LETTER TO THE EDITOR

Diagnostic challenges and proposed classification of myeloid neoplasms with overlapping features of thrombocytosis, ring sideroblasts and concurrent del(5q) and *SF3B1* mutations

Authors

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Panel	Genes
30-gene panel	*ASXL1, CBL, CEBPA, DNMT3A, ETV6, EZH2, FLT3, HRAS, IDH1, IDH2, JAK1, JAK2, JAK3, KIT, KRAS, MPL, NPM1, NRAS, PHF6, PTEN, RUNX1, SF3B1, SH2B3, SUZ12, TET1, TET2, TET3, TP53, TYK2, WT1*
49-gene panel	*ASXL1, BCOR, BCORL1, BRAF, CALR, CBL, CBLB, CEBPA, CSF3R, DNMT3A, ETV6, EZH2, FLT3, GATA1, GATA2, GNAS, HRAS, IDH1, IDH2, JAK1, JAK2, JAK3, KDM6A, KIT, KRAS, MAP2K1, MPL, MYD88, NOTCH1, NPM1, NRAS, PHF6, PML, PTEN, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2*
400-gene panel	*ABL1, ACTG1, AKT1, AKT2, AKT3, ALK, ALOX12B, AMER1, APC, AR, ARAF, ARHGEF28, ARID1A, ARID1B, ARID2, ARID3A, ARID3B, ARID3C, ARID4A, ARID4B, ARID5A, ARID5B, ASXL1, ASXL2, ATM, ATP6AP1, ATP6V1B2, ATR, ATRX, ATXN2, AURKA, AURKB, AXIN1, AXL, B2M, BACH2, BAP1, BARD1, BCL10, BCL11B, BCL2, BCL6, BCOR, BCORL1, BCR, BIRC3, BLM, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTG1, BTK, CALR, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD28, CD58, CD79A, CD79B, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1B, CDKN2Ap14ARF, CDKN2Ap16INK4A, CDKN2B, CDKN2C, CEBPA, CHEK1, CHEK2, CIC, CIITA, CRBN, CREBBP, CRKL, CRLF2, CSF1R, CSF3R, CTCF, CTNNB1, CUX1, CXCR4, CYLD, DAXX, DDR2, DDX3X, DIS3, DNMT3A, DOT1L, DTX1, DUSP22, EED, EGFR, EGR1, EP300, EP400, EPHA3, EPHA5, EPHA7, EPHB1, ERBB2, ERBB3, ERBB4, ERG, ESCO2, ESR1, ETNK1, ETV6, EZH2, FAM46C, FANCA, FANCC, FANCD2, FAS, FAT1, FBXO11, FBXW7, FGF19, FGF3, FGF4, FGFR1, FGFR2, FGFR3, FGFR4, FLCN, FLT1, FLT3, FLT4, FOXL2, FOXO1, FOXP1, FURIN, FYN, GATA1, GATA2, GATA3, GNA11, GNA12, GNA13, GNAQ, GNAS, GNB1, GRIN2A, GSK3B, HDAC1, HDAC4, HDAC7, HGF, HIF1A, HIST1H1B, HIST1H1C, HIST1H1D, HIST1H1E, HIST1H2AC, HIST1H2AG, HIST1H2AL, HIST1H2AM, HIST1H2BC, HIST1H2BD, HIST1H2BG, HIST1H2BJ, HIST1H2BK, HIST1H2BO, HIST1H3B, HIST1H3G, HLA-A, HNF1A, HRAS, ID3, IDH1, IDH2, IGF1, IGF1R, IGF2, IKBKE, IKZF1, IKZF3, IL7R, INPP4B, IRF1, IRF4, IRF8, IRS2, JAK1, JAK2, JAK3, JARID2, JUN, KDM5A, KDM5C, KDM6A, KDR, KEAP1, KIT, KMT2A, KMT2B, KMT2D, KMT2C, SETD8, KRAS, KSR2, LCK, LMO1, LTB, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K13, MAP3K14, MAPK1, MAPK3, MCL1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGA, MGAM, MITF, MLH1, MOB3B, MPEG1, MPL, MRE11A, MSH2, MSH6, MTOR, MUTYH, MYC, MYCL1, MYCN, MYD88, NBN, NCOR1, NCOR2, NCSTN, NF1, NF2, NFE2, NFE2L2, NKX2-1, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NRAS, NSD1, NT5C2, NTRK1, NTRK2, NTRK3, P2RY8, PAK7, PALB2, PARP1, PAX5, PBRM1, PCBP1, PDCD1, PDGFRA, PDGFRB, PDPK1, PDS5B, PHF6, PIGA, PIK3C2G, PIK3C3, PIK3CA, PIK3CG, PIK3R1, PIK3R2, PIM1, PLCG1, PLCG2, PMS2, PNRC1, POT1, PPP2R1A, PRDM1, PRKAR1A, PTCH1, PTEN, PTPN1, PTPN11, PTPN2, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD52, RAD54L, RAF1, RARA, RB1, REL, RET, RHOA, RICTOR, RNF43, ROBO1, ROS1, RPTOR, RRAGC, RTEL1, RUNX1, RUNX1T1, SAMHD1, SDHA, SDHB, SDHC, SDHD, SETBP1, SETD1A, SETD1B, SETD2, SETD3, SETD4, SETD5, SETD6, SETD7, SETDB1, SETDB2, SF3B1, SGK1, SH2B3, SMAD2, SMAD4, SMARCA4, SMARCB1, SMARCD1, SMC1A, SMC3, SMG1, SMO, SOCS1, SOX2, SP140, SPEN, SPOP, SRC, SRSF2, STAG1, STAG2, STAT3, STAT5A, STAT5B, STAT6, STK11, SUFU, SUZ12, SYK, TBL1XR1, TBX3, TERT, TET1, TET2, TET3, TGFBR2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TRAF2, TRAF3, TRAF5, TSC1, TSC2, TSHR, TYK2, U2AF1, U2AF2, UBR5, VAV1, VAV2, VHL, WHSC1, WT1, XBP1, XPO1, ZRSR2*

