SN-1, A Novel Leukemic Cell Line with t(11;16)(q23;p13): Myeloid Characteristics and Resistance to Retinoids and Vitamin D$_3$

Yasuhide Hayashi, Yoshio Honma, Nozomi Niitsu, Tomohiko Taki, Fumio Bessho, Masahiro Sako, Taijiro Mori, Masayoshi Yanagisawa, Kohichiro Tsuji, and Tatsutoshi Nakahata

Department of Pediatrics, Faculty of Medicine, University of Tokyo, Tokyo 113-8655 [Y. H., T. T., F. B., M. Y.]; Department of Chemotherapy, Saitama Cancer Research Center Institute, Saitama 362-8006 [Y. H., N. N.]; Department of Pediatrics, Osaka City General Hospital, Osaka 554-0021 [M. S.]; Department of Pediatrics, Keio University School of Medicine, Tokyo 160-0016 [T. M.]; and Department of Clinical Oncology, Institute of Medical Science, University of Tokyo, Tokyo 108-8659 [K. T., T. N.], Japan

ABSTRACT

The MLL gene is fused with the cAMP-responsive element binding protein-binding protein (CBP) gene in t(11;16)(q23;p13), which has been reported to be associated with therapy-related acute leukemia. We established a novel myeloid cell line, SN-1, from a patient with T-cell acute lymphoblastic leukemia with t(11;16)(q23;p13) having in-frame MLL-CBP fusion transcripts. The majority of the SN-1 cells were positive for myeloperoxidase when examined using an electron microscope and expressed CD13, CD33, CD56, and HLA-DR antigens, but not CD7, CD10, CD19, CD34, or CD41 antigens. Suggesting that these cells are of myeloid origin. SN-1 cells underwent functional and morphological differentiation when treated with actinomycin D or sodium butyrate, but not with all-trans-retinoic acid (ATRA) or 1α,25-dihydroxyvitamin D$_3$ (VD3). Exposure of SN-1 cells to ATRA hardly affected cell growth and differentiation, whereas the growth of HL-60 and NB4 cells treated with ATRA was effectively inhibited, and differentiation into mature granulocytes was induced. SN-1 cells were relatively insensitive to VD3 with respect to inhibiting the cell growth and inducing the ability to reduce nitroblue tetrazolium, lysosome activity, and morphological differentiation, although the expression of CD11b was slightly induced by VD3. These results suggest that the cell line was impaired in the signal transduction systems of ATRA and VD3. This cell line should be useful for the study of the role of CBP as a transcriptional regulator in leukemia differentiation and for the functional analysis of the MLL-CBP fusion gene, which will provide new insights into leukemogenesis caused by 11q23 translocations.

INTRODUCTION

A close association of specific chromosome translocations with particular subtypes of hematological malignancies has been reported (1–3). Recent molecular studies have revealed that some genes are involved in two different translocations, such as the AML1 gene in t(8;21) AML$^1$ (4) and t(12;21) ALL$^5$ (5). The MLL gene (Ref. 6; also called ALL-1, HRX, and Htrx-1) has been identified in 11q23 translocations (7–9), and its rearrangement is found in the majority of infant (10–12) and therapy-related leukemias (13, 14). This gene forms fusion transcripts with more than 15 partner genes (3, 15, 16). The CBP gene, encoding a transcriptional adaptor/coactivator protein, resides on 16p13 (17) and is mutated in patients with Rubinstein-Taybi syndrome (18). Recently, the CBP gene was found to be fused to MOZ in AML with t(8;16)(p11;p13) (19, 20) and MLL in therapy-related acute leukemia with t(11;16)(q23;p13) (21–24). Here we establish a t(11;16) myeloid cell line from childhood T-ALL that was impaired in the signal transduction systems of ATRA and VD3.

MATERIALS AND METHODS

Case Report. A boy (age, 2 years and 2 months) was admitted to the hospital with hepatosplenomegaly and cervical lymphadenopathy. His peripheral WBC was 24,500/μl with 4% lymphoblasts, 17% eosinophils, and 17% basophils. His bone marrow showed 65% lymphoblasts with an increased number of eosinophils and basophils. His leukemic cells were negative for MPO and expressed CD2, CD4, CD5, CD7, and CD8 antigens, but not CD3, CD19, CD33, CD34, CD15, CD38, or HLA-DR antigens. He was diagnosed as T-ALL (L1) according to the French-American-British classification. He was treated by ALL-oriented chemotherapy (ultra-high risk protocol) including vincristine, dexamethasone, and pirarubicin, but he did not achieve a complete remission. Six months later, he received a CD34-positive allogenic peripheral blood stem cell transplantation from his HLA-haploididentical father. After bone marrow recovery, leukemic blasts appeared in his peripheral blood, and he died of progressive disease 130 days after transplantation. Patient samples were obtained from bone marrow cells 2 months after chemotherapy.

