***NUP214* fusion genes in acute leukemia (Review)**

MIN-HANG ZHOU and QING-MING YANG

Department of Hematology and Oncology, The First Affiliated Hospital of the People's Liberation Army General Hospital, Beijing 100048, P.R. China

Received November 30, 2013; Accepted May 23, 2014

DOI: 10.3892/ol.2014.2263

Abstract. Nucleoporin 214 (*NUP214*), previously termed *CAN*, is required for cell cycle and nucleocytoplasmic transport. The genetic features and clinical implications of five *NUP214*-associated fusion genes are described in this review. *SET-NUP214* was most frequently observed in T-cell acute lymphoblastic leukemia (T-ALL), concomitant with the elevated expression of *HOXA* cluster genes. Furthermore, the fusion transcript may be regarded as a potential minimal residual disease marker for *SET-NUP214*-positive patients. Episomal amplifications of *NUP214-ABL1* are specific to T-ALL patients. The *NUP214-ABL1* gene is observed in ~6% of T-ALL, in children and adults. Targeted tyrosine kinase inhibitors plus standard chemotherapy appear to present a promising treatment strategy. *DEK-NUP214* is formed by the fusion of exon 2 of *DEK* and exon 6 of *NUP214*. Achieving molecular negativity of *DEK-NUP214* is of great importance for individual management. *SQSTM1-NUP214* and *NUP214-XKR3* were only identified in one T-ALL patient and one cell line, respectively. The *NUP214* fusions have significant diagnostic and therapeutic implications for leukemia patients. Additional *NUP214*-associated fusions require identification in future studies.

Contents

1. Introduction
2. *SET-NUP214* fusion gene
3. *NUP214-ABL1* fusion gene
4. *DEK-NUP214* fusion gene
5. *SQSTM1-NUP214* fusion gene
6. *NUP214-XKR3* fusion gene
7. Conclusion

Correspondence to: Dr Qing-Ming Yang, Department of Hematology and Oncology, The First Affiliated Hospital of the People's Liberation Army General Hospital, 51 Fucheng Road, Beijing 100048, P.R. China
E-mail: yangqm@medmail.com.cn

Key words: *NUP214*, acute lymphoblastic leukemia, fusion gene, acute myeloid leukemia

1. Introduction

Nucleoporin 214 (*NUP214*), also known as *CAN*, is an FG-repeat-containing nucleoporin. The encoded protein is found on the cytoplasmic side of the nuclear pore complex, and is necessary for the cell cycle and for transport of material between the nucleus and cytoplasm (1). The *NUP214* gene is located at band 9q34.1 and includes 36 exons numbered 1-36. Several novel *NUP214* partner genes have been described recently, and the present study provides a review on this topic.

2. *SET-NUP214* fusion gene

The *SET* gene was previously termed *TAF-I* or *TAF-Iβ*. The encoded protein inhibits cell apoptosis caused by cytotoxic T lymphocytes (2). Del(9)(q34.11q34.13) (3), or occasionally t(9; 9)(q34; q34), leads to the formation of the *SET-NUP214* fusion gene, and often predicts a poor outcome for patients (4,5). The fusion gene is most frequently observed in T-cell acute lymphoblastic leukemia (T-ALL) (4,6), but rarely in acute myeloid leukemia (AML) (7) or acute undifferentiated leukemia (8). Similar to the *PICALM-MLLT10* fusion gene, *MLL* rearrangements and the inv(7)(p15q34) aberration (9-11), the *SET-NUP214* fusion gene contributes to the occurrence of T-ALL by increasing the expression of *HOXA* cluster genes (6). Two cell lines, the T-ALL LOUCY cell line and the AML MEGAL cell line, are known to exhibit the *SET-NUP214* gene (3). The *SET-NUP214* gene in cell lines is formed as a result of the fusion of exon 7 of *SET* and exon 18 of *NUP214*. In addition, the fusion of *SET* exon 7 and *NUP214* exon 17 has also been identified in leukemia patients. The fusion gene inhibits hematopoietic cell differentiation (12,13). However, concurrent chromosomal abnormalities are also required to induce the development of leukemia (4,14).

