Taipei Veterans General Hospital

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Sample Information

Patient Name: 劉冠男
Gender: Male
ID No.: FA20189686
History No.: 44504587
Age: 38

Ordering Doctor: DOC1751J 蕭樑材
Ordering REQ.: H41PAFA
Signing in Date: 2022/01/21

Path No.: S111-98212
MP No.: MY22001
Assay: Oncomine Myeloid Assay
Sample Type: Blood
Date of blood drawing: 2022/01/12

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Myelodysplastic Syndrome

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Relevant Myelodysplastic Syndrome Variants

Gene	Finding	Gene	Finding
ASXL1	None detected	NPM1	None detected
BCOR	None detected	NRAS	None detected
CBL	None detected	NUP214	None detected
CREBBP	None detected	RUNX1	***RUNX1 p.(P298S) c.892C>T***
ETV6	None detected	SF3B1	None detected
EZH2	None detected	SRSF2	None detected
FLT3	None detected	STAG2	None detected
GATA2	None detected	TP53	None detected
IDH2	None detected	U2AF1	None detected
KIT	None detected	WT1	None detected
KMT2A	None detected	ZRSR2	None detected
MECOM	None detected		

Relevant Biomarkers

No clinically significant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
RUNX1 p.(P298S) c.892C>T

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
RUNX1	p.(P298S)	c.892C>T	.	chr21:36171673	51.75%	NM_001754.4	missense	1996
SH2B3	p.(T396=)	c.1188G>A	.	chr12:111885300	51.80%	NM_005475.3	synonymous	2000
BCOR	p.(P483L)	c.1448C>T	.	chrX:39933151	99.49%	NM_001123385.2	missense	1556

Biomarker Descriptions

RUNX1 (RUNX family transcription factor 1)

Background: The RUNX1 gene encodes the runt-related transcription factor (RUNX) 1, part of the RUNX family of transcription factors which also includes RUNX2 and RUNX3[1]. All RUNX proteins share several conserved regions with similar functionality including a highly conserved N-terminal 'runt' domain responsible for binding DNA, a C-terminal region composed of an activation domain, inhibitory domain, protein interacting motifs, and a nuclear matrix targeting signal[2]. Each of these proteins are capable of interacting with core binding factor beta (CBFβ) to form the core binding factor (CFB) complex. Consequently, RUNX1, RUNX2, and RUNX3 are collectively known as core binding factor alpha (CBFα) since they can each function as the alpha subunit of CBF. Specifically, CBFβ binds to the 'runt' domain of RUNX1 leading to RUNX1 stabilization and increased affinity of the CFB complex for promoters involved in hematopoietic differentiation and cell cycle regulation[3,4]. RUNX1 is frequently mutated in various hematological malignancies[4]. Germline mutations in RUNX1 result in a rare autosomal dominant condition known as familial platelet disorder, with predisposition to acute myeloid leukemia (FPD/AML)[5,6]. Somatic mutations and chromosomal translocations in RUNX1 are often observed in myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and chronic myelomonocytic leukemia (CMML)[4].

Alterations and prevalence: RUNX1 is frequently rearranged in hematological malignancies with over 50 different observed translocations[7]. The most recurrent translocation, t(12;21)(q34;q11), results in ETV6-RUNX1 fusion and is observed in 20-25% of childhood ALL[8,9,10]. This translocation is also observed in adult ALL at a lower frequency (2%)[9,10]. Another recurrent translocation, t(8;21)(q22;q22), results in RUNX1-RUNX1T1 fusion and is observed in 5-10% of AML[11]. The RUNX1-RUNX1T1 fusion, consists of the RHD domain of RUNX1 and the majority of RUNXT1, which promotes oncogenesis by altering transcriptional regulation of RUNX1 target genes[4,11]. Somatic mutations in RUNX1 include missense, nonsense, and frameshift mutations resulting in loss of function or dominant negative effects[4]. RUNX1 mutations are reported in approximately 10% of de novo AML as well as 10-15% of MDS[4,12,13,14].

Potential relevance: The t(8;21)(q22;q22.1)/RUNX1-RUNX1T1 translocation is recognized as a distinct AML disease category by the World Health Organization (WHO)[15]. Additionally, AML with RUNX1 mutations is a provisional entity in the WHO[15]. Translocations involving RUNX1, specifically t(8;21)(q22;q22)/RUNX1-RUNX1T1 in AML and t(12;21)(q34;q11)/ETV6-RUNX1 in ALL, are associated with favorable risk[12,16]. On the other hand, mutations in RUNX1 confer poor prognosis in AML, MDS, and systemic mastocytosis (SM)[12,13,17]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

References

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