Establishment of Cell Line in Suspension Culture. The methods used to culture the cells were described previously (25). Briefly, bone marrow leukemic cells obtained 2 months after chemotherapy were separated by density gradient sedimentation, seeded at 2 × 10$^6$ cells/liter in 20% FBS and RPMI 1640 medium, and incubated at 37°C in 5% CO$_2$. Fifty percent of the medium was exchanged for fresh medium once a week. Human myeloid leukemia HL-60 (26) and NB4 cells (27) were cultured in suspension in RPMI 1640 supplemented with 10% FBS at 37°C in a humidified atmosphere of 5% CO$_2$ in air.

Cell Morphology and Cytochemistry. For morphological studies, air-dried smears were prepared from bone marrow aspirates at diagnosis or from cell suspensions in culture medium using cytospin and were stained with May-Grunwald-Giemsa stain. Cytochemical studies were performed on fresh bone marrow smears at diagnosis and on cytospin preparations and included MPO, PAS, and NSE reaction using naphthyl butyrate as substrate.

Electron microscopic studies. After centrifugation of the cell suspension, the culture medium was replaced with 2.5% glutaraldehyde for morphological studies and with 1.5% glutaaldehyde for ultrastructural cytochemistry. After hardening, cell pellets removed from the centrifuge tubes were minced into small pieces and placed in the respective fresh fixative for a total of 60 min at 4°C. The peroxidase reaction and subsequent procedures were carried out as described previously (28). Ultrathin sections were stained with uranyl acetate and lead citrate for morphological observation or with lead citrate for detection of peroxidase reaction products and viewed with a Hitachi H-7000 electron microscope at an accelerating voltage of 75 kV.

Immunological Marker Studies. Marker studies were performed as described previously (29). The indirect rosette formation technique was performed by placing 1000 leukemic cells into each well of a test plate. The primary antibody was then added to each well at room temperature for 30 min. The cells were then washed twice with PBS containing 2% FBS. Next, bovine erythrocytes (5 × 10$^7$ cells) conjugated with antimouse IgG antibodies were added to the test plate wells. The cells were again incubated at room temperature for 30 min and then examined for rosette formation using a microscope. Positivity was defined as when >30% of the cells reacted to a given antibody.

Cytogenetic Studies. The chromosomes of bone marrow cells from the patient at diagnosis and of SN-1 cells after culture for 12 months were

Received 8/2/99; accepted 12/13/99.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Received 8/2/99; accepted 12/13/99.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Supported in part by the Children's Cancer Association of Japan, by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare of Japan, by a Grant-in-Aid for Scientific Research on Priority Areas, and by a Grant-in-Aid for Scientific Research (B) and (C) from the Ministry of Education, Science, Sports and Culture of Japan.

The abbreviations used are: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CBP, cAMP-responsive element binding protein-binding protein; RT-PCR, reverse transcription-PCR; ATRA, all-trans-retinoic acid; T-ALL, T-cell acute lymphoblastic leukemia; VD3, 1α,25-dihydroxyvitamin D$_3$; FBS, fetal bovine serum; MPO, myeloperoxidase; PAS, periodic acid Schiff; NSE, nonspecific esterase; TCR, T-cell receptor; NBT, nitroblue tetrazolium; RAR, retinoic acid receptor.

1	The abbreviations used are: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CBP, cAMP-responsive element binding protein-binding protein; RT-PCR, reverse transcription-PCR; ATRA, all-trans-retinoic acid; T-ALL, T-cell acute lymphoblastic leukemia; VD3, 1α,25-dihydroxyvitamin D$_3$; FBS, fetal bovine serum; MPO, myeloperoxidase; PAS, periodic acid Schiff; NSE, nonspecific esterase; TCR, T-cell receptor; NBT, nitroblue tetrazolium; RAR, retinoic acid receptor.

2	Supported in part by the Children's Cancer Association of Japan, by a Grant-in-Aid for Cancer Research from the Ministry of Health and Welfare of Japan, by a Grant-in-Aid for Scientific Research on Priority Areas, and by a Grant-in-Aid for Scientific Research (B) and (C) from the Ministry of Education, Science, Sports and Culture of Japan.