In a study of 256 ALL patients, two T-ALL patients with the *SET-NUP214* gene were identified using multiplex reverse transcription polymerase chain reaction (RT-PCR). Overexpression of the *HOX* genes (*HOXA7*, *HOXA9* and *HOXA10*) was also detected in the two patients (15). Wang *et al* (16) identified three patients with the *SET-NUP214* gene out of a total of 46 T-ALL patients. Notably, all three patients exhibited a mutation in *PHF*, a key tumor suppressor gene in T-ALL. An additional three patients with the *SET-NUP214* gene in a study by Van Vlierberghe *et al* (6) were found to exhibit the *NOTCH1* mutation, which occurs in almost 50% of T-ALL patients (17). Gorello *et al* (4) identified seven patients

with the *SET-NUP214* gene in 152 T-ALL patients. All seven patients exhibited ≥ 1 additional genetic abnormality, and the majority of patients succumbed to the disease within two years of diagnosis. A significant correlation between minimal residual disease (MRD), detected by the *SET-NUP214* fusion transcript, and the clonal *Ig/TCR* rearrangements was identified in fifteen follow-up bone marrow samples obtained from three pediatric patients with the *SET-NUP214* gene (18). The consistency of the two methods showed that the *SET-NUP214* fusion transcript may be regarded as a potential MRD marker for *SET-NUP214*-positive patients.

3. *NUP214-ABL1* fusion gene

The *ABL1* gene is fused to the *BCR* gene in >95% of chronic myeloid leukemia (CML) patients (19). With the exception of the *BCR-ABL1* gene, the *NUP214-ABL1* gene is the most common fusion gene in hematological malignancies involving the *ABL1* gene (20). The *NUP214-ABL1* protein cannot activate the *ABL1* kinase unless it interacts and competes with other nuclear pore proteins and thus, the amplification of *NUP214-ABL1* is necessary for neoplastic transformation (21). The episome is an extrachromosomal genetic element that has the ability to exist autonomously and freely replicate in the cytoplasm or be integrated with the chromosome and replicate with it (22,23). Episomal amplification of *NUP214-ABL1* is often evident in leukemia cells and varies even in the same patient, with 5-50 copies/cell (24,25). Episomes exhibiting the *NUP214-ABL1* gene are visible by fluorescence *in situ* hybridization (FISH) with specific probes or molecular analysis, but are undetectable by conventional cytogenetics (24).

The *NUP214-ABL1* gene is observed in ~6% of T-ALL, in children and adults (24). Patients with the *NUP214-ABL1* gene usually present with high-risk factors of T-ALL, including an elevated white blood cell count, a mediastinal mass and extramedullary involvement, often with early relapse and a poor outcome. The *NUP214-ABL1* gene is highly specific for T-ALL (21). The *NUP214-ABL1* gene has also been identified in B-cell ALL patients (26). Different types of the *NUP214-ABL1* gene have been found in patients with T-ALL. The most common gene found in previous studies was exon 31 of *NUP214* fused to exon 2 of *ABL1*, followed by exon 29 of *NUP214* fused to exon 2 of *ABL1*. The breakpoints of *NUP214* were variable, located between exon 23 and 34 (27-30). The *NUP214* gene was most frequently fused to exon 2 of *ABL1*, but rarely to exon 3 of *ABL1*. In addition, the fusion gene was observed in four cell lines (31), ALL-SIL and TALL-1024 (exon 32 of *NUP214* fused to exon 2 of *ABL1*) and PEER and BE-13 (exon 34 of *NUP214* fused to exon 2 of *ABL1*). The fusion gene was revealed by FISH at chromosome 9q34 as homogeneously staining regions and was found to replicate with the chromosome in all four cell lines. The fusion protein retains two coiled-coil domains of *NUP214* and the tyrosine kinase domain of *ABL1*.

