

Hereditary Bone Marrow Failure Panel, Sequencing and Deletion/Duplication

Last Literature Review: August 2022 Last Update: June 2025

Bone marrow failure (BMF) encompasses a heterogenous array of acquired and germline conditions characterized by qualitative or quantitative defects in one or more hematopoietic lineages resulting in cytopenias and hypocellular bone marrow. These include inherited syndromes such as Fanconi anemia (FA), telomere biology disorders (TBD) such as dyskeratosis congenita (DC), Schwachman-Diamond syndrome (SDS), Diamond-Blackfan anemia (DBA), congenital amegakaryocytic thrombocytopenia (CAMT), severe congenital neutropenia (SCN), aplastic anemia, and others.

This panel includes genes causative for hereditary BMF syndromes as well as genes associated with hereditary predisposition to myeloid neoplasms, as there is often clinical overlap between these two entities.

Featured ARUP Testing

Hereditary Bone Marrow Failure Panel, Sequencing and Deletion/Duplication 3001615 Method: Massively Parallel Sequencing

- Use to assess for inherited/germline DNA variants associated with bone marrow failure or hereditary predisposition to myeloid neoplasms.
- Preferred sample type is cultured skin fibroblasts; testing whole blood in affected patients may not definitively determine germline status.
- Not intended to detect somatic variants; refer to the Laboratory Test Directory for myeloid malignancy panel testing.

Disease Overview

Hereditary BMF syndromes are caused by germline pathogenic variants that disrupt DNA repair, telomere maintenance, ribosome biogenesis, and structural protein pathways. In addition to BMF, these conditions may also be accompanied by syndromic physical findings and predisposition to hematologic and other malignancies. While most patients with hereditary BMF present in childhood, these conditions may manifest at any age.

Genetics

Genes

For a list of genes tested, associated disorders, and inheritance, refer to the Genes Tested table.

Refer to Limitations for exons not covered by sequencing and genes for which deletion and/or duplication is not available.

Test Interpretation

Methodology

This test is performed using the following sequence of steps:

- Selected genomic regions, primarily coding exons and exon-intron boundaries, from the targeted genes are isolated from extracted genomic DNA using a probe-based hybrid capture enrichment workflow.
- Enriched DNA is sequenced by massively parallel sequencing (MPS; also known as next generation sequencing, or NGS) followed by pairedend read alignment and variant calling using a custom bioinformatics pipeline. The pipeline includes an algorithm for the detection of large deletions and duplications.
- Sanger sequencing is performed as necessary to fill in regions of low coverage and in certain situations, to confirm variant calls.
- Large deletion/duplication calls made using MPS are confirmed by an orthogonal exon-level microarray when sample quality and technical conditions allow.

Analytic Sensitivity/Specificity

Variant Class	Analytic Sensitivity (PPA) Estimate ^a (%) and 95% Credibility Region	Analytic Specificity (NPA) Estimate (%)
SNVs	>99 (96.9-99.4)	>99.9
Deletions 1-10 bp ^b	93.8 (84.3-98.2)	>99.9
Insertions 1-10 bp ^b	94.8 (86.8-98.5)	>99.9
Exon-level ^c deletions	97.8 (90.3-99.8) [2 exons or larger] 62.5 (38.3-82.6) [single exon]	>99.9
Exon-level ^c duplications	83.3 (56.4-96.4) [3 exons or larger]	>99.9

^aPPA values are derived from larger methods-based MPS and/or Sanger validations. These values do not apply to testing performed by multiplex ligation-dependent probe amplification (MLPA) unless otherwise indicated.

^bVariants greater than 10 bp may be detected, but the analytic sensitivity may be reduced.

