopenia, Anemia, Myelofibrosis	AR	-	-
MPL	Thrombocytopenia, Myelofibrosis, Thrombocytosis, Polycythemia Vera	AD,AR	100	55 of 55
MSH2	Lynch Syndrome, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome	AD,AR	99.99	1032 of 1057
MSH6	Colorectal Cancer, Endometrial Carcinoma, Mismatch Repair Cancer Syndrome, Lynch Syndrome, Muir-Torre Syndrome	AD,AR	99.28	613 of 641
MYH9	Deafness, May-Hegglin Anomaly	AD	100	144 of 145
MYSM1	Bone Marrow Failure Syndrome, Skeletal Dysplasia	AR	98.5	4 of 4
NAF1	Diskeratosis	-	99.74	2 of 2
NBN	Aplastic Anemia, Leukemia, Nijmegen Breakage Syndrome	AR,MU,P	100	200 of 200
NF1	Leukemia, Noonan Syndrome, Neurofibromatosis, Watson Syndrome, 17q11.2 Microduplication Syndrome, Pheochromocytoma-Paraganglioma	AD	97.97	3082 of 3166
NHP2	Dyskeratosis Congenita	AR	100	3 of 3
NOP10	Dyskeratosis Congenita	AR	100	1 of 1
NRAS	Colorectal Cancer, Thyroid Cancer, Epidermal Nevus, Noonan Syndrome, Autoimmune Lymphoproliferative Syndrome, Schimmelpenning-Feuerstein-Mims Syndrome, Melanocytic Nevus	AD	100	15 of 15
PALB2	Fanconi Anemia, Pancreatic Carcinoma, Breast And Ovarian Cancer	AD,AR	98.78	601 of 617
PARN	Dyskeratosis Congenita, Pulmonary Fibrosis, Bone Marrow Failure, Hoyeraal-Hreidarsson Syndrome, Idiopathic Pulmonary Fibrosis	AD,AR	99.98	33 of 33
PAX5	Gray Zone Lymphoma	-	100	8 of 8
PGM3	Immunodeficiency	AR	99.99	17 of 17
PIEZO1	Stomatocytosis, Lymphedema	AD,AR	99.98	107 of 107
PMS2	Colorectal Cancer, Mismatch Repair Cancer Syndrome, Lynch Syndrome	AD,AR	97.17	264 of 285
POT1	Glioma, Melanoma	AD	99.76	42 of 47
PRF1	Aplastic Anemia, Hemophagocytic Lymphohistiocytosis, Lymphoma Non-Hodgkin	AR	99.99	196 of 196
PTPN11	Myelomonocytic Leukemia, Leopard Syndrome, Metachondromatosis, Noonan Syndrome	AD	100	150 of 151
PTPRJ	Colorectal Cancer	AD	97.97	9 of 10
PUS1	Mitochondrial Myopathy, Sideroblastic Anemia	AR	99.58	13 of 14
RAB27A	Griscelli Syndrome	AR	100	54 of 55
RAC2	Hypogammaglobulinemia, Neutrophil Immunodeficiency Syndrome	AD,AR	100	5 of 5
RAD51	Breast And Ovarian Cancer, Fanconi Anemia, Mirror Movements	AD	99.98	16 of 16

RAD51C	Breast-Ovarian Cancer, Fanconi Anemia	AR	100	130 of 130
RAD51D	Breast And Ovarian Cancer	-	100	97 of 97
RBBP6	Retinoblastoma, Esophageal Cancer	-	99.38	6 of 6
RBM8A	Thrombocytopenia, Absent Radius Syndrome	AR	100	4 of 4
RFWD3	Fanconi Anemia	AR	99.99	2 of 2
RMRP	Anauxetic Dysplasia, Hypoplasia, Omenn Syndrome	AR	-	-
RPL11	Diamond-Blackfan Anemia	AD	100	52 of 52
RPL15	Diamond-Blackfan Anemia	AD	99.74	8 of 9
RPL26	Diamond-Blackfan Anemia	AD	92.97	1 of 1
RPL27	Diamond-Blackfan Anemia	AD	100	2 of 2
RPL31	Blackfan-Diamond Anemia	-	100	0 of 1
RPL35	Diamond-Blackfan Anemia	AD	100	1 of 1
RPL35A	Diamond-Blackfan Anemia	AD	100	12 of 12
RPL5	Diamond-Blackfan Anemia	AD	100	95 of 95
RPL9	Diamond-Blackfan Anemia	-	100	2 of 2
RPS10	Diamond-Blackfan Anemia	AD	100	7 of 7
RPS15A	Diamond-Blackfan Anemia	AD	98.74	1 of 1
RPS17	Diamond-Blackfan Anemia	AD	0	0 of 7
RPS19	Diamond-Blackfan Anemia	AD	78	159 of 165
RPS24	Diamond-Blackfan Anemia	AD	90.17	11 of 14
RPS26	Diamond-Blackfan Anemia	AD	100	28 of 29
RPS27	Diamond-Blackfan Anemia	AD	99.85	1 of 1
RPS28	Diamond-Blackfan Anemia, Mandibulofacia Dysostasis	AD	100	1 of 1
RPS29	Diamond-Blackfan Anemia	AD	100	4 of 4
RPS7	Diamond-Blackfan Anemia	AD	100	7 of 10
RTEL1	Dyskeratosis Congenita, Pulmonary Fibrosis, Bone Marrow Failure, Hoyeraal-Hreidarsson Syndrome	AD,AR	99.73	127 of 131
RUNX1	Leukemia, Platelet Disorder, Systemic Mastocytosis	AD	99.83	90 of 90
SAMD9	Mirage Syndrome, Tumoral Calcinosis	AD,AR	99.72	45 of 46
SAMD9L	Ataxia-Pancytopenia Syndrome	AD	99.81	39 of 39
SBDS	Aplastic Anemia, Shwachman-Diamond Syndrome	AR	100	77 of 79
SBF2	Charcot-Marie-Tooth Disease	AR	99.98	44 of 44
SEC23B	Anemia, Cowden Syndrome	AD,AR	100	119 of 127
SETBP1	Mental Retardation, Schinzel-Giedion Syndrome	AD	98.61	43 of 43
SH2B3	Erythrocytosis, Myelofibrosismyelofibrosis With Myeloid Metaplasia, Thrombocythemia	AD	93.59	17 of 17
SH2D1A	Lymphoproliferative Syndrome	X,XR,G	99.94	-
SLC19A2	Thiamine-Responsive Megaloblastic Anemia Syndrome	AR	99.99	67 of 68
SLC25A38	Anemia	AR	100	32 of 32
SLC35C1	Congenital Disorder Of Glycosylation	AR	99.73	8 of 8
SLC37A4	Glycogen Storage Disease	AR	99.97	112 of 112
SLX4	Fanconi Anemia	AR	99.92	76 of 76
SMARCD2	Specific Granule Deficiency	AR	91.58	1 of 1
SRP54	Neutropenia, Shwachman-Diamond Syndrome	AD,AR	99.95	8 of 8