The development of acute leukemia with the *NUP214-ABL1* gene is partly due to the increased tyrosine kinase activity. Therefore, targeted therapy with specific tyrosine kinase inhibitors may be effective in the treatment of the disease (30,32). Imatinib, the first tyrosine kinase inhibitor, has considerable efficacy against CML exhibiting the *BCR-ABL1*

gene (33). The *NUP214-ABL1* fusion is a late event and not the only aberration in T-ALL, often in combination with the deletion of the important tumor suppressor genes *CDKN2A* and *PTPN2* (34) and the overexpression of *TLX1* or *TLX3* (27,32), increasing the risk of a poor survival time (28). Therefore, in contrast to CML, monotherapy with imatinib is inadequate for treating T-ALL patients with the *NUP214-ABL1* gene. In addition, the easy and usual amplifications of the *NUP214-ABL1* gene on episomes are beneficial for the development of relapse and resistance. In a study by Clarke *et al*, a total daily dose of 600 mg imatinib was administered in combination with vincristine and prednisolone to a male T-ALL patient with the *NUP214-ABL1* fusion gene who relapsed three months after a sibling allograft (35). The patient achieved rapid hematological remission and remained in remission for six months prior to a secondary relapse. Overall, the patient exhibited a brief, but initially favorable response to imatinib. De Keersmaecker *et al* (36) revealed that the SRC family kinase LCK was crucial for the proliferation and survival of T-ALL cells with the *NUP214-ABL1* gene. Dasatinib and bosutinib, dual *ABL1*/SRC kinase inhibitors (37), are considered to be important in the treatment of *NUP214-ABL1*-positive disease. Deenik *et al* (38) reported the case of a young male T-ALL patient with the *NUP214-ABL1* fusion gene who was treated with dasatinib monotherapy (70 mg twice daily), while chemotherapy was postponed due to the surgical removal of a ruptured spleen. The patient achieved a complete hematological response and cytogenetic remission three weeks later. Therefore, dasatinib in combination with standard chemotherapy appears to present a promising treatment strategy.

4. *DEK-NUP214* fusion gene

DEK is involved in DNA duplication and mRNA processing. The *DEK-NUP214* gene, which results from t(6;9)(p22.3;q34.1), is associated with 1% of AML and myelodysplastic syndromes (39,40). Sandén *et al* (41) demonstrated that the *DEK-NUP214* gene increased cell proliferation via the upregulation of mammalian target of rapamycin complex 1 (mTORC1) activity, and that the *DEK-NUP214* induced proliferation was reversed by the mTORC1 inhibitor. Therefore, the mTOR inhibitor may be suitable for the treatment of the patients with the *DEK-NUP214* gene. The *DEK-NUP214* gene is generated from the rare fusion between exon 2 of *DEK* and exon 6 of *NUP214* (42). Patients with this fusion gene are characterized by a young age, marrow basophilia, preceding myelodysplasia and a poor prognosis (39,43,44). It has been found that ~70% of patients with the fusion gene exhibit internal tandem duplications of the tyrosine kinase *FLT3*, as well as higher numbers of white blood cells and bone marrow blasts, and markedly lower complete remission rates (39,45). The *DEK-NUP214* gene is most frequently observed in patients with AML-M2, according to the French-American-British classification (44).

Garçon *et al* (46) applied the quantitative PCR (qPCR) method to analyze 79 bone marrow and peripheral blood samples of 12 patients (ten AML and two myelodysplastic syndrome patients) with the *DEK-NUP214* gene. Five patients exhibited an absence of the *DEK-NUP214* gene (sensitivity,

$<10^5$). All five patients underwent allogeneic hematopoietic stem cell transplantation (allo-HSCT) and four showed consistent molecular negativity with a median follow-up time of 18.5 months. By contrast, the additional seven patients who did not achieve *DEK-NUP214* negativity all succumbed to the disease following a median time of 12 months from diagnosis. It was demonstrated that monitoring the *DEK-NUP214* fusion transcript by qPCR was a useful method for individual management. Four patients with the positive *DEK-NUP214* gene had survived prior to transplantation, indicating that allo-HSCT may overcome the poor prognosis of the *DEK-NUP214* fusion gene and that allo-HSCT is critical for the increased survival times of patients with the *DEK-NUP214* gene.

