LETTER TO THE EDITOR

Identification of a novel *MYO1F::MLLT10* fusion in adult acute monocytic leukemia

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Supplemental Table 1. Comparison of *MYO1F*::*MLLT10* and *MLLT10*::*MYO1F* reciprocal fusions (in-frame)

Parameter	**MYO1F::MLLT10**	**MLLT10::MYO1F**
Breakpoint Coordinates (hg19)	5′ (MYO1F): chr19:8642191 (-) 3′ (MLLT10): chr10:22015173 (+)	5′ (MLLT10): chr10:22022016 (+) 3′ (MYO1F): chr19:8590446 (-)
Transcript IDs (GENCODE v19)	MYO1F: ENST00000338257.8 MLLT10: ENST00000307729.7	MLLT10: ENST00000377072.3 MYO1F: ENST00000338257.8
Base Pairs at Breakpoints	MYO1F: 8642191 (3′ splice-site) MLLT10: 22015173 (5′ splice-site)	MLLT10: 22022016 (3′ splice-site) MYO1F: 8590446 (5′ splice-site)
Transcript Length (bp, aa, exons)	MYO1F-001: 4303 bp, 1098 aa, 28 exons MLLT10-002: 5032 bp, 1068 aa, 23 exons	MLLT10-001: 5126 bp, 1027 aa, 24 exons MYO1F-001: 4303 bp, 1098 aa, 28 exons
Exons Involved	MYO1F: Exon 1 (chr19:8642191–8642357, –) MLLT10: Exon 15/16 (chr10:22015173–22015284, +)	MLLT10: Exon 18/19 (chr10:22021828–22022016, +) MYO1F: Exon 25 (chr19:8590363–8590446, –)
Domains Retained (PFAM)	MYO1F: 5′ UTR and ATG start codon MLLT10: PHD-finger, leucine zipper	MLLT10: PHD-finger, zf-HC5HC2H, Jnk-SapK_ap_N MYO1F: C-terminal exon 25 (part of Myosin tail)

Parameter	**MYO1F::MLLT10**	**MLLT10::MYO1F**
Length of Fusion Protein	443 amino acids (including stop codon) 1 amino acid (0.2%) from 5′MYO1F; 442 from 3′MLLT10	839 amino acids (including stop codon) 816 (97%) from 5′ MLLT10; 23 from 3′ MYO1F
Amino Acid Sequence	See sequence block below Table 1	See sequence block below Table 1
Fusion Structure & Mechanism	MYO1F exon 1 (5′ UTR, start codon) fuses to MLLT10 exon 15/16, resulting in a chimeric transcript with minimal MYO1F coding sequence and MLLT10 C-terminal region. Promoter/enhancer elements from MYO1F5′ UTR drive MLLT10 expression, enhancing oncogenic activity.	MLLT10 exon 18/19 fuses to MYO1Fexon 25, resulting in a chimeric transcript with MLLT10 N-terminal region and MYO1FC-terminal exons. MLLT10 regulatory domains may confer fusion stability or minor functions but lack key oncogenic domains.
Functional & Expression	In-frame, 443 amino acids; 1 aa from MYO1F (start codon), 442 aa from MLLT10’s C-terminal oncogenic domains (PHD-finger, leucine zipper)	In-frame (STAR-Fusion, FusionCatcher), 839 amino acids; N-terminal MLLT10domains (PHD-finger, zf-HC5HC2H) with regulatory potential; lacks oncogenic leucine zipper
FFPM & Coverage	FFPM: 13.4276 (STAR-Fusion); Arriba: high coverage (284/220), strong expression	FFPM: 9.3126 (STAR-Fusion), Arriba: moderate coverage (309/85), intermediate expression

Parameter	**MYO1F::MLLT10**	**MLLT10::MYO1F**
Oncogenicity	Primary driver: MLLT103′ domains drive leukemogenesis, akin to KMT2A::MLLT10	Secondary: MLLT105′ domains less critical for leukemogenesis
Biological/Clinical Significance	Likely novel driver in AML/ALL.MLLT103′ domains promote transformation via transcriptional dysregulation. High expression suggests major oncogenic event, validating experimental targeting.	Reciprocal product; potentially functional but less oncogenic due toMLLT105′ domains. Moderate expression fits secondary role; may stabilize translocation or confer regulatory effects.

