QuanDx®

MOLECULAR DIAGNOSTICS INNOVATOR

LEUKEMIA FUSION GENES (Q30)

SCREENING KIT

FUSION GENE DETECTION

CE IVD

Many hematologic malignancies carry characteristic chromosomal translocations. Correct identification of fusion genes can ensure an accurate diagnosis and prognosis is made, and can assist treatment decisions, stratification and disease monitoring.

Current methodologies used to detect fusion genes can be laborious and time consuming, typically involving karyotyping, followed by fluorescence-in situ hybridization (FISH) and molecular analysis based on reverse transcriptase polymerase chain reaction (RT-PCR).

QuanDx's novel Leukemia Fusion Gene (Q30) Screening Kit reduces the time, complexity, and costs associated with fusion gene detection for CML, AML, and ALL, yielding rapid results at a fraction of the cost of FISH.

DISEASE RELEVANCE

- ***Chronic Myeloid Leukemia (CML)***
- ***Acute Myeloid Leukemia (AML)***
- ***Acute Lymphoblastic Leukemia (ALL)***

KEY FEATURES

- ***Multiplexing:*** Allows simultaneous detection of 30 fusion genes with 140+ breakpoints.
- ***Compatibility:*** Compatible with most current real-time qPCR instruments.
- ***Rapid:*** Results can be obtained in 2-3 hours.
- ***Simple***: Easy to perform for routine screening.
- ***Cost Effective***: Can be performed for a fraction of the cost of FISH.

PRODUCT SPECIFICATIONS

FUSION VARIANTS	MLL-AF9, MLL-AF4, MLL-MLLT1, MLL-MLLT10, PML-RARA, TEL-AML1, BCR-ABL1, CBFB-MYH11, AML1-ETO, E2A-PBX1, STIL-TAL1, AML1-EVI1, FIP1L1-PDGFRA, MLL-SEPT6, MLL-AF17, MLL-AF1P, DEK-NUP214, MLL-ELL, MLL-MLLT11, MLL-MLLT4, SET-NUP214, TLS-ERG, NPM1-RARA, TEL-ABL1, E2A-HLF, TEL-PDGFRB, ZBTB16-RARA, AML1-EAP, NPM1-MLF1, AML1-CBFA2T3
SAMPLE TYPES	Bone marrow, peripheral blood, FFPE, and cell lines
REACTION TIME	2-3 hours
INTERNAL CONTROL	GUSB internal control, one positive control and one negative control
INSTRUMENTS	Compatible with Bio-Rad CFX96, iCycler, ABI7500, Stratagene Mx3000P/Mx3005P, and other commonly used RT-qPCR instruments
DETECTION CHANNELS	FAM, HEX, ROX, CY5