^cIn most cases, a single exon deletion or duplication is less than 450 bp and 3 exons span a genomic region larger than 700 bp.

bp, base pairs; NPA, negative percent agreement; PPA, positive percent agreement; SNVs, single nucleotide variants

Limitations

- A negative result does not exclude a diagnosis of bone marrow failure.
- Diagnostic errors can occur due to rare sequence variations.
- Interpretation of this test result may be impacted if this patient received an allogeneic stem cell transplant unless the sample analyzed is definitively from the recipient, such as cultured skin fibroblasts.
- The germline or somatic status of a detected variant cannot be definitively determined in patients with hematologic malignancy if the assay is performed on blood or other tissue that may be contaminated by clonal or malignant cells; testing a definitively germline specimen such as cultured fibroblasts may be recommended in such cases.
- The following will not be evaluated:
 - · Variants outside the coding regions and intron-exon boundaries of targeted genes
 - SBDS gene associated with Schwachman-Diamond syndrome
 - Regulatory region and deep intronic variants
 - SNVs and small insertions/deletions will not be called in the following exons due to technical limitations of the assay:
 - CXCR4 (NM_001348056) exon 2
 - CXCR4 (NM_001348059) exon 2
 - DNAJC21 (NM_001348420) partial exon 9 (Chr5:34945827-34945845)
 - ERCC6L2 (NM_001375291) exon 19
 - *ERCC6L2* (NM_001375292) exon 19
 - *ERCC6L2* (NM_001375293) exon 18
 - *ERCC6L2* (NM_001375294) exon 18
 - FANCA (NM_001018112) exon 11
 - FANCA (NM_001351830) exon 10
 - *FANCD2* (NM_033084) exons 14, 17, 21, 22
 - FANCD2 (NM_001018115) exons 14, 17, 21, 22
 - FANCD2 (NM_001319984) exons 14, 17, 21, 22
 - FANCD2 (NM_001374253) exons 14, 17, 20, 21
 - FANCD2 (NM_001374254) exons 14, 17, 21, 22
 - FANCD2 (NM_001374255) exon 10
 - FANCL (NM_001374615) exon 8
 - Deletions/duplications in CEBPA, NOP10, RMRP, and RPL15 genes
 - Duplications in the TERC gene
 - Breakpoints of large deletions/duplications
- The following may not be detected:
- Deletions/duplications/insertions of any size by massively parallel sequencing
- Large duplications less than 3 exons in size

- Noncoding transcripts
- Some variants due to technical limitations in the presence of pseudogenes and/or repetitive/homologous regions
- Low-level somatic variants

Genes Tested

Gene	MIM #	Disorders	Inheritance
ACD	609377	Dyskeratosis congenita	AD, AR
ALAS2	301300	Sideroblastic anemia Erythropoietic protoporphyria	XL
ANKRD26	610855	Thrombocytopenia 2	AD
ATM	607585	Ataxia-telangiectasia	AR
BLM	604610	Bloom syndrome	AR
BRCA1	113705	Fanconi anemia, complementation group S	AR
		Hereditary breast and ovarian cancer syndrome	AD
BRCA2	600185	Fanconi anemia, complementation group D1	AR
		Hereditary breast and ovarian cancer syndrome	AD
BRIP1	605882	Fanconi anemia, complementation group J	AD
CBL	165360	Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia	AD
CEBPA	116897	Familial acute myeloid leukemia	AD
CSF3R	138971	Severe congenital neutropenia 7	AR
CTC1	613129	Dyskeratosis congenita Coats plus syndrome	AR
CXCR4	162643	WHIM syndrome	AD
DDX41	608170	Familial myeloproliferative/lymphoproliferative neoplasms	AD
DKC1	300126	Dyskeratosis congenita	XL
DNAJC21	617048	Bone marrow failure syndrome 3	AR
ELANE	130130	Cyclic neutropenia Severe congenital neutropenia 1	AD
ERCC4	133520	Xeroderma pigmentosum, group F Fanconi anemia, complementation group Q	AR
ERCC6L2	615667	Bone marrow failure syndrome 2	AR
ETV6	600618	Thrombocytopenia 5	AD
FANCA	607139	Fanconi anemia, complementation group A	AR
FANCB	300515	Fanconi anemia, complementation group B	XL
FANCC	613899	Fanconi anemia, complementation group C	AR
FANCD2	613984	Fanconi anemia, complementation group D2	AR
FANCE	613976	Fanconi anemia, complementation group E	AR