Supplemental Table S1. List of genes included in the NGS assays.

	MN w/ low blasts and *SF3B1* mutation (n=27)	MDS with low blasts and isolated del(5q) (n=9)	Overlap cases (n=5)
Age, median years (range)	73 (54-88)	70 (62-76)	69 (57-78)
Sex (M:F)	19:8	4:5	2:3
Therapy related, number (%)	1 (3.7%)	2 (22.2%)	0/5 (0%)
Blood counts			
Hb, median g/dL (IQR)	9.1 (7.8-10.1)*	10.4 (9.6-12.8)	8.6 (8.2-10.3)
Maximum platelet count, median (IQR)	319 (165-364)	216 (180-291)	528 (357-581)^
ANC, median K/uL (IQR)	3.6 (2.8-4.8)^	1.3 (1.0-2.8)	1.4 (1.3-4.9)
AMC, median K/uL (IQR)	0.3 (0.2-0.5)	0.3 (0.2-0.5)	0.2 (0.1-0.3)
Blasts, median % (IQR)	0	0	0
Bone marrow findings			
Dysplastic megakaryocytes	9/27 (33.3%)	9/9 (100%)#	5/5 (100%)#
Ring sideroblasts (if evaluable)			
Any ring sideroblasts	21/24 (87.5%)^	1/8 (12.5%)	4/5 (80%)^
Present but <5%	2/24 (8.3%)	1/8 (12/5%)	2/5 (40%)
Present with 5-15%	1/24 (4.2%)	0/8 (0%)	0/5 (0%)
Present with >15%	18/24 (75%)	0/8 (0%)	2/5 (40%)
Blasts, %, median (IQR)	2% (1-3%)	2% (1-4%)	3% (0-4%)
Fibrosis, 2+ out of 3 or higher (%)	9/27 (33.3%)	1/9 (11.1%)	2/5 (40%)
Genetic findings, number (%)			
Deletion 5q	N/A	9/9 (100%)	5/5 (100%)
SF3B1 mutation	27 (100%)	N/A	5/5 (100%)
Exon 14	12/27 (44.4%)	N/A	3/5 (60%)
Exon 15	13/27 (48.1%)	N/A	2/5 (40%)
Other spliceosome gene mutation	1/27 (3.2%)	0/9 (0%)	0/5 (0%)
JAK2, *CALR*, *MPL* mutations	4/27 (14.8%)	0/9 (0%)	2/5 (40%)
Complex karyotype	1/27 (3.2%)	0/9 (0%)	0/5 (0%)

Supplemental Table S2: Clinicopathologic features of all patients.
Abbreviations: MN – Myeloid neoplasm; MDS – Myelodysplastic Syndrome; ANC – absolute neutrophil count; AMC – absolute monocyte count; N/A – not applicable
*Significantly decreased compared to MDS with low blasts and del(5q)
^ Significantly increased compared MDS with low blasts and del(5q)
# Statistically increased compared to MN with low blasts and *SF3B1* mutation