*** Amino acid sequence of chimeric *MYO1F::MLLT10* Fusion protein**

MANTLSGSSLSQAPSHMYGNRSNSSMAALIAQSENNQTDQDLGDNSRNLVGRGSSPRGSLS
PRSPVSSLQIRYDQPGNSSLENLPPVAASIEQLLERQWSEGQQFLLEQGTPSDILGMLKSLHQL
QVENRRLEEQIKNLTAKKERLQLLNAQLSVPFPTITANPSPSHQIHTFSAQTAPTTDSLNSSKSP
HIGNSFLPDNSLPVLNQDLTSSGQSTSSSSALSTPPPAGQSPAQQGSGVSGVQQVNGVTVGA
LASGMQPVTSTIPAVSAVGGIIGALPGNQLAINGIVGALNGVMQTPVTMSQNPTPLTHTTVPPN
ATHPMPATLTNSASGLGLLSDQQRQILIHQQQFQQLLNSQQLTPEQHQAFLYQLMQHHHQQH
HQPELQQLQIPGPTQIPINNLLAGTQAPPLHTATTNPFLTIHGDNASQKVARLSDKTGPVAQEKS
*

**** Amino acid sequence of chimeric *MLLT10::MYO1F* Fusion protein**

MVSSDRPVSLEDEVSHSMKEMIGGCCVCSDERGWAENPLVYCDGHGCSVAVHQACYGIVQV
PTGPWFCRKCESQERAARVRCELCPHKDGALKRTDNGGWAHVVCALYIPEVQFANVSTMEPI
VLQSVPHDRYNKTCYICDEQGRESKAATGACMTCNKHGCRQAFHVTCAQFAGLLCEEEGNG
ADNVQYCGYCKYHFSKLKKSKRGSNRSYDQSLSDSSSHSQDKHHEKEKKKYKEKDKHKQKH
KKQPEPSPALVPSLTVTTEKTYTSTSNNSISGSLKRLEDTTARFTNANFQEVSAHTSSGKDVSE
TRGSEGKGKKSSAHSSGQRGRKPGGGRNPGTTVSAASPFPQGSFSGTPGSVKSSSGSSVQS
PQDFLSFTDSDLRNDSYSHSQQSSATKDVHKGESGSQEGGVNSFSTLIGLPSTSAVTSQPKSF
ENSPGDLGNSSLPTAGYKRAQTSGIEEETVKEKKRKGNKQSKHGPGRPKGNKNQENVSHLSV
SSASPTSSVASAAGSITSSSLQKSPTLLRNGSLQSLSVGSSPVGSEISMQYRHDGACPTTTFSE
LLNAIHNDRGDSSTLTKQELKFIGIYNSNDVAVSFPNVVSGSGSSTPVSSSHLPQQSSGHLQQV
GALSPSAVSSAAPAVATTQANTLSGSSLSQAPSHMYGNRSNSSMAALIAQSENNQTDQDLGD
NSRNLVGRGSSPRGSLSPRSPVSSLQIRYDQPGNSSLENLPPVAASIEQLLERQWSEGQQFLL
EQGTPSDILGMLKSLHQLQVENRRLEEQIKNLTAKKERLQLLNAQLSVPFPTITANPSPSHQIHT

FSAQTEPTRKGMAKGKPRRSSQAPTRAAPAPPRGMDRNGVPPSARGGPLPLEIMSGGGTHR
PPRGPPSTSLGASRRPRARPPSEHNTEFLNVPDQGMAGMQRKRSVGQRPVPGVGRPKPQP
RTHGPRCRALYQYVGQDVDELSFNVNEVIEILMEDPSGWWKGRLHGQEGLFPGNYVEKI*

Abbreviations:
UTR, untranslated region; PFAM, protein family database; PHD, plant homeodomain; zf-HC5HC2H, zinc finger domain; FFPM, fragments per million; bp, base pairs; aa, amino acids; AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia.