Gene	MIM #	Disorders	Inheritance
FANCF	613897	Fanconi anemia, complementation group F	AR
FANCG	602956	Fanconi anemia, complementation group G	AR
FANCI	611360	Fanconi anemia, complementation group I	AR
FANCL	608111	Fanconi anemia, complementation group L	AR
G6PC3	611045	Dursun syndrome Severe congenital neutropenia 4	AR
GATA1	305371	Dyserythropoietic anemia and thrombocytopenia	XL
GATA2	137295	Familial acute myeloid leukemia and myelodysplastic syndrome	AD
GFI1	600871	Severe congenital neutropenia 2	AD
HAX1	605998	Severe congenital neutropenia 3	AR
HOXA11	142958	Radioulnar synostosis with amegakaryocytic thrombocytopenia 1	AD
IKZF1	603023	Common variable immunodeficiency 13	AD
KRAS	190070	Noonan syndrome	AD
MBD4	603574	Susceptibility to acute myeloid leukemia	Unknown
MPL	159530	Congenital amegakaryocytic thrombocytopenia (CAMT)	AR
МҮН9	160775	Macrothrombocytopenia and granulocyte inclusions with or without nephritis or sensorineural hearing loss	AD
NBN	602667	Aplastic anemia Nijmegen breakage syndrome	AR
NHP2	606470	Dyskeratosis congenita	AR
NOP10	606471	Dyskeratosis congenita	AR
NRAS	164790	Noonan syndrome	AD
PALB2	610355	Fanconi anemia, complementation group N	AR
PARN	604212	Dyskeratosis congenita	AR
		Pulmonary fibrosis and/or bone marrow failure	AD
PTPN11	176876	Noonan syndrome	AD
RAD51C	602774	Fanconi anemia, complementation group O	AR
RMRP	157660	Aplastic anemia Cartilage-hair hypoplasia	AR
RPL11	604175	Diamond-Blackfan anemia 7	AD
RPL15	604174	Diamond-Blackfan anemia 12	AD
RPL26	603704	Diamond-Blackfan anemia 11	AD
RPL35A	180468	Diamond-Blackfan anemia 5	AD
RPL5	603634	Diamond-Blackfan anemia 6	AD
RPS10	603632	Diamond-Blackfan anemia 9	AD