5. *SQSTM1-NUP214* fusion gene

The protein encoded by *SQSTM1* mediates the activation of the nuclear factor- κ B signaling pathway in response to upstream signals (47). Gorello *et al* (48) reported the case of a 20-year-old male with chemoresistant T-ALL, with an overall survival time of 16 months. Gene expression profiles showed that the patient was clustered tightly with the *SET-NUP214*-positive T-ALL patients, exhibiting an elevated expression level of the *HOXA* cluster genes (*HOXA7*, *HOXA9* and *HOXA10*). However, the patient exhibited certain common clinical characteristics with the *SET-NUP214*-positive patients, including an immature phenotype and a poor outcome (4). Metaphase FISH revealed an unbalanced translocation, der(5)t(5;9)(q35;q34). Furthermore, RT-PCR and sequencing confirmed a novel fusion gene with exon 5 of *SQSTM1* fused to exon 33 of *NUP214*. In contrast to the *SET-NUP214* gene with 42/44 *NUP214* FG repeats (49), the *SQSTM1-NUP214* gene exhibited only 14/44 FG repeats (50) and thus, the leukemogenic mechanisms of the two *NUP214* fusion genes appeared to be markedly different. A total of 136 T-ALL patients were screened by nested RT-PCR, and no other patients with the *SQSTM1-NUP214* gene were identified, suggesting that the fusion gene was an extremely rare event in the T-ALL patients. Further study on the incidence and clinical implications of the *SQSTM1-NUP214* gene in ALL is required.

6. *NUP214-XKR3* fusion gene

XKR3 is a membrane transporter in the XK/Kell complex of the Kell blood group system, located at chromosome 22q11.1 (51). Levin *et al* (52) investigated gene fusions in the cDNA Illumina data (Illumina, Inc., San Diego, CA, USA) of K562 (a CML cell line) using targeted RNA sequencing. In addition to the *BCR-ABL1* fusion gene, a novel *NUP214-XKR3* fusion gene was identified in the cDNA library. A total of four *NUP214-XKR3* fusion transcript isoforms were detected, and all four transcripts were confirmed by Sanger sequencing RT-PCR. However, only the fusion gene between exon 29 of *NUP214* and exon 4 of *XKR3* retained an open reading frame downstream of the fusion gene. However, the functional significance of the fusion gene was not reported in the literature and the occurrence of the *NUP214-XKR3* gene in leukemia patients has not yet been reported.

7. Conclusion

In the present review, five *NUP214*-associated fusion genes that have been identified in leukemia patients were described. The majority of the fusion genes were observed in T-ALL patients. Identifying *NUP214* fusions is extremely important due to the diagnostic and therapeutic significance for leukemia patients. The *SQSTM1-NUP214* and *NUP214-XKR3* fusion genes were described in only one patient and one cell line, respectively. To investigate the incidence and the clinical implications in leukemia patients, further investigations are required. Additional partner genes of *NUP214* remain to be identified in the future.

