



Sample Information

Patient Name: 劉洪幸子
Gender: Female
ID No.: F202853712
History No.: 49468431
Age: 84

Ordering Doctor: DOC6266E 徐千富
Ordering REQ.: OCLBEAS
Signing in Date: 2023/05/25

Path No.: M112-00112
MP No.: MY23027
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/05/18

Reporting Doctor: DOC5444B 楊靜芬 (Phone: 8#5444)

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	None detected
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

TET2 p.(Q1524*) c.4570C>T, DNMT3A c.1554+1G>A

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
DNMT3A	p.(?)	c.1554+1G>A	.	chr2:25468121	21.95%	NM_022552.4	unknown	2000
TET2	p.(Q1524*)	c.4570C>T	.	chr4:106196237	23.95%	NM_001127208.2	nonsense	2000

Biomarker Descriptions

DNMT3A (DNA methyltransferase 3 alpha)

Background: The DNMT3A gene encodes the DNA methyltransferase 3 alpha which functions as a de novo methyltransferase (DNMT) with equal methylation efficiency for unmethylated and hemimethylated DNA¹. Methylation of DNA occurs at CpG islands, a region of DNA consisting of sequential cytosine/guanine dinucleotide pairs. CpG island methylation plays an important role in development as well as stem cell regulation. Alterations to global DNA methylation patterns are dependent on DNMTs, which are associated with cancer initiation and progression^{2,3}.

Alterations and prevalence: DNMT3A mutations are observed in approximately 25% of all acute myeloid leukemia (AML) including 29-34% of AML with normal karyotype (NK-AML)^{4,5,6,7,8,9,10}. Mutations in DNMT3A are also reported in 12-18% of myelodysplastic syndromes (MDS) as well as 4-6% of melanoma, lung adenocarcinoma, and uterine cancer^{9,11}. The majority of mutations in DNMT3A are missense however, frameshift, nonsense, and splice site mutations have also been reported^{4,9}. Missense mutations at R882 are most prevalent and are observed to coexist with NPM1 and FLT3 mutations^{12,13}. The R882 mutations occur at the dimer/tetramer interface within the catalytic domain, which leads to disruption of DNMT3A tetramerization and loss of CpG methylation^{14,15}. However, DNMT3A mutations observed in AML at positions other than R882 also contribute to pathogenesis by mechanisms that do not involve methyltransferase activity¹⁶.

Potential relevance: DNMT3A mutations confer shorter overall survival (OS) in patients with AML including those with NK-AML^{4,7,8,13}. DNMT3A mutations are a useful in the diagnosis of angioimmunoblastic T-cell lymphoma (AITCL) when trying to differentiate from other peripheral T-cell lymphomas (PTCL)¹⁷.

TET2 (tet methylcytosine dioxygenase 2)

Background: TET2 encodes the tet methylcytosine dioxygenase 2 protein and belongs to a family of ten-eleven translocation (TET) proteins that also includes TET1 and TET3¹⁸. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine^{19,20}. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded β -helix domain (DSBH)²¹. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies^{18,19,20}.

Alterations and prevalence: Somatic TET2 mutations, including nonsense, frameshift, splice site, and missense, are observed in 20-25% of myelodysplastic syndrome (MDS) associated diseases, including 40%-60% chronic myelomonocytic leukemia (CMML)¹¹. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies^{19,22}. TET2 mutations are also observed in 9% of uterine, 8% of melanoma and acute myeloid leukemia (AML), as well as 6% of diffuse large B-cell lymphoma (DLBCL).

Potential relevance: The presence of TET2 mutations may be used as one of the major diagnostic criteria in pre-primary myelofibrosis (pre-PMF) and overt PMF in the absence of JAK2/CALR/MPL mutations^{23,24}. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia^{24,25}.

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