RPS70 60347 Namod Blackfan amenia 1 Apple RPS24 602412 Namod Blackfan amenia 3 Apple RPS74 60300 Namod Blackfan amenia 10 Apple RPS74 60383 Namod Blackfan amenia 2000 menia 900 menia	Gene	MIM #	Disorders	Inheritance
RPS26 603701 Dimond-Blackfan anemia 10 AD RPS7 603658 Dimond-Blackfan anemia 8 AD RTE1 60832 Pulmonary fibrosis and/or bone marrow failure AD RTE1 60832 Pulmonary fibrosis and/or bone marrow failure AD RTM7 15138 Familial platelet disorder with associated myeloid malignancy AD RUN7 15138 Familial platelet disorder with associated myeloid malignancy AD SMMD9 010450 Monosomy 7 myeloidysplasia and leukemia syndrome AD SMMD91 011070 Monosomy 7 myeloidysplasia and leukemia syndrome AD SKAMD91 011702 Monosomy 7 myeloidysplasia and leukemia syndrome AD SKAMD91 011702 Monosomy 7 myeloidysplasia and leukemia syndrome AD SKAMD91 011702 Monosomy 7 myeloidysplasia and leukemia syndrome AD SKAMD91 011702 Monosomy 7 myeloidysplasia and leukemia syndrome AD SKAMD91 011702 Bone marow failure syndrome 1 AD SKAMD91 011702 Bone marow failure syndrome 3 AD SKAMD91 0128 Dyekeratosis congenita AD SKAT 16292 Dyekeratosis congenita AD SKAT 111702	RPS19	603474	Diamond-Blackfan anemia 1	AD
RPS7 60858 Diamond-Blackfan anemia 8 AD RTE1 60858 Pulmonary fibrosis and/or bore marrow failure AD RTMX1 51305 Familial platelet disorder with associated myeloid malignancy AD SMMDPL 151305 Monosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61010 Monosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61127 Monosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61127 Monosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61127 Nonosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61127 Nonosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61127 Nonosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMMDPL 61278 Sonosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMP2 61278 Sonosomy 7 myelodysplasia and leukemia syndrome MRRGE syndrome AD SMP2 61278 Sonosomy 7 myelodysplasia and leukemia syndrome Multimanary fibrosis AD SMP2 61278 Sonosomy 7 myelodysplasia and leukemia syndrome Multimanary fibrosis AD TFAT 1928 So	RPS24	602412	Diamond-Blackfan anemia 3	AD
RTEL1 69833 [Pulmonary fibrosis and/or bone marrow failure AD Queerators congenita AD, AR RUXX 15136 Familial platelet disorder with associated myeloid malignancy AD SAMDP 610450 Monosomy 7 myelodysplasia and leukemia syndrome AD SAMDPL 610450 Monosomy 7 myelodysplasia and leukemia syndrome AD SAMDPL 610370 Monosomy 7 myelodysplasia and leukemia syndrome AD SAMDPL 611270 Monosomy 7 myelodysplasia and leukemia syndrome AD SAMDPL 611270 Ansonomy 7 myelodysplasia and leukemia syndrome AD SAMDPL 611270 Ansonomy 7 myelodysplasia and leukemia syndrome AD SRP72 60128 Panconianemia, complementation group P AD SRP72 60212 posterators congenita AD, AR TFR 18720 posterators congenita AD, AR TFR 18720 posterators congenita AD TFR 18720 posterators congenita neutropenia AD TFR3 10120 posterators congenita neutropenia	RPS26	603701	Diamond-Blackfan anemia 10	AD
Image: Participant service AD, AR RUX1 15136 Familial platelet disorder with associated myeloid malignary AD SMADP 61045 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61050 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61170 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61170 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61170 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61170 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61170 Monosomy 7 myelodysplasia and leukemia syndrome AD SMADPL 61272 61283 Faconi anemia, complementation group P AD TFAT 17270 Oyskeratosis congenita Monodeficiency AD TFAT 17281 Oyskeratosis congenita AD TFAT 161281 Inframeni syndrome AD TFAT 161281 Inframeni syndrome AD UB271 161281 </td <td>RPS7</td> <td>603658</td> <td>Diamond-Blackfan anemia 8</td> <td>AD</td>	RPS7	603658	Diamond-Blackfan anemia 8	AD