References

1. Kraemer D, Wozniak RW, Blobel G and Radu A: The human CAN protein, a putative oncogene product associated with myeloid leukemogenesis, is a nuclear pore complex protein that faces the cytoplasm. *Proc Natl Acad Sci USA* 91: 1519-1523, 1994.
2. Fan Z, Beresford PJ, Oh DY, Zhang D and Lieberman J: Tumor suppressor NM23-H1 is a granzyme A-activated DNase during CTL-mediated apoptosis, and the nucleosome assembly protein SET is its inhibitor. *Cell* 112: 659-672, 2003.
3. Quentmeier H, Schneider B, Röhrs S, *et al*: SET-NUP214 fusion in acute myeloid leukemia- and T-cell acute lymphoblastic leukemia-derived cell lines. *J Hematol Oncol* 2: 3, 2009.
4. Gorello P, La Starza R, Varasano E, *et al*: Combined interphase fluorescence *in situ* hybridization elucidates the genetic heterogeneity of T-cell acute lymphoblastic leukemia in adults. *Haematologica* 95: 79-86, 2010.
5. Chae H, Lim J, Kim M, *et al*: Phenotypic and genetic characterization of adult T-cell acute lymphoblastic leukemia with del(9)(q34):SET-NUP214 rearrangement. *Ann Hematol* 91: 193-201, 2012.
6. 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. *Blood* 111: 4668-4680, 2008.
7. Rosati R, La Starza R, Barba G, *et al*: Cryptic chromosome 9q34 deletion generates TAF-Ialpha/CAN and TAF-Ibeta/CAN fusion transcripts in acute myeloid leukemia. *Haematologica* 92: 232-235, 2007.
8. von Lindern M, Breems D, van Baal S, Adriaansen H and Grosveld G: Characterization of the translocation breakpoint sequences of two DEK-CAN fusion genes present in t(6;9) acute myeloid leukemia and a SET-CAN fusion gene found in a case of acute undifferentiated leukemia. *Genes Chromosomes Cancer* 5: 227-234, 1992.
9. Okada Y, Jiang Q, Lemieux M, Jeannotte L, Su L and Zhang Y: Leukaemic transformation by CALM-AF10 involves upregulation of Hoxa5 by hDOT1L. *Nat Cell Biol* 8: 1017-1024, 2006.
10. Speleman F, Cauwelier B, Dastugue N, *et al*: A new recurrent inversion, inv(7)(p15q34), leads to transcriptional activation of HOXA10 and HOXA11 in a subset of T-cell acute lymphoblastic leukemias. *Leukemia* 19: 358-366, 2005.
11. Ferrando AA, Armstrong SA, Neuberg DS, *et al*: Gene expression signatures in MLL-rearranged T-lineage and B-precursor acute leukemias: dominance of HOX dysregulation. *Blood* 102: 262-268, 2003.
12. Kandilci A, Mientjes E and Grosveld G: Effects of SET and SET-CAN on the differentiation of the human promonocytic cell line U937. *Leukemia* 18: 337-340, 2004.
13. Saito S, Nouno K, Shimizu R, Yamamoto M and Nagata K: Impairment of erythroid and megakaryocytic differentiation by a leukemia-associated and t(9;9)-derived fusion gene product, SET/TAF-Ibeta-CAN/Nup214. *J Cell Physiol* 114: 322-333, 2008.
14. De Keersmaecker K, Marynen P and Cools J: Genetic insights in the pathogenesis of T-cell acute lymphoblastic leukemia. *Haematologica* 90: 1116-1127, 2005.
15. Liu F, Gao L, Jing Y, *et al*: Detection and clinical significance of gene rearrangements in Chinese patients with adult acute lymphoblastic leukemia. *Leuk Lymphoma* 54: 1521-1526, 2013.