3	To whom requests for reprints should be addressed, at Department of Pediatrics, Faculty of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Phone: 03-3815-5411, ext. 33452; Fax: 03-3816-4108.

4	The abbreviations used are: AML, acute myeloid leukemia; ALL, acute lymphoblastic leukemia; CBP, cAMP-responsive element binding protein-binding protein; RT-PCR, reverse transcription-PCR; ATRA, all-trans-retinoic acid; T-ALL, T-cell acute lymphoblastic leukemia; VD3, 1α,25-dihydroxyvitamin D$_3$; FBS, fetal bovine serum; MPO, myeloperoxidase; PAS, periodic acid Schiff; NSE, nonspecific esterase; TCR, T-cell receptor; NBT, nitroblue tetrazolium; RAR, retinoic acid receptor.
Fig. 1. Morphological changes of SN-1 cells treated with 1.5 mM sodium butyrate (B), 0.9 μM VD3 (C), or 1 nM actinomycin D (D) for 6 days. A, untreated cells.

Fig. 2. An electron micrograph showing ultrastructural evidence of peroxidase. All cells in this field show peroxidase reaction products. The distribution of the peroxidase reaction products, i.e., their presence in the nuclear envelope and endoplasmic reticulum as well as in cytoplasmic granules, shows that these cells are at the promyelocytic stage of differentiation. Cells were stained with lead citrate (×3900).
analyzed by the regular trypsin-Giemsa banding method as described previously (12, 21).

**Southern Blot Analyses.** High molecular weight DNA was extracted from SN-1 by proteinase K digestion and phenol/chloroform extraction. Ten μg of DNA were digested with appropriate restriction enzymes, subjected to electrophoresis on 0.8% agarose gels, transferred to charged nylon filters (Pall BioSupport), and hybridized to DNA probes labeled by the random hexamer method (12, 21). A 0.9-kb BamHI fragment derived from MLL cDNA (30) and

![Fig. 3. The karyotype of the SN-1 cell line was 47, XY, +8, t(11;16) (q23;p13) after culturing for 12 months. Arrows indicate abnormal chromosomes 11 and 16.](image3)

![Fig. 4. A, Southern blot of DNA digested with BamHI and probed with the 0.9-kb fragment of the MLL gene. Control, peripheral lymphocytes. SN-1 exhibited a rearranged band (arrow) with this probe. B, identification of fusion transcripts by RT-PCR. The primers used were MLL-7S and CBP-1A (MLL-CBP; Lane 1), and CBP-2S and MLL-11A (CBP-MLL; Lane 2). C, partial sequences at the chimeric junctions from three cDNAs (longer and shorter fragments of MLL-CBP and CBP-MLL). longer, longer fragment of 521 bp; shorter, shorter fragment of 407 bp. Arrows indicate the fusion points of each cDNA.](image4)
a 3.7-kb HindIII fragment containing the TCR β1 gene were used as a probe (21).

RT-PCR. Total cellular RNA was extracted by the acid guanidine isothiocyanate-phenol-chloroform method (21) from bone marrow cells of the patient at diagnosis and at 2 months after chemotherapy and from SN-1 cells after they were cultured for 6 months. Four μg of total RNA were reverse-transcribed to cDNA in a total volume of 20 μl with random hexamers and 20 units of reverse transcriptase (avian myeloblastosis virus; Boehringer Mannheim). One-twentieth of the cDNA was amplified by PCR in a total volume of 100 μl with 50 mM KCl, 1.5 mM MgCl2, 10 mM Tris-HCl (pH 9.0 at room temperature), each primer at 25 μM, each deoxynucleotide triphosphate at 75 μM, and 2.5 units of Taq polymerase (Boehringer Mannheim). After 30 rounds of PCR (30 s at 94°C, 30 s at 55°C, and 1 min at 72°C), 5 μl of PCR product were electrophoresed in a 3% agarose gel (21, 31). The primers used were as reported previously (21).

Cloning and Sequencing of PCR Products. PCR products were cloned into the TA cloning vector (Invitrogen). Nucleotide sequences were determined by the fluorometric method (Dye Terminator Cycle Sequencing Kit; Applied Biosystems; Refs. 21 and 31).

Chemicals and Differentiation Inducers. ATRA and NBT were purchased from Sigma Chemical Co. (St. Louis, MO), and VD3 was purchased from Wako Pure Chemicals (Osaka, Japan).

