Supplementary Materials for:

Assessment of technical heterogeneity among diagnostic tests to detect germline risk variants for hematopoietic malignancies

Contents:

S1. Inherited Bone Marrow Failure Syndromes (IBMFS) Assay Characteristics

Company / Institution	Preferred Specimen	# Genes Included	List Price (USD)	Turnaround (days)	CNV Resolution / Limitations	CNV Confirmation	SNV Confirmation
Laboratory I	WB[a]	39	250[b]	10-21	Single exon resolution	MLPA	Long-read sequencing
Laboratory J	WB, purified DNA, saliva[a]	135	1700	28	May not reliably detect partial exon CNVs or indels > 50 bp	ddPCR	Upon Review
Laboratory K	SF	63	3000	42	May not reliably detect partial-exon CNVs or rearrangements < 400 bp	MLPA, qPCR	Sanger
Laboratory L	WB, SF, purified DNA	86	3350	28-42	Single exon resolution	Upon Review	Upon Review
Laboratory M	SF, WB, saliva[a]	116	Not Disclosed	42	Not Detected	Not Detected	Sanger
Laboratory N	SF	133	1450	18	~80% sensitivity for CNVs < 4 exons	aCGH, MLPA	Upon Review
Laboratory O	WB	90	3090.70	42	Reliably detects CNVs of 3+ exons	MLPA/ddPCR	Sanger
Laboratory P	WB, saliva, buccal[a]	60	Not Disclosed	21-35	Not Detected	MLPA, qPCR	Sanger

Eight commercially available IMBFS assays were identified. Data were collected from laboratory websites, test requisition forms, and test information sheets. Laboratory representatives were contacted to verify the data. 7/8 laboratory representatives provided responses to our queries. Multiple tissue specimen types were accepted. Some laboratories (a) indicated the need for non-blood specimens in patients with active hematopoietic malignancies or who had received allogeneic transplants Genes included reflect those on primary IMBFS panels for each laboratory and excluded “add-on” genes. Price reflects the list price before the application of health insurance cost reductions or maximum out-of-pocket (b) policies adopted by some entities. ‘Upon review’ indicates that variants are not reflexively validated but are instead confirmed by secondary methodology only if internal quality standards are not met. “Not Provided” indicates that no information was available on publicly available resources and no response to multiple email inquiries was received at the time of manuscript submission. ‘USD; US dollars, WB; whole blood, SF; skin fibroblasts, CNV; copy number variant, SNV; single nucleotide variant, indel; insertion/deletion, aCGH; array comparative genomic hybridization, MLPA; multiplex ligation-dependent probe amplification, qPCR; quantitative polymerase chain reaction, ddPCR; droplet digital polymerase chain reaction. Commercial IBMFS assays were offered by the following laboratories: Blueprint Genetics Bone Marrow Failure Syndrome Panel, University of Chicago Medical Center Inherited Bone Marrow Failure Panel, Cincinnati Children’s Hospital Bone Marrow Failure Gene Sequencing Panel, Fulgent Bone Marrow Failure NGS Panel, Invitae Bone Marrow Failure Syndromes

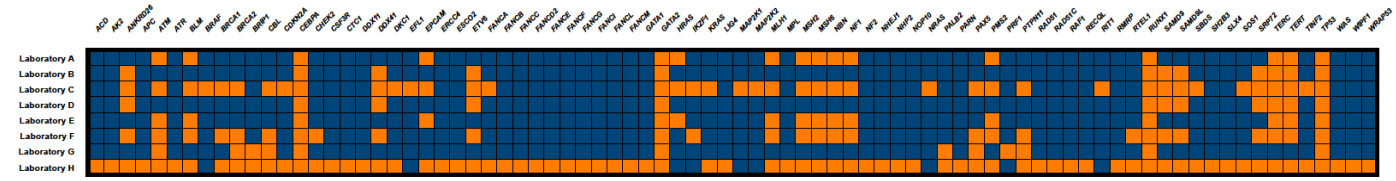
Panel, Children's Hospital of Philadelphia Bone Marrow Failure Panel, Prevention Genetics Inherited Bone Marrow Failure Panel, and University of Washington MarrowSeq Hereditary Bone Marrow Failure Panel, which are ordered randomly and anonymized above.

S2. ClinVar queries for genes included in 4/8 MDS/AL panels. Data collected Dec 2019.