SRP72	Bone Marrow Failure Syndrome	AD	99.95	3 of 3
STAT3	Autoimmune Disease, Leukemia, Hyper-Ige Syndrome, Diabetes Mellitus	AD	100	171 of 171
STIM1	Immune Dysfunction, T-Cell Inactivation, Myopathy, Stormorken Syndrome	AD,AR	100	28 of 28
STN1	Cerebroretinal Microangiopathy, Idiopathic Pulmonary Fibrosis	AR	99.87	-
STX11	Hemophagocytic Lymphohistiocytosis	AR	100	24 of 24
STXBP2	Hemophagocytic Lymphohistiocytosis	AR	99.17	88 of 93
TAZ	Barth Syndrome, Dilated Cardiomyopathy	X,XR,G	100	-
TCIRG1	Osteopetrosis, Neutropenia, Dysosteosclerosis	AR	100	140 of 146
TERC	Dyskeratosis Congenita, Pulmonary Fibrosis, Bone Marrow Failure, Aplastic Anemia, Idiopathic Pulmonary Fibrosis	AD	-	-
TERF2IP	Familial Melanoma	-	94.94	6 of 6
TERT	Aplastic Anemia, Dyskeratosis Congenita, Leukemia, Melanoma, Meningioma, Pulmonary Fibrosis, Bone Marrow Failure, Hoyeraal-Hreidarsson Syndrome	AD,AR	99.09	194 of 197
TET2	Myelodysplastic Syndrome, Sideroblastic Anemia, Mastocytosis, Essential Thrombocythemia, Polycythemia Vera, Primary Myelofibrosis, Refractory Anemia	-	99.96	15 of 15
THPO	Thrombocythemia	AD	100	11 of 11
TINF2	Dyskeratosis Congenita, Revesz Syndrome, Hoyeraal-Hreidarsson Syndrome	AD	99.94	47 of 47
TP53	Bone Marrow Failure, Glioma, Li-Fraumeni Syndrome, Nasopharyngeal Carcinoma, Papilloma Of Choroid Plexus, Essential Thrombocythemia, Multiple Cancer Types	AD,MU,P	98.92	557 of 563
TRNT1	Retinitis Pigmentosa, Erythrocytic Microcytosis, Sideroblastic Anemia, B-Cell Immunodeficiency, Periodic Fevers, Developmental Delay	AR	99.47	22 of 27
TSR2	Diamond-Blackfan Anemia	X,XR,G	99.96	-
TUBB1	Macrothrombocytopenia	AD	100	13 of 13
UBE2T	Fanconi Anemia	AR	100	4 of 4
UNC13D	Hemophagocytic Lymphohistiocytosis	AR	99.78	197 of 202
USB1	Poikiloderma, Neutropenia, Dyskeratosis Congenita	AR	100	24 of 24
VPS13B	Cohen Syndrome	AR	99.98	182 of 190
VPS45	Neutropenia	AR	100	4 of 4
WAS	Neutropenia, Thrombocytopenia, Wiskott-Aldrich Syndrome	X,XR,G	100	-
WDR1	Periodic Fever, Immunodeficiency, Thrombocytopenia	AR	100	9 of 9
WIPF1	Wiskott-Aldrich Syndrome	AR	99.79	3 of 3
WRAP53	Dyskeratosis Congenita	AR	100	10 of 10
XIAP	Lymphoproliferative Syndrome	X,XR,G	99.94	-
XRCC2	Fanconi Anemia, Male Infertility With Azoospermia Or Oligozoospermia	AR	98.39	28 of 28
YARS2	Myopathy, Sideroblastic Anemia	AR	100	22 of 22
ZCCHC8	Pulmonary Fibrosis, Bone Marrow Failure	AD	98.53	2 of 2

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

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