Assay of Cell Growth and Differentiation. Cell numbers were counted with a Model ZM counter (Coulter Electronics, Luton, United Kingdom) after culturing for the indicated times. Myelomonocytic differentiation was assessed by monitoring the reduction of NBT, nonspecific α-naphthyl acetate esterase, lysozyme, and morphology using light microscopy of Cytospin preparations stained with May-Grünwald-Giemsa solution (Merck, Darmstadt, Germany; Ref. 32). Surface expression of myelomonocytic antigen CD11b was determined by indirect immunofluorescence staining and flow cytometry. Cells were incubated for 30 min at 4°C in the presence of an appropriate monoclonal antibody. After three washes with PBS, cells were incubated for 30 min at 4°C with goat antimouse IgG labeled with fluorescein and then analyzed in an Epics EX flow cytometer (Coulter Electronics, Hialeah, FL; Ref. 32).

RESULTS

Cell Culture. Cell growth became apparent 10 weeks after seeding the patient’s bone marrow cells in flasks supplemented with 20% FBS. The cell line designated as SN-1 showed a rapid growth rate with a doubling time of 28 h. The concentration of FBS was gradually reduced, and the cell line has since been continuously maintained in 10% FBS in RPMI 1640.

Morphology and Cytochemistry of ALL and SN-1 Cells. Leukemic cells at diagnosis were round and had scanty cytoplasm. A small percentage of the cells contained fine cytoplasmic granules, and the appropriate stains revealed that MPO, PAS, and NSE reactivity was negative. Notably, an increased number of eosinophils and basophils were found in his bone marrow cells. The morphology of the SN-1 cells is shown in Fig. 1A. The majority of cells had a high nuclear:cytoplasmic ratio and oval or reniform nuclei with one or two prominent nucleoli. A small fraction of SN-1 cells contained cytoplasmic granules, and 5% of the cells were positive for MPO. The SN-1 cells lacked PAS and NSE reactivity.

Ultrastructural Studies. SN-1 cells exhibited the characteristics of immature myeloid cells. Although only 5% of the cells were positive for MPO by light microscopy, more than 90% were positive for MPO when examined using an electron microscope. MPO reaction products were clearly demonstrated in the perinuclear envelope, endoplasmic reticulum, Golgi apparatus, and cytoplasmic granules (Fig. 2).

Immunological Marker Studies. SN-1 cells expressed CD13, CD33, CD56, and HLA-DR antigens, which are considered to be specific markers for myeloid leukemia cells, and did not express CD1, CD2, CD3, CD5, CD7, CD8, CD10, CD14, CD19, CD20, CD22, CD34, CD36, CD41, or CD42 antigens, which suggests that they were of myeloid origin.

Chromosomal Analysis of the Patient and SN-1 Cells. The karyotype of the bone marrow cells from the patient at diagnosis was 45, XY, −7 in 15 cells and 46, XY in 3 cells, whereas that of SN-1 cells was 45, XY, −7, t(11;16)(q23;p13) in 15 cells and 46, XY, t(11;16) in 3 cells after culturing for 3 months and 45, XY, −7, t(11;16) in 9 cells and 47, XY, +8, t(11;16) in 11 cells (Fig. 3) after culturing for 12 months.

The TCR β, MLL, and CBP Genes Are Involved in Fresh T-ALL and SN-1 Cells. Rearrangements of the TCR β gene were found in fresh T-ALL and SN-1 cells (data not shown). Rearrangement of the MLL gene was found in SN-1 cells (Fig. 4A), but not in leukemic cells at diagnosis by Southern blotting using a MLL cDNA probe.

Detection of MLL-CBP Fusion Transcripts. Using the sense primer for MLL exon 7 (MLL-7S) and the antisense primer for CBP (CBP-1A), we obtained PCR products of 521 and 407 bp from SN-1 cells (Fig. 4B), but not from the patient’s bone marrow cells at diagnosis. Interestingly, PCR products of 521 and 407 bp were weakly present in the patient’s bone marrow cells 2 months after therapy, from which SN-1 cell line was established. Nucleotide sequencing analysis of these amplified fragments demonstrated 197 bp of MLL exons 7 and 8 in the 5′ region, 324 bp of CBP exon in the 3′ region of the longer fragment, 83 bp of MLL exon 7 in the 5′ region, and 324 bp of the CBP exon in the 3′ region of the shorter fragment from the patient’s bone marrow cells and SN-1 cells. These findings indicate that the two chimeric products are generated by alternative splicing of the MLL gene transcript, which has also been observed in other 11q23 translocations (15, 31). The reciprocal PCR products of the CBP-MLL

![Graphs showing results](https://cancerres.aacrjournals.org/)
fusion transcripts were generated by RT-PCR using the sense primer for CBP (CBP-2S) and the antisense primer on MLL exon 11 (MLL-11A; Fig. 4B).