RURX1151385Familial platelet disorder with associated myeloid malignancyADSAMD961056Monosomy 7 myelodysplasia and leukenia syndromeADSAMD9L61170Monosomy 7 myelodysplasia and leukenia syndromeADSAMD9L61170Monosomy 7 myelodysplasia and leukenia syndromeADSLX4613278Fanconi anemia, complementation group PARSRP7260212Bone marrow failure syndrome 1ADTERC60232Dyskeratosis congenitaADTERT187270Dyskeratosis congenitaADTER761283ImmunodeficiencyARTER761283ImmunodeficiencyADTER761319Dyskeratosis congenitaADTER761328ImmunodeficiencyADTER761329Dyskeratosis congenitaADTER761330Dyskeratosis congenitaADTER761330Dyskeratosis congenitaADTER761330Dyskeratosis congenitaADTER761430Dyskeratosis congenitaADTER761538Fanconi anemia, complementation group TARUE2761538Fanconi anemia, complementation group TARUS8161035Severe congenital neutropeniaARUFS4561035Severe congenital neutropeniaARUFS45Silvisot Aldrich syndrome, Severe congenital neutropeniaALUS82Viskott Aldrich syndrome, Severe congenital neutropeniaALUS84Sev	RTEL1	608833	Pulmonary fibrosis and/or bone marrow failure	AD
SAMD9610456Monosomy 7 myelodysplasia and leukemia syndromeADSAMD94611170Monosomy 7 myelodysplasia and leukemia syndromeADSLX4613278Facconi anemia, complementation group PARSRP72602120Bone marrow failure syndrome 1ADTERC602322Dyskeratosis congenitaADTERT187270Dyskeratosis congenitaADTER716239munodeficiencyADTINF260419Dyskeratosis congenitaADTINF260439Dyskeratosis congenitaADTINF260439Dyskeratosis congenitaADTINF261039Dyskeratosis congenitaADTINF261039Dyskeratosis congenitaADTINF261039Dyskeratosis congenitaADTINF261039Dyskeratosis congenitaADTINF261039Dyskeratosis congenitaADTINF261039Severe congenital neutropeniaARUBE2761035Severe congenital neutropeniaARVPS4561005Severe congenital neutropeniaARVPS4561005Severe congenital neutropeniaALVISA0T-LAtrich Syndrome, Severe congenital neutropeniaSevere congenital neutropeniaALVISA0T-LAtrich Syndrome, Severe congenital neutropeniaSevere congenital neutropeniaSevere congenital neutropenia			Dyskeratosis congenita	AD, AR
MIRAGE syndromeSAMD9L61170Monosomy 7 myelodysplasia and leukernia syndrome Ataxia-pancytopenia syndromeADSLX4613278Fanconi anemia, complementation group PARSRP72602122Bone marrow fallure syndrome 1ADTRRC602322Dyskeratosis congenita Pulmonary fibrosisADTER7187270Dyskeratosis congenita Pulmonary fibrosisAD, ARTER7187270Dyskeratosis congenita Pulmonary fibrosisAD, ARTF7261239ImmunodeficiencyAD, ARTF7319170Li-Fraumeni syndrome 5ADTVF2461039Fanconi anemia, complementation group TARUBE277610359Fanconi anemia, complementation group TARUSB71610359Fanconi anemia, complementation group TARVFS454610359Severe congenital neutropeniaARVFS454610359Severe congenital neutropeniaARVFS454SouseSevere congenital neutropeniaALVFS454SouseSevere congenital neutropeniaALVFS454SouseSevere congenital neutropeniaALVFS454SouseSevere congenital neutropeniaALVFS454SouseSevere congenital neutropeniaSevere congenital neutropeniaVFS454SouseSevere congenital neutropeniaSevere congenital neutropeniaVFS454SouseSevere congenital neutropeniaSevere congenital neutropeniaVFS454SouseSevere congenital ne	RUNX1	151385	Familial platelet disorder with associated myeloid malignancy	AD
SLX4613278Fanconi anemia, complementation group PARSRP72602122Bone marrow failure syndrome 1ADTERC602322Dyskeratosis congenita Pulmonary fibrosisADTERT187270Dyskeratosis congenita Pulmonary fibrosisAD,ARTERT187270Dyskeratosis congenita Pulmonary fibrosisAD,ARTERT187270Dyskeratosis congenita Pulmonary fibrosisAD,ARTERT187270Dyskeratosis congenita Pulmonary fibrosisAD,ARTERT187270Dyskeratosis congenita Pulmonary fibrosisAD,ARTINF261439Dyskeratosis congenitaADTINF261439Dyskeratosis congenita Pulmonary fibrosisADTINF261035ExercongenitaADUBE2T61035Fanconi anemia, complementation group TARUSB161035Severe congenital neutropeniaARVPS4561035Severe congenital neutropeniaARVMSSilviskott-Aldrich syndrome, Severe congenital neutropenia TrombocytopeniaXL Specifical neutropenia	SAMD9	610456		AD
