# Two rare cases of acute myeloid leukemia with t(8;16)(p11.2;p13.3) and 1q duplication: case presentation and literature review

**Meng Liu**
the First Hospital of China Medical University
**Yuan Ren**
China Medical University
**Xianfu Wang**
University of Oklahoma Health Sciences Center
**Xianglan Lu**
University of Oklahoma Health Sciences Center
**Ming Li**
the Second Hospital of Jilin University
**Young Mi Kim**
University of Oklahoma Health Sciences Center
**Shibo Li**
University of Oklahoma Health Sciences Center
**Lijun Zhang** ( lzhang202003@163.com )
the First Hospital of China Medical University https://orcid.org/0000-0002-9821-1863

**Research**

**Keywords:** 1q duplication; acute myeloid leukemia; t(8;16)(p11.2;p13.3); prognostic factor

**Posted Date:** July 15th, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-24639/v2



**Version of Record:** A version of this preprint was published on August 25th, 2020. See the published version at https://doi.org/10.1186/s13039-020-00507-0.

# Abstract

**Background**: Acute myeloid leukemia (AML) is a complex hematological disease characterized by genetic and clinical heterogeneity. The identification and understanding of chromosomal abnormalities are important for the diagnosis and management of AML patients. Compared to recurrent chromosomal translocations in AML, t(8;16)(p11.2;p13.3) can be found in any age group, but is very rare and typically associated with poor prognosis.

**Methods**: Conventional cytogenetic studies were performed among 1,824 AML patients from our oncology database in the last 20 years. Fluorescence in situ hybridization (FISH) was carried out to demonstrate the translocation fusion. Array comparative genome hybridization (aCGH) was carried out to further characterize the duplication of chromosomes.

**Results**: We identified three AML patients with t(8;16)(p11.2;p13.3) by chromosome analysis. Two of the three patients with additional 1q duplication were detected by FISH and aCGH. aCGH characterized a 46.7 Mb and 49.9 Mb gain of chromosome 1 at bands q32.1q44 in these two patients, respectively. One patient achieved a complete remission (CR) but relapsed three months later. The other patient never experienced a CR and died two years after diagnosis.

**Conclusion**: 1q duplication were detected in two of three AML patients with t(8;16)(p11.2;p13.3), suggesting that 1q duplication can be a recurrent event in AML patients with t(8;16). In concert with the findings of previous studies of similar patients, our work suggests that 1q duplication may also be an unfavorable prognostic factor of the disease.


# Background

Acute myeloid leukemia (AML) is a common disease characterized by immature myeloid cell proliferation and bone marrow failure, which can be subdivided into 9 to 11 pathogenetically different subtypes [1]. Over the past two decades, the incidence rate has increased by 30% [2,3]. Furthermore, AML has a poor long-term survival with a high relapse rate [4]. So, AML represents a substantial health problem that requires strict monitoring and innovative treatment strategies. The development of newer effective treatment strategies is necessary in AML.

To present, detection of cytogenetic abnormalities has been regarded as a critical prognostic tool for AML treatment [5]. Hence, it is intensively necessary to identify chromosomal rearrangements in AML patients and provide whole spectrum of cytogenetic abnormalities for AML[6]. According to the World Health Organization classification updated in 2008, AML with recurrent genetic abnormalities including t(8;21)(q22;q22), t(11q23)/*MLL*, t(15;17)(q24;q21), inv(16)(p13.1q22), and t(16;16)(p13.1;q22) were identified [7,8]. Non-random chromosomal abnormalities, such as deletions and translocations, has been detected in approximately 52% of all adult AML patients. More than that, chromosomal abnormalities have been recognized as the genetic events which can cause and promote this disease [9]. Certain cytogenetic abnormalities including t(8;21)(q22;q22), t(15;17)(q24;q21) and inv(16)(p13.1;q22) are shown to be