Fusion Genes	No. of Break Points	Target Disease	Chromosome Alteration	Description
MLL-AF9	16	**AML**	t(9;11)(p22;q23)	MLL-AF9 is the most frequent MLL rearrangement in childhood acute myeloid leukemia (AML) and it may be also found in acute lymphoblastic leukemia (ALL) of patients younger than 1-year-old (infants).[1,2,3,4,5,6]
PML-RARA	3	**APL**	t(15;17)(q24;q21)	The PML–RARA fusion protein is found in approximately 97% of patients with acute promyelocytic leukemia (APL). Diagnosis of APL is based on the detection of t(15;17). Depending on the location of breakpoints within the PML site, intron 6, exon 6 and intron 3, the respective PML-RARa transcript subtypes referred to as long (L or bcr1), variant (V or bcr2) and short (S or bcr3), may be formed.[7,8,9,10]
AML-ETO	1	**AML**	t(8;21)(q22;q22)	The AML1-ETO rearrangement t(8;21)(q22;q22) has been reported in acute myeloid leukemia (AML) subtype M2. Synonyms for AML1 (acute myeloid leukemia 1 gene) are PEBP2a (polyoma enhancer binding protein 2 subunit a) or CBFA2 (core binding factor subunit A2) and for ETO (eight twenty one) CDR (cyclin D-related gene) or MTG8 (myeloid translocation gene on chromosome 8). The breakpoints of AML1 are located between exon 5 and 6 and upstream of exon 2 regarding ETO.[11]
MLL-AF4	10	**ALL**	t(4;11)(q21;q23)	The t(4;11)(q21;q23) involving the genes MLL and AF4 (alias for AFF1) is detected in 50–70% of infant leukemia. The MLL status of acute leukemia, including precise identification of the partner gene, is used in clinincal research studies to enable investigations that may provide information relating to therapy decisions.[12,13]
TEL-AML1	4	**ALL**	t(12;21)(p13;q22)	TEL gene rearrangement due to the 12;21 chromosome translocation is believed to be the most common molecular genetic abnormality in childhood acute lymphoblastic leukemia (ALL).[14,15]
E2A-PBX1	2	**ALL**	t(1;19)(q23;p13)	The t(1;19) translocation yields a fusion between E2A and PBX1 genes and occurs in 5% of acute lymphoblastic leukemia in children and adults.[16,17,18,19]
MLL-ENL	8	**ALL**	t(11;19)(q23;p13)	The translocation t(11;19) is a recurrent feature of a subgroup of acute leukemiasoccurring in infants. This event fuses the genes MLL and ENL and creates the leukemogenic oncoprotein MLL-ENL.[20,21]
BCR-ABL1	8	**CML/ALL**	t(9;22)(q34;q11)	Philadelphia chromosome is a specific chromosomal abnormality that is associated with chronic myelogenousleukemia (CML). It is the result of a reciprocal translocation between chromosome 9 and 22, and is specifically designated t(9;22)(q34;q11). Three BCR-ABL transcripts have been found and are designated p210, p190 and p230.[23-34]
SIL-TAL1	2	**T-ALL**	del(1)(p32)	SIL-TAL1 fusion gene and the ectopic expression of HOX11L2 are common molecular abnormalities in T-cell acute lymphoblastic leukemia (T-ALL). [35,36]
MLL-AF10	18	**ALL/AML**	t(10;11)(p12;q23)	Translocations involving the MLL gene on chromosome 11q23 occur in 5-10% of human leukemias, and involve fusion with more than 30 different partner genes. The MLL-AF10 fusion produced by the t(10;11)(p12;q23) or ins(10;11)(p12;q23q13) occurs in a small percentage of acute leukemias, most commonly acute myelogenous leukemia (AML) of the M5 FAB subtype.[37,38,39]
CBF-MYH11	10	**AML**	t(16;16)(p13;q22)	Pericentric inversion of chromosome 16, translocation (16;16) and del(16q), resulting in a chimerical fusion of CBF and MYH11 genes, are typically seen in the M4Eo FrenchAmerican-British (FAB) classification subset of acute myelogenous leukemia (AML).[40,41,42]
AML1-MDS1/ EV11	2	**CML**	t(3;21)(q26;q22)	The (3;21)(q26;q22) translocation associated with treatmentrelated myelodysplastic syndrome, treatment-related acute myeloid leukemia, and blast crisis of chronic myeloid leukemia results in the expression of the chimeric genes AML1/EAP, AML1/MDS1, and AML1/EVI1. AML1 (CBFA2), which codes for the alpha subunit of the heterodimeric transcription factor CBF, is also involved in the t(8;21), and the gene coding for the beta subunit (CBFB) is involved in the inv(16). These are two of the most common recurring chromosomal rearrangements in acute myeloid leukemia.[43,44,45]
FIP1L1-PDG-FRA	4	**CEL**	del(4)(q12)	(FIP1L1-PDGFRA), which results in a constitutively activated platelet-derived growth factor receptor-alpha (PDGFRA), has been invariably associated with a primary eosinophilic disorder.[46-49]