SRP7260212Bone marrow failure syndrome 1ADTERC602322Dyskeratosis congenita Pulmonary fibrosisADTERT187270Dyskeratosis congenitaAD, ARTET2612839ImmunodeficiencyARTINF2604319Dyskeratosis congenitaADTP53191170LiFraumeni syndrome Bone marrow failure syndrome 5ARUBE2T610305Severe congenital neutropeniaARVPS45610305Severe congenital neutropeniaARWAS303922Wiskott-Aldrich syndrome, Severe congenital neutropeniaXL	SAMD9L	611170		AD
TERC602322Dyskeratosis congenita Pulmonary fibrosisADTERT187270Dyskeratosis congenitaAD, ARTET2612839ImmunodeficiencyARTINF2604319Dyskeratosis congenitaADTINF2604319Dyskeratosis congenitaADTINF2610310Li-Fraumeni syndrome Bone marrow failure syndrome 5ADUBE27610538Fanconi anemia, complementation group TARUSB1610325Severe congenital neutropeniaARVPS45610035Severe congenital neutropeniaARWAS30392Wiskott-Aldrich syndrome, Severe congenital neutropenia ThrombocytopeniaXL	SLX4	613278	Fanconi anemia, complementation group P	AR
Function of spanning Pulmonary fibrosisPulmonary fibrosisTERT187270Dyskeratosis congenitaAD, ARTET2612839ImmunodeficiencyARTINF2604319Dyskeratosis congenitaADTP53191170Li-Fraumeni syndrome Bone marrow failure syndrome 5ADUBE27610538Fanconi anemia, complementation group TARUSB1610355Severe congenital neutropeniaARVPS45610035Severe congenital neutropeniaARWAS30392Wiskott-Aldrich syndrome, Severe congenital neutropenia Thrombocytopenia ThrombocytopeniaXL	SRP72	602122	Bone marrow failure syndrome 1	AD
TET2612839ImmunodeficiencyARTINF2604319Dyskeratosis congenitaADTP53191170Li-Fraumeni syndrome Bone marrow failure syndrome 5ADUBE2T610538Fanconi anemia, complementation group TARUSB1613276Poikiloderma with neutropeniaARVPS45610035Severe congenital neutropeniaARWAS300392Wiskott-Aldrich syndrome, Severe congenital neutropenia ThrombocytopeniaXL	TERC	602322		AD
TINF2604319Dyskeratosis congenitaADTP53191170Li-Fraumeni syndrome Bone marrow failure syndrome 5ADUBE2T610538Fanconi anemia, complementation group TARUSB1613276Poikiloderma with neutropeniaARVPS45610035Severe congenital neutropeniaARWAS30392Wiskott-Aldrich syndrome, Severe congenital neutropenia ThrombocytopeniaXL	TERT	187270	Dyskeratosis congenita	AD, AR
TP5319170Li-Fraumeni syndrome Bone marrow failure syndrome 5ADUBE2T610538Fanconi anemia, complementation group TARUSB1613276Poikiloderma with neutropeniaARVPS45610035Severe congenital neutropeniaARWAS300392Wiskott-Aldrich syndrome, Severe congenital neutropeniaXL	TET2	612839	Immunodeficiency	AR
Bone marrow failure syndrome 5UBE2T610538Fanconi anemia, complementation group TARUSB1613276Poikiloderma with neutropeniaARVPS45610035Severe congenital neutropeniaARWAS300392Wiskott-Aldrich syndrome, Severe congenital neutropeniaXL	TINF2	604319	Dyskeratosis congenita	AD
USB1613276Poikiloderma with neutropeniaARVPS45610035Severe congenital neutropeniaARWAS300392Wiskott-Aldrich syndrome, Severe congenital neutropenia ThrombocytopeniaXL	TP53	191170		AD
VPS45 610035 Severe congenital neutropenia AR WAS 300392 Wiskott-Aldrich syndrome, Severe congenital neutropenia Thrombocytopenia XL	UBE2T	610538	Fanconi anemia, complementation group T	AR
WAS 300392 Wiskott-Aldrich syndrome, Severe congenital neutropenia XL Thrombocytopenia Thrombocytopenia	USB1	613276	Poikiloderma with neutropenia	AR
Severe congenital neutropenia Thrombocytopenia	VPS45	610035	Severe congenital neutropenia	AR
WRAP53 612661 Dyskeratosis congenita AR	WAS	300392	Severe congenital neutropenia	XL
	WRAP53	612661	Dyskeratosis congenita	AR

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108 (800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com

© 2025 ARUP Laboratories. All Rights Reserved.