associated with longer remission and survival, while alterations of chromosomes 5, 7, 11q23 and complex karyotypes are associated with poor response to therapy and shorter overall survival [10]. Chromosomal translocations as t(15;17)/*PML-RARA*, t(8;21)/*RUNX1-RUNX1T1*, inv(16)/*CBFB-MYH11* and t(11q23)/*MLL* are usually found in AML patients [11,12]. However, AML with t(8;16)(p11.2;p13.3)/*KAT6A-CREBBP* is a very rare AML subtype and can be found in any age group, from newborn to the eighth decade of life, with a female predominance [13-17]. A majority of adult patients with t(8;16)(p11.2;p13.3) are therapy related [14-17], and pediatric patients tend to be *de novo* [13]. There are approximately 160 cases reported in works of literatures [13-17], and the first t(8;16)(p11.2;p13.3) in an infant was described in 1983 [18]. Some AML patients with t(8;16) (p11.2;p13.3) have a bleeding tendency and disseminated intravascular coagulopathy, which is overlapping clinical features that mimic acute promyelocytic leukemia (APL) [17]. Unlike APL, AML with t(8;16)(p11.2;p13.3) has unfavorable treatment and outcome [14,19]. As a sole chromosomal anomaly, t(8;16)(p11.2;p13.3) is found in more than 50% of reported cases, and one or more additional chromosomal anomalies can be seen in the remaining cases [20]. The most common secondary chromosomal anomalies are found to be trisomy 8 or partial trisomy 8, and monosomy 7 or deletion of the long arm or short arm of chromosome 7[13-16,19]. Comparatively, the gain of 1q in variable sizes were also frequently noticed in patients with t(8;16)(p11.2;p13.3) in these large studies [13-15,19].

Recurrent cytogenetic abnormality t(8;16)(p11.2;p13.3) is seldom associated with AML, and the 1q duplication in AML patients with t(8;16)(p11.2;p13.3) has never been discussed. In the present study, a total of 1,824 *de novo* or treatment-related AML patients were collected from our laboratory oncology database. Among them, three patients were detected with t(8;16)(p11.2;p13.3)/*KAT6A-CREBBP*, and two of these three showed an additional copy of partial chromosome 1q.

# Methods

### Patients

This study was approved by the Institutional Review Board (IRB) of Oklahoma University (IRB Number: 2250). A total of 1,824 AML patient samples were studied cytogenetically from 2000 to 2019 at the Genetics Laboratory of Oklahoma University Health Sciences Center. Bone marrow samples were obtained from three of the 1,824 patients who had t(8;16)(p11.2;p13.3).

### Conventional cytogenetic analysis

Short-term cultures of unstimulated bone marrow samples were set up and harvested according to the standard laboratory protocols. Karyotype analysis was performed using giemsa and trypsin technique for G-banding. The cytogenetic abnormalities were described according to the International System for Human Cytogenetic Nomenclature (ISCN 2016).

### Fluorescence in situ hybridization analysis

Fluorescence in situ hybridization (FISH) assays were performed according to the manufactures' instruction in combination with our established laboratory protocols. The *PML/RARA* dual-color, dual-

fusion translocation probe (Abbott Molecular Inc., Des Plaines, IL, USA), the sub-telomere specific probes for chromosome 3 p-arm and q-arm, and the whole chromosome painting (WCP) probes for chromosome 1, 3 and 14 were purchased from Cytocell Ltd, NY, USA. A spectrum green-labeled probe mapping to the 8p11.21 region and a spectrum orange-labeled probe mapping to the 16p13.3 region was created in house, respectively with the following BAC/PAC clones: RP11-642I24[chr8: 41,676,336-41,856,494(hg19)] and RP11-589C21[chr8: 41,873,702-42,036,222(hg19)], RP11-619A23[chr16: 3,720,076-3,914,571(hg19)] and RP11-95J11[chr16: 3,860,374-4,025,510(hg19)] (Children's Hospital Oakland Research Institute, Oakland, CA, USA). The *KAT6A* gene located on 8p11.21 and the *CREBBP* gene located on 16p13.3 was covered by the green-labeled and red-labeled home-brewed probe, respectively. All probes were validated before use. Chromosome spreads were counterstained with 4,6-diamidino-2-phenylindole (DAPI4) in an antifade medium (Vector Laboratories Inc., CA, USA). Digital images carrying specific hybridization signals were captured and processed on CytoVision version 7.0 (Applied Spectral Imaging, Carlsbad, CA, USA).