Fusion Genes	No. of Break Points	Target Disease	Chromosome Alteration	Description
SET-CAN	1	**AUL/ AML/ALL**	del(9)(q34)	SET-CAN is the product of the t(9;9) in Acute Undifferentiated Leukemia.[50,51,52]
E2A-HLF	2	**ALL**	t(17;19)(q23;p13)	The chimeric transcription factor E2a-Hlf is an oncoprotein associated with a subset of acute lymphoblastic leukemias of early B-lineage derivation.[53-56]
DEK-CAN	1	**AML**	t(6;9)(p23;q34)	The t(6;9) associated DEK/CAN fusion protein targets a population of long-term repopulating hematopoietic stem cells for leukemogenic transformation.[57-60]
MLL-SEPT6	5	**MLL**	t(X;11)q24;q23)	SEPT6 is ubiquitously expressed in tissues and one of the fusion partner genes of MLL in the 11q23 translocations implicated in acute leukemia.[61,62,63]
TLS-ERG	6	**ALM/ ALL/CML**	t(16;21)(p11;q22)	TLS-ERG fusion protein is derived from the t(16;21) translocation found in human myeloid leukemia.[64-68]
TEL-PDGFRB	3	**CEL**	t(5;12)(q33;p13)	Constitutive activation of platelet-derived growth factor receptor (PDGFR) is one of the features of myeloproliferative disease (MPD). PDGFR is a member of type III receptor tyrosine kinase that transmits mitotic signals in cells of mesenchymal origin. Both PDGFRA and PDGFRB genes, located on chromosomes 4q12 and 5q33 respectively, form fusion gene as a result of chromosome translocation. Representative examples are TEL-PDGFRB in t(5;12) (q33;p13) 4 and FIP1L1-PDGFRA in del(4)(q12),both of the gene products known to have ligand-independent kinase activity. The former is observed in chronic myelomonocytic leukaemia (CMMoL) as well as other MPDs with eosinophilia, whereas the latter has been reported in hypereosinophilic syndrome (HES).[69,70,71]
MLL-ELL	6	**ALL**	t(11;19)(q23;p13)	The (11;19)(q23;p13.1) translocation in acute leukemia results in the formation of a chimeric MLL-ELL fusion protein.[72,73]
MLL-AF17	18	**AML**	t(11;17)(q23;p13	The development of acute leukemias is associated with MLL gene alterations in about 10% of all leukemia cases of ALL and AML.[74,75]
NPM-RARA	1	**APL**	t(5;17)(q32;q21)	The t(5;17) variant of acute promyelocytic leukemia expresses a nucleophosmin-retinoic acid receptor fusion.[76,77]
NPM-MLF1	1	**AML**	t(3;5)(q25;q35)	The t(3;5)(q25.1;q34) of myelodysplastic syndrome and acute myeloid leukemia produces a novel fusion gene, NPM-MLF1.[78]
PLZF-RARA	2	**APL**	t(11;17)(q23;q21)	Acute promyelocytic leukemia (APL) is typified by the t(15;17) translocation, which leads to the formation of thePML/RARA fusion gene and predicts a beneficial response to retinoids. However, approximately 10% of all APL cases lack the classic t(15;17). This group includes (1) cases with cryptic PML/RARA gene rearrangements and t(5;17) that leads to the NPM/RARA fusion gene, which are retinoid-responsive, and (2) cases with t(11;17)(q23;q21) that are associated with the PLZF/RARA fusion gene, which are retinoid-resistant.[79,80,81]
MLL-AF1q	4	**ALL**	t(1;11)(q21;q23)	MLL-AF1q fusion resulting from t(1;11) in acute leukemia.[82]
MLL-AF1P	8	**AML**	t(1;11)(p32;q23)	The t(1;11) (MLL-EPS15=MLL-AF1p) translocation is rare with a small number of clinical cases published and three reports of molecular characterization at the transcriptional level. MLL-AF1p AMLs exhibit a more myeloproliferative phenotype than do the other MLL subtypes.[83,84]
TEL-ABL	2	**AML/ ALL/CML**	t(9;12)(q34;p13)	ETV6 A gene on 12p13 that encodes a transcription factor required for haematopoiesis and for maintaining developing vasculature. ETV6 is involved in an array of chromosomal rearrangements linked to leukaemia and congenital fibrosarcoma.[85,86]
AML1-MTG16	2	**AML**	t(16;21)(q24;q22)	AML1/MTG16 fusion gene from a t(16;21)(q24;q22) translocation in treatment-induced leukemia after breast cancer.[87,88]
AML-EAP	1	**AML**	t(3;21)(q26,q22)	The chimeric genes AML1/MDS1 and AML1/EAP inhibit AML1B activation at the CSF1R promoter, but only AML1/MDS1 has tumor-promoter properties.[89]

ORDERING INFORMATION

LEUKEMIA FUSION GENES (Q30) SCREENING KIT

Cat. No.	Description	Size
1-100-10020	Leukemia Fusion Genes (Q30) Screening Kit	20 reactions

Leukemia Fusion Genes (Q30) Screening Kit is a CE-IVD product for in vitro diagnostic use.
USA Research Use Only.