16. Wang Q, Qiu H, Jiang H, *et al*: Mutations of PHF6 are associated with mutations of NOTCH1, JAK1 and rearrangement of SET-NUP214 in T-cell acute lymphoblastic leukemia. *Haematologica* 96: 1808-1814, 2011.
17. Weng AP, Ferrando AA, Lee W, *et al*: Activating mutations of NOTCH1 in human T cell acute lymphoblastic leukemia. *Science* 306: 269-271, 2004.
18. Li WJ, Cui L, Gao C, *et al*: MRD analysis and treatment outcome in three children with SET-NUP214-positive hematological malignancies. *Int J Lab Hematol* 33: e25-e27, 2011.
19. de Klein A, van Kessel AG, Grosveld G, *et al*: A cellular oncogene is translocated to the Philadelphia chromosome in chronic myelocytic leukaemia. *Nature* 300: 765-767, 1982.
20. De Braekeleer E, Douet-Guilbert N, Rowe D, *et al*: ABL1 fusion genes in hematological malignancies: a review. *Eur J Haematol* 86: 361-371, 2011.
21. De Keersmaecker K, Rocnik JL, Bernad R, *et al*: Kinase activation and transformation by NUP214-ABL1 is dependent on the context of the nuclear pore. *Mol Cell* 31: 134-142, 2008.
22. Maurer BJ, Lai E, Hamkalo BA, Hood L and Attardi G: Novel submicroscopic extrachromosomal elements containing amplified genes in human cells. *Nature* 327: 434-437, 1987.
23. Carroll SM, DeRose ML, Gaudray P, *et al*: Double minute chromosomes can be produced from precursors derived from a chromosomal deletion. *Mol Cell Biol* 8: 1525-1533, 1988.
24. Graux C, Stevens-Kroef M, Lafage M, *et al*: Groupe Francophone de Cytogénétique Hématologique; Belgian Cytogenetic Group for Hematology and Oncology: Heterogeneous patterns of amplification of the NUP214-ABL1 fusion gene in T-cell acute lymphoblastic leukemia. *Leukemia* 23: 125-133, 2009.
25. Eyre T, Schwab CJ, Kinstrie R, *et al*: Episomal amplification of NUP214-ABL1 fusion gene in B-cell acute lymphoblastic leukemia. *Blood* 120: 4441-4443, 2012.
26. Roberts KG, Morin RD, Zhang J, *et al*: Genetic alterations activating kinase and cytokine receptor signaling in high-risk acute lymphoblastic leukemia. *Cancer Cell* 22: 153-166, 2012.
27. Burmeister T, Gökbuget N, Reinhardt R, Rieder H, Hoelzer D and Schwartz S: NUP214-ABL1 in adult T-ALL: the GMALL study group experience. *Blood* 108: 3556-3559, 2006.
28. Ballerini P, Landman-Parker J, Cayuela JM, *et al*: Impact of genotype on survival of children with T-cell acute lymphoblastic leukemia treated according to the French protocol FRALLE-93: the effect of TLX3/HOX11L2 gene expression on outcome. *Haematologica* 93: 1658-1665, 2008.
29. Ballerini P, Busson M, Fasola S, *et al*: NUP214-ABL1 amplification in t(5;14)/HOX11L2-positive ALL present with several forms and may have a prognostic significance. *Leukemia* 19: 468-470, 2005.
30. Graux C, Cools J, Melotte C, *et al*: Fusion of NUP214 to ABL1 on amplified episomes in T-cell acute lymphoblastic leukemia. *Nat Genet* 36: 1084-1089, 2004.
31. Hagemeijer A and Graux C: ABL1 rearrangements in T-cell acute lymphoblastic leukemia. *Genes Chromosomes Cancer* 49: 299-308, 2010.
32. Quintás-Cardama A, Tong W, Manshouri T, *et al*: Activity of tyrosine kinase inhibitors against human NUP214-ABL1-positive T cell malignancies. *Leukemia* 22: 1117-1124, 2008.
33. Druker BJ: Translation of the Philadelphia chromosome into therapy for CML. *Blood* 112: 4808-4817, 2008.
34. Kleppe M, Lahortiga I, El Chaar T, *et al*: Deletion of the protein tyrosine phosphatase gene PTPN2 in T-cell acute lymphoblastic leukemia. *Nat Genet* 42: 530-535, 2010.