Supplemental Table 2: Parameters supporting detection of *MYO1F*::*MLLT10* and *MLLT10*::*MYO1F* fusions across multiple fusion-calling algorithms.

Parameter	***MYO1F::MLLT10***	***MLLT10::MYO1F***
Breakpoints (hg19)	FusionCatcher: chr19:8642191 (-), chr10:22015173 (+) STAR-Fusion: chr19:8642191 (-), chr10:22015173 (+) Arriba: chr19:8642191 (-), chr10:22015173 (+)	FusionCatcher: chr10:22022016 (+), chr19:8590446 (-) STAR-Fusion: chr10:22022016 (+), chr19:8590446 (-) Arriba: chr10:22022016 (+), chr19:8590446 (-)
Junction Type	FusionCatcher: Exon-exon STAR-Fusion: ONLY_REF_SPLICE (GT/AG) Arriba: CDS/splice-site	FusionCatcher: Exon-exon STAR-Fusion: ONLY_REF_SPLICE (GT/AG) Arriba: CDS/splice-site
Read Support	STAR-Fusion: 39 junction reads, 23 spanning fragments Arriba: 6/27 split reads, 9 discordant mates FusionCatcher: 19 unique reads, 42 spanning pairs	STAR-Fusion: 40 junction reads, 3 spanning fragments Arriba: 14/8 split reads, 2 discordant mates FusionCatcher: 12 unique reads, 42 spanning pairs
Total Supporting Fragments	FusionCatcher: 61 STAR-Fusion: 62 (FFPM 13.4276) Arriba: 42 (coverage 284/220)	FusionCatcher: 54 STAR-Fusion: 43 (FFPM 9.3126) Arriba: 24 (coverage 309/85)
Confidence	FusionCatcher: High (multiple aligners) STAR-Fusion: High (Presence of Long Double Anchor Support) Arriba: High	FusionCatcher: High (multiple aligners) STAR-Fusion: High (Presence of Long Double Anchor Support) Arriba: High
Filters	FusionCatcher: None STAR-Fusion: None Arriba: duplicates (19), inconsistently clipped (1), mismatches (14)	FusionCatcher: None STAR-Fusion: None Arriba: duplicates (25), mismatches (1)

Functional Effect	FusionCatcher: In-frame STAR-Fusion: In-frame Arriba: In-frame	FusionCatcher: In-frame STAR-Fusion: In-frame Arriba: Out-of-frame* Due to transcript selection ending at exon 25 (short isoform)
Retained Protein Domains	FusionCatcher: Not provided STAR-Fusion: None Arriba: None	FusionCatcher: Not provided STAR-Fusion: PHD-finger, zf-HC5HC2H (MLLT10) Arriba: PHD-finger, SH3 (MLLT10)
Annotations	FusionCatcher: cancer, tumor, t17, exon-exon, reciprocal STAR-Fusion: ["MLLT10: Oncogene"], INTERCHROMOSOMAL [chr19--chr10] Arriba: None	FusionCatcher: cancer, tumor, t17, exon-exon, reciprocal STAR-Fusion: ["MLLT10: Oncogene"], INTERCHROMOSOMAL [chr10--chr19] Arriba: None
Transcript	FusionCatcher: ENSE00003459507 (MYO1F), ENSE00001612483 (MLLT10) STAR-Fusion: ENST00000338257.8 (MYO1F), ENST00000307729.7 (MLLT10) Arriba: ENST00000338257.8 (MYO1F), ENST00000377072.3 (MLLT10)	FusionCatcher: ENSE00001750689 (MLLT10), ENSE00003182580 (MYO1F) STAR-Fusion: ENST00000377072.3 (MLLT10), ENST00000338257.8 (MYO1F) Arriba: ENST00000377072.3 (MLLT10), ENST00000596245.1 (MYO1F)

Abbreviations:
UTR, untranslated region; PHD, plant homeodomain; zf-HC5HC2H, zinc finger domain; SH3, Src homology 3 domain; FFPM, fragments per million; CDS, coding sequence; bp, base pairs; aa, amino acids.