REFERENCES

1. Genes on chromosomes 4, 9, and 19 involved in 11q23 abnormalities in acute leukemia share sequence homology and/or common motifs. Nakamura T, Alder H, Gu Y, Prasad R, Canaani O, Kamada N, Gale RP, Lange B, Crist WM, Nowell PC, et al. Proc Natl Acad Sci USA. 1993 May 15;90(10):4631-5. 2. MLLT3 gene on 9p22 involved in t(9;11) leukemia encodes a serine/proline rich protein homologous to MLLT1 on 19p13. Iida S, Seto M, Yamamoto K, Komatsu H, Tojo A, Asano S, Kamada N, Ariyoshi Y, Takahashi T, Ueda R. Oncogene. 1993 Nov;8(11):3085-92. 3. A reverse transcriptase-polymerase chain reaction detects heterogeneous chimeric mRNAs in leukemias with 11q23 abnormalities. Yamamoto K, Seto M, Iida S, Komatsu H, Kamada N, Kojima S, Kodera Y, Nakazawa S, Saito H, Takahashi T, et al. Blood. 1994 May 15;83(10):2912-21. 4. Incidence and characterization of MLL gene (11q23) rearrangements in acute myeloid leukemia M1 and M5. Poirel H, Rack K, Delabesse E, Radford-Weiss I, Troussard X, Debert C, Leboeuf D, Bastard C, Picard F, Veil-Buzyn A, Flandrin G, Bernard O, Macintyre E. Blood. 1996 Mar 15;87(6):2496-505. 5. Monitoring of minimal residual leukemia in patients with MLL-AF9 positive acute myeloid leukemia by RT-PCR. Mitterbauer G1, Zimmer C, Fonatsch C, Haas O, Thalhammer-Scherrer R, Schwarzinger I, Kalhs P, Jaeger U, Lechner K, Mannhalter C. Leukemia. 1999 Oct;13(10):1519-24. 6. A novel AF9 breakpoint in MLL-AF9-positive acute monoblastic leukemia. Alonso CN, Longo PL, Gallego MS, Medina A, Felice MS. Pediatr Blood Cancer. 2008 Apr;50(4):869- 71. 7. Molecular analysis of acute promyelocytic leukemia breakpoint cluster region on chromosome 17. Borrow J, Goddard AD, Sheer D, Solomon E. Science. 1990 Sep 28;249(4976):1577-80. 8. The t(15;17) translocation of acute promyelocytic leukaemia fuses the retinoic acid receptor alpha gene to a novel transcribed locus. de Thé H, Chomienne C, Lanotte M, Degos L, Dejean A. Nature. 1990 Oct 11;347(6293):558-61. 9. Cloning and characterization of the t(15;17) translocation breakpoint region in acute promyelocytic leukemia. Lemons RS, Eilender D, Waldmann RA, Rebentisch M, Frej AK, Ledbetter DH, Willman C, McConnell T, O'Connell P. Genes Chromosomes Cancer. 1990 Jul;2(2):79-87. 10. Rearrangements and aberrant expression of the retinoic acid receptor alpha gene in acute promyelocytic leukemias. Longo L, Pandolfi PP, Biondi A, Rambaldi A, Mencarelli A, Lo Coco F, Diverio D, Pegoraro L, Avanzi G, Tabilio A, et al. J Exp Med. 1990 Dec 1;172(6):1571-5. 11. Identification of breakpoints in t(8;21) acute myelogenous leukemia and isolation of a fusion transcript, AML1/ETO, with similarity to Drosophila segmentation gene, runt. Erickson P, Gao J, Chang KS, Look T, Whisenant E, Raimondi S, Lasher R, Trujillo J, Rowley J, Drabkin H. Blood. 1992 Oct 1;80(7):1825-31. 12. The t(4;11) chromosome translocation of human acute leukemias fuses the ALL-1 gene, related to Drosophila trithorax, to the AF-4 gene. Gu Y, Nakamura T, Alder H, Prasad R, Canaani O, Cimino G, Croce CM, Canaani E. Cell. 1992 Nov 13;71(4):701-8. 