Induction of Myelomonocytic Differentiation. A number of myeloid leukemia cell lines have been shown to differentiate in response to various compounds (26, 27, 32–34). Therefore, we examined the effects of some inducers of differentiation on SN-1 cells, as compared with the effects on typical myeloid leukemia cell lines (HL-60 and NB4). ATRA at clinically useful concentrations was effective in induction of NBT reduction activity in HL-60 and NB4 cells, but SN-1 cells were less sensitive to ATRA (Fig. 5). The sensitivity of SN-1 cells to VD3 was also extremely low for inducing NBT reduction activity. On the other hand, actinomycin D and sodium butyrate significantly induced NBT reduction activity (Fig. 5). Expression of CD11b, another typical myelomonocytic differentiation marker, was greatly enhanced by actinomycin D, but not by ATRA (Fig. 6). VD3 slightly induced expression of the surface antigen in SN-1 cells, although it hardly induced NBT reduction activity. Morphological examination revealed that butyrate induced granulocytic differentiation of SN-1 cells, mainly into myelocytes and metamyelocytes (Fig. 1). On the other hand, monocytic differentiation of the cells was induced by actinomycin D (Fig. 1). This was confirmed by the finding that α-naphthyl acetate esterase activity was detected in the treated cells (data not shown). Neither ATRA nor VD3 alone induced the lysozyme activity of SN-1 cells, even at high concentrations of the drugs, but actinomycin D and butyrate effectively induced the activity in a dose-dependent manner. In SN-1 cells incubated with actinomycin D for 8 days, lysozyme activity was increased about 7-fold (Fig. 7), and the cell growth was dose-dependently inhibited, with $0.22 \pm 0.03$ nM actinomycin D causing a 50% inhibition (IC$_{50}$). SN-1 cells were fairly resistant to the growth-inhibitory effects of ATRA and VD3: the IC$_{50}$s of ATRA and VD3 were $>1$ µM when added to cultures of SN-1 cells for 4 days.

To understand the relationship between the resistance to ATRA and the expression of retinoid receptor genes, we examined the expression of RAR and retinoid X receptor mRNAs by RT-PCR. Untreated SN-1 cells expressed significant amounts of RARα but not RARβ or RARγ mRNA, suggesting that the resistance to ATRA is not due to a lack of RAR expression. ATRA did not significantly affect the expression of these mRNAs in the cells (data not shown).

DISCUSSION

A large number of human lymphoid cell lines and a few myeloid cell lines have been described thus far (25, 35–42). However, only a few cell lines derived from acute leukemia with 11q23 translocations have been reported (37–42). A t(11;16) translocation was reported in one patient with therapy-related ALL and in nine AML patients by us (21) and by others (13, 22–24). In the present study, we established a t(11;16) myeloid cell line that expressed a MLL-CBP chimeric transcript from a T-ALL patient (21). Interestingly, more than 90% of SN-1 cells showed MPO positivity ultrastructurally, although only 5% of the cells were positive for MPO by light microscopy. Immunophenotyping showed a shift from the T-cell phenotype seen at diagnosis to a myeloid phenotype in SN-1 cells. Similar leukemias have been reported previously (43, 44). The karyotype of leukemic cells at diagnosis was 45, XY, −7, whereas that of SN-1 cells was 45, XY, −7, t(11;16)(q23;p13) in 15 cells and 46, XY, t(11;16) in 3 cells after culturing for 3 months and 45, XY, −7, t(11;16) in 9 cells and 47, XY, +8, t(11;16) in 11 cells after culturing for 12 months. These karyotypes commonly included 7 monosomy, although t(11;16) was found only in SN-1 cells. One of the explanations for the different karyotype between leukemic cells and SN-1 cells is that t(11;16) appeared in the cell line culture. Another explanation is that a small percentage of t(11;16) cells had a growth advantage after chemotherapy. Notably, the rearranged bands of TCR β gene were found in SN-1 cells as well as in T-ALL cells at diagnosis, and weak PCR products of 521 and 407 bp found in SN-1 cells were observed in the patient’s bone marrow cells 2 months after chemotherapy, suggesting that the SN-1 cell lines were derived from the T-ALL patient.