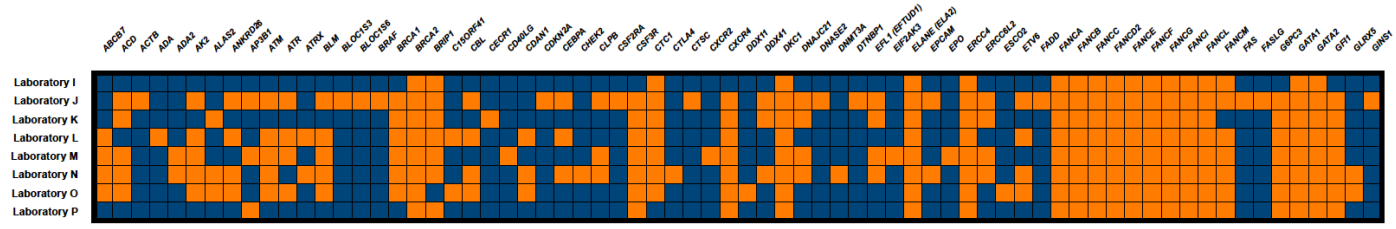
Gene	ClinVar listing?	Pathogenic/likely pathogenic germline/ *de novo* mutations (#)	ClinVar SNVs?	ClinVar CNVs?
ANKRD26	Yes	6	Yes	Yes
ATM	Yes	915	Yes	Yes
BLM	Yes	70	Yes	Yes
BRCA2	Yes	3398	Yes	Yes
CBL	Yes	24	Yes	Yes
CEBPA	Yes	6	No	Yes
DDX41	Yes	18	Yes	Yes
EPCAM	Yes	56	Yes	Yes
ETV6	Yes	17	Yes	Yes
GATA2	Yes	50	Yes	Yes
MLH1	Yes	878	Yes	Yes
MSH2	Yes	962	Yes	Yes
MSH6	Yes	703	Yes	Yes
NBN	Yes	164	Yes	Yes
NF1	Yes	1284	Yes	Yes
PAX5	Yes	10	No	Yes
PMS2	Yes	344	Yes	Yes
PTPN11	Yes	111	Yes	No
RUNX1	Yes	47	Yes	Yes
SAMD9	Yes	11	Yes	No
SAMD9L	Yes	5	Yes	No
SRP72	Yes	4	Yes	Yes
TERC	Yes	19	Yes	Yes
TERT	Yes	53	Yes	Yes
TP53	Yes	414	Yes	Yes

S3. Matrix showing each gene of interest by individual laboratory for all MDS/AL genes (n=82).

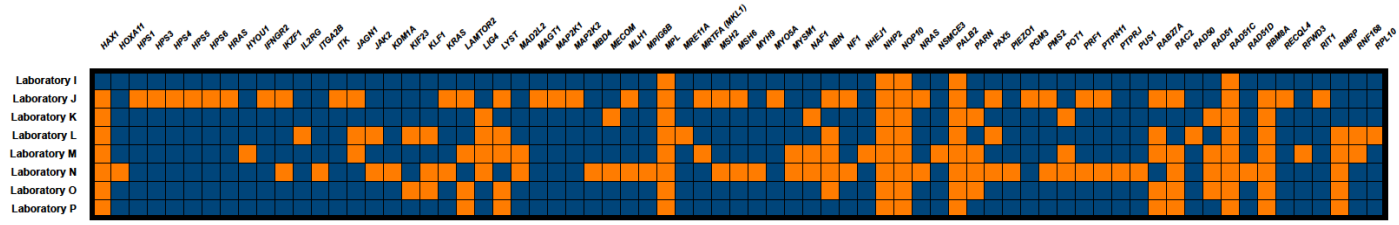
Orange: gene analyzed; Blue: gene omitted.



S4. Matrix showing each IBMFS gene of interest by individual laboratory (part 1, total n for all parts = 212). Orange: gene analyzed; Blue: gene omitted.



S5. Matrix showing each IBMFS gene of interest by individual laboratory (part 2, total n for all parts = 212). Orange: gene analyzed; Blue: gene omitted.



S6. Matrix showing each IBMFS gene of interest by individual laboratory (part 3, total n for all parts = 212). Orange: gene analyzed; Blue: gene omitted.