13. Exon/intron structure of the human AF-4 gene, a member of the AF-4/LAF-4/FMR-2 gene family coding for a nuclear protein with structural alterations in acute leukaemia. Nilson I, Reichel M, Ennas MG, Greim R, Knörr C, Siegler G, Greil J, Fey GH, Marschalek R. Br J Haematol. 1997 Jul;98(1):157-69. 14. Fusion of the TEL gene on 12p13 to the AML1 gene on 21q22 in acute lymphoblastic leukemia. Golub TR, Barker GF, Bohlander SK, Hiebert SW, Ward DC, Bray-Ward P, Morgan E, Raimondi SC, Rowley JD, Gilliland DG. Proc Natl Acad Sci U S A. 1995 May 23;92(11):4917-21. 15. The t(12;21) of acute lymphoblastic leukemia results in a tel-AML1 gene fusion. Romana SP, Mauchauffé M, Le Coniat M, Chumakov I, Le Paslier D, Berger R, Bernard OA. Blood. 1995 Jun 15;85(12):3662-70. 16. A new homeobox gene contributes the DNA binding domain of the t(1;19) translocation protein in pre-B ALL. Kamps MP, Murre C, Sun XH, Baltimore D. Cell. 1990 Feb 23;60(4):547-55. 17. Chromosomal translocation t(1;19) results in synthesis of a homeobox fusion mRNA that codes for a potential chimeric transcription factor. Nourse J, Mellentin JD, Galili N, Wilkinson J, Stanbridge E, Smith SD, Cleary ML. Cell. 1990 Feb 23;60(4):535-45. 18. Cytogenetics of pre-B-cell acute lymphoblastic leukemia with emphasis on prognostic implications of the t(1;19). Raimondi SC, Behm FG, Roberson PK, Williams DL, Pui CH, Crist WM, Look AT, Rivera GK. J Clin Oncol. 1990 Aug;8(8):1380-8. 19. Characterisation of genomic translocation breakpoints and identification of an alternative TCF3/PBX1 fusion transcript in t(1;19)(q23;p13)-positive acute lymphoblastic leukaemias. Paulsson K1, Jonson T, Ora I, Olofsson T, Panagopoulos I, Johansson B. Br J Haematol. 2007 Jul;138(2):196-201. 20. Involvement of a homolog of Drosophila trithorax by 11q23 chromosomal translocations in acute leukemias. Tkachuk DC, Kohler S, Cleary ML. Cell. 1992 Nov 13;71(4):691-700. 21. Two distinct portions of LTG19/ENL at 19p13 are involved in t(11;19) leukemia. Yamamoto K, Seto M, Komatsu H, Iida S, Akao Y, Kojima S, Kodera Y, Nakazawa S, Ariyoshi Y, Takahashi T, et al. Oncogene. 1993 Oct;8(10):2617-25. 22. Nowell P, Hungerford D. A minute chromosome in human chronic granulocytic leukemia [J]. Science, 1960,132:1497. 23. Nowell P, Hungerford D. Chromosome studies in human leukemia. II. Chronic granulocytic leukemia [J]. J Natl Cancer Inst, 1961,27:1013-1035. 24. Tough IM, Court Brown WM, Baikie AG, et al. Cytogenetic studies in chronic myeloid leukaemia and acute leukaemia associated with monogolism [J]. Lancet, 1961,1(7174):411-417. 25. Rowley JD. Letter: A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining [J]. Nature, 1973, 243(5405):290-293. 26. de Klein A, van Kessel AQ Grosveld G, et al. A cellular oncogene is translocated to the Philadelphia chromosome in chronic myelocytic leukaemia [J]. Nature, 1982, 300(5894):765-767. 27. Groffen J, Stephenson JR, Heisterkamp N, et al. Philadelphia chromosomal breakpoints are clustered within a limited region, bcr, on chromosome 22 [J]. Cell, 1984,36(l):93-99. 28. Shtivelman E, Lifshitz B, Gale RP, et al. Fused transcript of abl and bcr genes in chronic myelogenous leukaemia [J], Nature, 1985,315(6020):550-554.

