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Sample Information

Patient Name: 謝明枝
Gender: Male
ID No.: T101588840
History No.: 46781399
Age: 71

Ordering Doctor: DOC3174E 廖映庭
Ordering REQ.: 0BERZBG
Signing in Date: 2021/04/15

Path No.: S110-98597
MP No.: MY21004
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2021/04/09
Note:

Sample Cancer Type: Myelodysplastic/Myeloproliferative Neoplasm

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Relevant Myelodysplastic/Myeloproliferative Neoplasm Variants

Gene	Finding
PDGFRA	Not detected
PDGFRB	Not detected

Relevant Biomarkers

No clinically significant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
*TET2 p.(N191Lfs*3) c.571_572delAA, TET2 p.(D1730Efs*15) c.5190delT, TET2 p.(R550*) c.1648C>T, SRSF2 p.(P95H) c.284C>A, TET2 p.(Q684Sfs*9) c.2049_2050insT*

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
TET2	p.(N191Lfs*3)	c.571_572delAA	.	chr4:106155669	24.67%	NM_001127208.2	frameshift Deletion	1998
TET2	p.(R550*)	c.1648C>T	.	chr4:106156747	43.19%	NM_001127208.2	nonsense	1998
TET2	p.(Q684Sfs*9)	c.2049_2050insT	.	chr4:106157144	8.69%	NM_001127208.2	frameshift Insertion	1991
TET2	p.(D1730Efs*15)	c.5190delT	.	chr4:106196856	8.22%	NM_001127208.2	frameshift Deletion	1995
SRSF2	p.(P95H)	c.284C>A	COSM211504	chr17:74732959	50.23%	NM_003016.4	missense	1957
NF1	p.(R765H)	c.2294G>A	.	chr17:29554278	51.40%	NM_001042492.2	missense	2000

Biomarker Descriptions

SRSF2 (serine and arginine rich splicing factor 2)

Background: The SRFS2 gene encodes the serine/arginine (SR)-rich splicing factor 2, a member of the SR-rich family of pre-mRNA splicing factors which make up part of the spliceosome. SRFS2 contains an RNA recognition motif (RRM) that recognizes and binds exonic splicing enhancers (ESE) in a sequence-specific manner[1]. SR proteins are essential regulators of alternative RNA splicing due to their ability to bind RNA and interact with other splicing factors. These proteins can influence the exclusion of cassette exons, a form of alternative splicing also known as exon skipping, which allows for the production of different protein isoforms[1,2]. SRSF2 is the target of somatic missense mutations and in-frame deletions in hematological malignancies, particularly myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), and myeloproliferative neoplasms (MPN)[3,4,5]. Such mutations in SRSF2 result in a differential gain of function which influences cassette exon exclusion, thereby supporting an oncogenic role in cancer[6].

Alterations and prevalence: Mutations in SRSF2 are observed in approximately 10% of MDS cases and 30-40% of CMML[4,7,8]. Missense mutations at P95 are most recurrent, which leads to an amino acid change from proline to histidine (H), leucine (L), or arginine (R)[8]. Specifically, the P95H substitution alters SRSF2 affinity for ESEs and drives preferential recognition of cassette exons containing C- versus G-rich ESEs[5,6]. Although less prevalent, recurrent in-frame deletions (P95H_R102del) are observed in primary myelofibrosis (PMF)[9]. This mutation results in the deletion of 8 amino acids which has been shown to exhibit greater variation of splicing events relative to the P95 missense mutation alone[10].

Potential relevance: In CMML, SRSF2 mutations are often enriched and can be used to support diagnosis[11,12]. SRSF2 mutations confer poor prognosis in MDS and systemic mastocytosis (SM) and are associated with decreased overall survival (OS)[12,13,14]. In MPN, SRSF2 mutations are considered high-risk mutations and are independently associated with inferior OS as well as leukemia-free survival[15,16]. Additionally, SRSF2 mutations are predictive of leukemic transformation in patients with PMF[15].

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 TET3[17]. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine[18,19]. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded ß-helix domain (DSBH)[20]. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies[17,18,19]

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)[12]. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies[18,21]. 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[11,15]. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia[15,22]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

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