35. Clarke S, O'Reilly J, Romeo G and Cooney J: NUP214-ABL1 positive T-cell acute lymphoblastic leukemia patient shows an initial favorable response to imatinib therapy post relapse. *Leuk Res* 35: e131-e133, 2011.
36. De Keersmaecker K, Porcu M, Cox L, *et al*: NUP214-ABL1 mediated cell proliferation in T-cell acute lymphoblastic leukemia is dependent on the LCK kinase and various interacting proteins. *Haematologica* 99: 85-93, 2013.
37. De Keersmaecker K, Versele M, Cools J, Superti-Furga G and Hantschel O: Intrinsic differences between the catalytic properties of the oncogenic NUP214-ABL1 and BCR-ABL1 fusion protein kinases. *Leukemia* 22: 2208-2216, 2008.
38. Deenik W, Beverloo HB, van der Poel-van de Luytgaarde SC, *et al*: Rapid complete cytogenetic remission after upfront dasatinib monotherapy in a patient with a NUP214-ABL1-positive T-cell acute lymphoblastic leukemia. *Leukemia* 23: 627-629, 2009.
39. Slovak ML, Gundacker H, Bloomfield CD, *et al*: A retrospective study of 69 patients with t(6;9)(p23;q34) AML emphasizes the need for a prospective, multicenter initiative for rare 'poor prognosis' myeloid malignancies. *Leukemia* 20: 1295-1297, 2006.
40. Cho YU, Chi HS, Park CJ, Jang S and Seo EJ: Rapid detection of prognostically significant fusion transcripts in acute leukemia using simplified multiplex reverse transcription polymerase chain reaction. *J Korean Med Sci* 27: 1155-1161, 2012.
41. Sandén C, Ageberg M, Petersson J, Lennartsson A and Gullberg U: Forced expression of the DEK-NUP214 fusion protein promotes proliferation dependent on upregulation of mTOR. *BMC Cancer* 13: 440, 2013.
42. von Lindern M, Fornerod M, van Baal S, *et al*: The translocation (6;9), associated with a specific 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. *Mol Cell Biol* 12: 1687-1697, 1992.
43. Rowley JD: Recurring chromosome abnormalities in leukemia and lymphoma. *Semin Hematol* 27: 122-136, 1990.
44. Chi Y, Lindgren V, Quigley S and Gaitonde S: Acute myelogenous leukemia with t(6;9)(p23;q34) and marrow basophilia: an overview. *Arch Pathol Lab Med* 132: 1835-1837, 2008.
45. Thiede C, Steudel C, Mohr B, *et al*: Analysis of FLT3-activating mutations in 979 patients with acute myelogenous leukemia: association with FAB subtypes and identification of subgroups with poor prognosis. *Blood* 99: 4326-4335, 2002.
46. Garçon L, Libura M, Delabesse E, *et al*: DEK-CAN molecular monitoring of myeloid malignancies could aid therapeutic stratification. *Leukemia* 19: 1338-1344, 2005.
47. Pursiheimo JP, Rantanen K, Heikkinen PT, Johansen T and Jaakkola PM: Hypoxia-activated autophagy accelerates degradation of SQSTM1/p62. *Oncogene* 28: 334-344, 2009.
48. Gorello P, La Starza R, Di Giacomo D, *et al*: SQSTM1-NUP214: a new gene fusion in adult T-cell acute lymphoblastic leukemia. *Haematologica* 95: 2161-2163, 2010.
49. Saito S, Miyaji-Yamaguchi M and Nagata K: Aberrant intracellular localization of SET-CAN fusion protein, associated with a leukemia, disorganizes nuclear export. *Int J Cancer* 111: 501-507, 2004.
50. Fornerod M, Boer J, van Baal S, Morreau H and Grosveld G: Interaction of cellular proteins with the leukemia specific fusion proteins DEK-CAN and SET-CAN and their normal counterpart, the nucleoporin CAN. *Oncogene* 13: 1801-1808, 1996.
51. Calenda G, Peng J, Redman CM, Sha Q, Wu X and Lee S: Identification of two new members, XPLAC and XTES, of the XK family. *Gene* 370: 6-16, 2006.
52. Levin JZ, Berger MF, Adiconis X, *et al*: Targeted next-generation sequencing of a cancer transcriptome enhances detection of sequence variants and novel fusion transcripts. *Genome Biol* 10: R115, 2009.