29. Davis RL, Konopka JB, Witte ON. Activation of the c-abl oncogene by viral transduction or chromosomal translocation generates altered c-abl proteins with similar in vitro kinase properties [J],Mol Cell Biol, 1985,5(1):204-213. 30. Ben-Neriah Y, Daley GQ, Mes-Masson AM, et al. The chronic myelogenous leukemiaspecific P210 protein is the product of the bcr/abl hybrid gene [J]. Science, 1986, 233(4760):212-214. 31. Daley GQ, Van Etten RA, Baltimore D. Induction of chronic myelogenous leukemia in mice by the P210bcr/abl gene of the Philadelphia chromosome [J]. Science, 1990,247(4944):824-830. 32. Rowley JD. Chromosomal translocations: revisited yet again [J]. Blood, 2008, 112(6):2183-2189. 33. Rowley JD. Identificaton of a translocation with quinacrine fluorescence in a patient with acute leukemia [J]. Ann Genet, 1973,16(2): 109-112. 34. Erickson P, Gao J, Chang KS, et al. Identification of breakpoints in t(8;21) acute myelogenous leukemia and isolation of a fusion transcript, AML1/E70, with similarity to Drosophila segmentation gene, runt [J]. Blood, 1992, 80(7): 1825-1831. 35. Brown L, Cheng JT, Chen Q, et al. Site-specific recombination of the tal-1 gene is a common occurrence in human T cell leukemia [J], EMBO J, 1990,9(10):3343-3351. 36. Delabesse E, Bernard M, Landman-Parker J, et al. Simultaneous SIL-TAL1 RT-PCR detection of all tal(d) deletions and identification of novel tal(d) variants [J]. Br J Haematol, 1997,99(4):901-907. 37. Chaplin T, Ayton P, Bernard OA et al. A novel class of zinc finger/leucine zipper genes identified from the molecular cloning of the t(10;ll) translocation in acute leukemia [J]. Blood, 1995, 85(6): 1435-1441. 38. Chaplin T, Bernard O, Beverloo HB, et al. The t(10;ll) translocation in acute myeloid leukemia (M5) consistently fuses the leucine zipper motif of AF10 onto the HRX gene [J]. Blood, 1995, 86(6):2073-2076. 39. Shibuya N, Taki T, Mugishima H, et al. t(10;1 l)-acute leukemias with MLL-AF10 and MLLABl1 chimeric transcripts: specific expression patterns of ABl1 gene in leukemia and solid tumor cell lines [J]. Genes Chromosomes Cancer, 2001,32(1):1-10. 40. Liu P, Tarle SA, Hajra A, et al. Fusion between transcription factor CBF beta/PEBP2 beta and a myosin heavy chain in acute myeloid leukemia [J]. Science, 1993,261(5124):1041- 1044. 41. Monma F, Nishii K, Shiga J, et al. Detection of the CBFB/MYH11 fusion gene in de novo acute myeloid leukemia (AML): a single-institution study of224 Japanese AML patients [J]. Leuk Res, 2007, 31(4):471-476. 42. Park TS, Lee ST, Song J, et al. Detection of a novel CBFB/MYH11 variant fusion transcript (K-type) showing partial insertion of exon 6 of CBFB gene using two commercially available multiplex RT-PCR kits [J]. Cancer Genet Cytogenet, 2009,189(2):87-92. 43. Nucifora Q Begy CR, Kobayashi H, et al. Consistent intergenic splicing and production of multiple transcripts between AML1 at 21q22 and unrelated genes at 3q26 in (3;21)(q26;q22) translocations [J]. Proc Natl Acad Sci U S A, 1994,91(9):4004–4008. 44. Mitani K, Ogawa S, Tanaka T, et al. Generation of the AML1-EVI-1 fusion gene in the t(3;21)(q26;q22) causes blastic crisis in chronic myelocytic leukemia [J]. EMBO J, 1994, 13(3):504-510. 45. Nucifora G Rowley JD. AML1 and the 8;21 and 3;21 translocations in acute and chronic myeloid leukemia [J], Blood, 1995, 86(1):1-14. 46. Gotlib J, Cools J. Five years since the discovery of FIP1L1-PDGFRA: what we have learned about the fusion and other molecularly defined eosinophilias [J]. Leukemia, 2008,22(11):1999-2010. 47. Lierman E, Cools J. Recent breakthroughs in the understanding and management of chronic eosinophilic leukemia [J]. Expert Rev Anticancer Ther, 2009,9(9): 1295-1304. 48. Lambert F, Heimann P, Herens C, et al. A case of FIPIL-PDGFRA-positive chronic eosinophilic leukemia with a rare FIP1L1 breakpoint [J]. J Mol Diagn, 2007,9(3):414-419. 49. Jovanovic JV, Score J, Waghorn K, et al. Low-dose imatinib mesylate leads to rapid induction of major molecular responses and achievement of complete molecular remission in FIPIL-PDGFRA-positive chronic eosinophilic leukemia [J]. Blood, 2007,109(ll):4635-4640. 50. von Lindern M, van Baal S, Wiegant J, et al. Can, a putative oncogene associated with myeloid leukemogenesis, may be activated by fusion of its 3' half to different genes: characterization of the set gene [J]. Mol Cell Biol, 1992,12(8):3346-3355. 