The MLL gene, a human homologue of the Drosophila trithorax gene, is frequently rearranged in infant acute leukemia (10–12) and in therapy-related acute leukemias induced by inhibitors of topoisomerase II (13, 14). Thus far, 15 partner genes for MLL have been cloned from leukemia cells with 11q23 translocations (15, 16, 21–24, 31). They include putative transcriptional factors (AF-4, AF-9, AF-10, AF-17, and ENL; Refs. 7–9 and 16), a target gene for Ras (AF-6; Ref. 45), and an RNA polymerase II elongation factor (ELL; Ref. 46). The
functions of the normal MLL gene and the fusion transcripts remain unknown except in the case of AML developed in chimeric mice carrying the mouse Mll-AF9 fusion gene (47). Rearrangements of the MLL gene found in ALL, AML, and myelodysplastic syndrome suggest that these chimeric proteins play a causative role in the dysregulation of differentiation along both lymphoid and myeloid pathways.

CBP, a member of the p300 transcriptional coactivator family (48), contains three separate cysteine/histidine (C/H)-rich regions and an adenosiviral oncprotein E1A-binding domain (49, 50) and functions by linking the basal transcriptional machinery to various signal-responsive transcriptional factors, such as the cAMP-responsive element binding protein (17), nuclear hormone receptors, STAT1, STAT2, c-jun, c-fos, myb, nuclear factor κB, and MyoD. CBP normally associates with p300/CBP-associated factor, which has intrinsic histone acetyltransferase activity (48). p300/CBP-associated factor, as well as p300, inhibits cell cycle progression (49, 50), suggesting that CBP may also be involved in the regulation of the cell cycle. Moreover, mutation of CBP leads to the development of Rubinstein-Taybi syndrome (18), whose victims have an increased risk of malignant tumors (51). Thus, CBP is considered to be a tumor suppressor gene. Fusion of CBP to translocated MOZ sequences is associated with specific subtypes of AML with t(8;16) (19, 20), and this leukemogenesis may also be associated with dysfunction of CBP.

Several myelomonocytic leukemia cell lines can be induced to differentiate by ATRA and VD3, whereas the SN-1 cell line is resistant to these differentiation inducers. CBP and p300 are extremely versatile in their ability to bridge DNA-binding factors and basal transcription machinery physically, resulting in transcriptional transactivation. They make contact with and connect the functions of many transcription factors, including receptors for retinoids and VD3 (52, 53). The MLL-CBP fusion protein may be defective in these functions. The resistance of SN-1 cells to ATRA and VD3 may be due to a defect in the fusion protein.

We conclude that this cell line may be useful for the study of the role of CBP as a transcriptional regulator in leukemic differentiation and for the functional analysis of the MLL-CBP fusion gene, which will provide new insights into leukemogenesis caused by 11q23 translocations.

ACKNOWLEDGMENTS

We thank M. Seto (Laboratory of Chemotherapy, Aichi Cancer Center Research Institute, Nagoya, Japan) for providing the MLL cDNA probe, S. Sohma for technical assistance with cell culture, and K. Fukuda for excellent technical assistance with electron microscopy.

REFERENCES

12. Taki, T., Ida, K., Bessho, H., Hanada, R., Kikuchi, A., Yamamoto, K., Sako, M., Tsuchida, M., Seto, M., Ueda, R., and Hayashi, Y. Frequency and clinical significance of the MLL gene rearrangements in infant acute leukemia. Leukemia (Balti-

Downloaded from cancerres.aacrjournals.org on July 22, 2017. © 2000 American Association for Cancer Research.
LTG19/ENL at 19p13 are involved in t(11;19) leukemia. Oncogene, 8: 2617–2625, 1993.


SN-1, A Novel Leukemic Cell Line with t(11;16)(q23;p13): Myeloid Characteristics and Resistance to Retinoids and Vitamin D₃

Yasuhide Hayashi, Yoshio Honma, Nozomi Niitsu, et al.

*Cancer Res* 2000;60:1139-1145.

**Updated version**
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/60/4/1139

**Cited articles**
This article cites 53 articles, 26 of which you can access for free at:
http://cancerres.aacrjournals.org/content/60/4/1139.full#ref-list-1

**Citing articles**
This article has been cited by 4 HighWire-hosted articles. Access the articles at:
http://cancerres.aacrjournals.org/content/60/4/1139.full#related-urls

**E-mail alerts**
Sign up to receive free email-alerts related to this article or journal.

**Reprints and Subscriptions**
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

**Permissions**
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.