51. Rosati R, La Starza R, Barba Q et al. Cryptic chromosome 9q34 deletion generates TAF-lalpha/CAN and TAF-lbeta/CAN fusion transcripts in acute myeloid leukemia [J], Haematologica, 2007,92(2):232-235. 52. Van Vlierberghe P, van Grotel M, Tchinda J, et al. The recurrent SET-NUP214 fusion as a new HOXA activation mechanism in pediatric T-cell acute lymphoblastic leukemia [J]. Blood, 2008, lll(9):4668-4680. 53. Hunger SP, Ohyashiki K, Toyama K, et al. Hlf, a novel hepatic bZIP protein, shows altered DNA-binding properties following fusion to E2A in t(l 7;19) acute lymphoblastic leukemia [J], Genes Dev, 1992,6(9): 1608-1620. 54. Inaba T, Roberts WM, Shapiro LH, et al. Fusion of the leucine zipper gene HLF to the E2A gene in human acute B-lineage leukemia [J]. Science, 1992,257(5069):531-534. 55. Takahashi H, Goto H, Eunabiki T, et al. Expression of two types of E2A-HLF fusion proteins in YCUB-2, a novel cell line established from B-lineage leukemia with t(17;19) [J]. Leukemia, 2001, 15(6):995-997. 56. Yeung J, Kempski H, Neat M, et al. Characterization of the t(17;19) translocation by gene-specific fluorescent in situ hybridization-based cytogenetics and detection of the E2A-HLF fusion transcript and protein in patients' cells [J]. Haematologica, 2006, 91(3):422-424. 57. von Lindern M, Fornerod M, van Baal S, et al. The translocation (6;9), associated with aspecific subtype of acute myeloid leukemia, results in the fusion of two genes, dek and can, and the expression of a chimeric, leukemia-specific dek-can mRNA [J]. Mol Cell Biol, 1992,12(4): 1687-1697. 58. Soekarman D, von Lindern M, Daenen S, et al. The translocation (6;9) (p23;q34) shows consistent rearrangement of two genes and defines a myeloproliferative disorder with specific clinical features [J]. Blood, 1992,79(ll):2990-2997. 59. Chi Y, Lindgren V, Quigley S, et al. Acute myelogenous leukemia with t(6;9)(p23;q34) and marrow basophilia: an overview [J]. Arch Pathol Lab Med, 2008,132(11):1835-1837. 60. Garcon L, Libura M, Delabesse E, et al. DEK-CAN molecular monitoring of myeloid malignancies could aid therapeutic stratification [J]. Leukemia, 2005,19(8):1338-1344. 61. Borkhardt A, Teigler-Schlegel A, Fuchs U, et al. An ins(X;llXq24;q23) fuses the MLL and the Septin 6/KIAA0128 gene in an infant with AML-M2 [J]. Genes Chromosomes Cancer, 2001, 32(l):82-88. 62. Ono R, Taki T, Taketani T, et al. SEPTIN6, a human homologue to mouse Septin6, is fused to MLL in infant acute myeloid leukemia with complex chromosomal abnormalities involving llq23 and Xq24 [J]. Cancer Res, 2002,62(2):333-337. 63. Cerveira N, Micci F, Santos J, et al. Molecular characterization of the MLL-SEPT6 fusion gene in acute myeloid leukemia: identification of novel fusion transcripts and cloning of genomic breakpoint junctions [J] ^Haematologica, 2008,93(7): 1076-1080. 64. Ichikawa H, Shimizu K, Hayashi Y, et al. An RNA-binding protein gene, TLS/FUS, is fused to ERG in human myeloid leukemia with t(16;21) chromosomal translocation [J]. Cancer Res, 1994, 54(ll):2865-2868. 65. Panagopoulos I, Aman P, Fioretos T, et al. Fusion of the FUS gene with ERG in acute myeloid leukemia with t(16;21)(p11;q22) [J]. Genes Chromosomes Cancer, 1994, ll(4):256-262. 66. Oh SH, Park TS, Choi JR, et al. Two childhood cases of acute leukemia with t(16;21Xpl 1.2;q22): second case report of infantile acute lymphoblastic leukemia with unusual type of FUS-ERG chimeric transcript [J]. Cancer Genet Cytogenet, 2010,200(2): 180-183. 67. Kong XT, Ida K, Ichikawa H, et al. Consistent detection of TLS/FUS-ERG chimeric transcripts in acute myeloid leukemia with t(16;21Xpll;q22) and identification of a novel transcript [J], Blood, 1997,90(3): 1192-1199. 68. Berg T, Kalsaas AH, Buechner J, et al. Ewing sarcoma-peripheral neuroectodermal tumor of the kidney with a FUS-ERG fusion transcript [J], Cancer Genet Cytogenet, 2009,194(l):53-57. 69. Cross NC, Reiter A. Fibroblast growth factor receptor and platelet-derived growth factor receptor abnormalities in eosinophilic myeloproliferative disorders [J], Acta Haematol, 2008,119(4): 199-206. 70. Golub TR, Barker GF, Lovett M, et al. Fusion of PDGF receptor beta to a novel ets-like gene, tel, in chronic myelomonocytic leukemia with t(5;12) chromosomal translocation [J]. Cell, 1994, 77(2):307-316. 71. Gallagher Q Horsman DE, Tsang P, et al. Fusion of PRKG2 and SPTBN1 to the plateletderived growth factor receptor beta gene (PDGFRB) in imatinib-responsive atypical myeloproliferative disorders [J]. Cancer Genet Cytogenet, 2008,181(1):46-51. 72. Thirman MJ, Levitan DA Kobayashi H, et al. Cloning of ELL, a gene that fuses to MLL in a t(ll;19Xq23;pl3.1) in acute myeloid leukemia [J]. Proc Natl Acad Sci U S A, 1994, 91(25): 12110-12114. 73. Kakihana K, Kubo F, Wakabayashi S, et al. A novel variant form of MLL-ELL fusion transcript with t(ll;19Xq23;pl3.1) in chronic myelomonocytic leukemia transforming to acute myeloid leukemia [J]. Cancer Genet Cytogenet, 2008,184(2): 109-112. 74. Prasad R, Leshkowitz D, Gu Y, et al. Leucine-zipper dimerization motif encoded by the AF17 gene fused to ALL-1 (MLL) in acute leukemia [J]. Proc Natl Acad Sci USA, 1994,91(17):8107-8111. 75. Strehl S, Konig M, Meyer C, et al. Molecular dissection of t(ll;17) in acute myeloid leukemia reveals a variety of gene fusions with heterogeneous fusion transcripts and multiple splice variants [J]. Genes Chromosomes Cancer, 2006,45(11):1041-1049. 76. Redner RL, Rush EA, Faas S, et al. The t(5;17) variant of acute promyelocytic leukemia expresses a nucleophosmin-retinoic acid receptor fusion [J]. Blood, 19%, 87(3):882-886. 77. Lim Q Choi JR, Kim MJ, et al. Detection of t(3;5) and NPM1/MLF1 rearrangement in an elderly patient with acute myeloid leukemia: clinical and laboratory study with review of the literature [J]. Cancer Genet Cytogenet, 2010,199(2):101-109. 78. Yoneda-Kato N, Look AT, Kirstein MN, et al. The t(3;5Xq25.1;q34) of myelodysplastic syndrome and acute myeloid leukemia produces a novel fusion gene, NPM-MLF1 [J], Oncogene, 1996, 12(2):265-275. 79. Chen Z, Brand NJ, Chen A, et al. Fusion between a novel Kruppel-like zinc finger gene and the retinoic acid receptor-alpha locus due to a variant t(ll;17) translocation associated with acute promyelocytic leukaemia [J]. EMBO J, 1993,12(3): 1161-1167. 80. Licht JD, Chomienne C, Goy A, et al. Clinical and molecular characterization of a rare syndrome of acute promyelocytic leukemia associated with translocation (11;17) [J]. Blood, 1995, 85(4): 1083-1094. 81. Grimwade D, Biondi A, Mozziconacci MJ, et al. Characterization of acute promyelocytic leukemia cases lacking die classic t(15;17): results of the European Working Party. Groupe Francais de Cytogenetique Hematologique, Groupe de Francais d'Hematologie Cellulaire, UK Cancer Cytogenetics Group and BIOMED 1 European Community-Concerted Action "Molecular Cytogenetic Diagnosis in Haematological Malignancies" [J]. Blood, 2000,96(4):1297-1308. 82. Tse W, Zhu W, Chen HS, et al. A novel gene, AFlq, fused to MLL in t(ll;l) (q21;q23), is specifically expressed in leukemic and immature hematopoietic cells [J]. Blood, 1995,85(3):650-656. 83. Bernard OA, Mauchauffe M, Mecucci C, et al. A novel gene, AF-lp, fused to HRX in t(1; 11 Xp32;q23), is not related to AF-4, AF-9 nor ENL [J]. Oncogene, 1994,9(4): 1039- 1045. 84. Wong WT, Kraus MH, Carlomagno F, et al. The human epsl5 gene, encoding a tyrosine kinase substrate, is conserved in evolution and maps to lp31-p32 [J]. Oncogene, 1994,9(6): 1591 -1597. 85. Papadopoulos P, Ridge SA, Boucher CA, et al. The novel activation of ABL by fusion to an ets-related gene, TEL [J]. Cancer Res, 1995,55(l):34-38. 86. Zuna J, Zaliova M, Muzikova K, et al. Acute leukemias with ETV6/ABL1 (TEL/ABL) fusion: poor prognosis and prenatal origin [J]. Genes Chromosomes Cancer, 2010,49(10):873-884. 87. Gamou T, Kitamura E, Hosoda F, et al. The partner gene of AML1 in t(16;21) myeloid malignancies is a novel member of the MTG8(ETO) family [J]. Blood, 1998,91(1l):4028-4037. 88. Park IT, Park JE, Kim HJ, et al. Acute myeloid leukemia with t(16;21Xq24;q22) and eosinophilia: case report and review of the literature [J]. Cancer Genet Cytogenet, 2010,196(1):105-108. 89. Nucifora G Begy CR, Erickson P, et al. The 3;21 translocation in myelodysplasia results in a fusion transcript between the AML1 gene and the gene for EAP, a highly conserved protein associated with the Epstein-Barr virus small RNA EBER 1 [J], Proc Natl Acad Sci U S A, 1993, 90(16):7784-7788. 90. Prasad R, Gu Y, Alder H, et al. Cloning of the ALL-1 fusion partner, the AF-6 gene, involved in acute myeloid leukemias with the t(6;ll) chromosome translocation [J]. Cancer Res, 1993,53(23):5624-5628.

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