### aCGH analysis

Genomic DNA was extracted from each three patient's bone marrow pellet according to the standard operating procedure using the phenol and chloroform method with a commercially-available DNA extraction kit (Puregene blood kit, Qiagen, Valencia, CA) or Nucleic Acid Isolation System (QuickGene-610L, FUJIFILM Corporation, Tokyo, Japan). Two aCGH platforms including NimbleGen and Agilent were used in this study. For the NimbleGen aCGH platform, human reference genomic DNA was purchased from Promega Corporation (Promega Corporation, Madison, WI, USA). The patient's DNA and the reference DNA were labeled with either Cyanine 3 (Cy-3) or Cyanine 5 (Cy-5) by random priming, and then equal quantity of both labeled products were mixed and loaded onto a 720 K oligonucleotide chip (Roche NimbleGen Inc., Madison, WI, USA) to hybridize at 42°C for 40 h in a MAUI hybridization system (BioMicro Systems, Salt Lake City, UT) according to the manufacturer's protocols with minor modifications. The slides were washed with washing buffers (Roche NimbleGen Inc.) after hybridization and scanned using Roche Scanner MS200 (Roche NimbleGen Inc.). Images were analyzed using software from NimbleScan software version 2.6 and the SignalMap software version 1.9 (Roche NimbleGen Inc.). The genomic positions were determined using GRCh36/hg18, UCSC Genome Browser. For the Agilent aCGH platform, human reference genomic DNA was purchased from Agilent Corporation (Agilent Corporation, Santa Clara, CA, USA). The patient's DNA and the purchased reference DNA were labeled with either cyanine 3 (Cy-3) or cyanine 5 (Cy-5) by random priming (Agilent Corporation). Patient DNA (labeled with Cy-3) was combined with a normal control DNA sample (labeled with Cy-5) of the same sex and hybridized to an Agilent 2 × 400 K oligo microarray chip (Agilent Technologies) by incubating in Agilent's Microarray Hybridization Ovens (Agilent Technologies). After a 40 h of hybridization at 67°C, the slides were washed and scanned using the NimbleGen MS 200 Microarray Scanner (Roche NimbleGen Inc.). Agilent's CytoGenomics 2.7 software (Agilent Technologies.) was applied for data analysis. The genomic positions were determined using GRCh37/hg19, UCSC Genome Browser.

## Case Presentation

**Case 1**: An 82-year-old male presented with anemia and referred to us for AML evaluation. His following lab results and hospital records were not available in our clinical database.

**Case 2**: A 28-year-old female presented with disseminated intravascular coagulopathy and referred to rule out APL. Her complete blood examination and bone marrow aspirate smears were not available. Flow cytometry revealed 57% monocytic cells positive for CD4, CD11b (partial), CD13 (bright), CD14 (partial), CD15, CD33 (bright) and HLA-DR (partial), but negative for CD3, CD7, CD34, CD117, MPO and TdT, consistent with a diagnosis of AML with monocytic differentiation (subtype M5). The patient achieved a hematological CR on day 15 and a cytogenetic CR on day 33 after induction chemotherapy, then relapsed three months later.

**Case 3**: A 69-year-old female with medical history of breast cancer post-lumpectomy, chemotherapy and radiation presented with generalized weakness, pancytopenia and fever. A complete blood examination showed a white blood cell count of $21610^9$/L with 53% blasts, a hemoglobin count of 66 g/L and a platelet count of $3110^9$/L. Her bone marrow aspirate smear demonstrated over 90% myeloblasts. Flow cytometry revealed 69% blast cells expressed CD45 (moderate) , CD34 (dim) , CD38, HLA-DR, CD13, CD15, CD33, negative for CD117, consistent with the diagnosis AML with monocytic differentiation(subtype M5). The patient started consolidation chemotherapy, but had a spontaneous regression and died 2 years after AML diagnosis.

# Results

In case 1, routine chromosome analysis detected an abnormal karyotype with a translocation between short arms of chromosome 8 and 16 (Fig. 1a) in 17 of 20 cells, consistent with the diagnosis of AML with t(8;16)(p11.2;p13.3). The nomenclature of the cytogenetic findings in patient 1 was t(8;16)(p11.2;p13.3)[17]/46,XY[3]. No other consistent karyotypic aberrations were detected. Thus, this male patient was excluded for subsequent FISH and aCGH analyses.

In case 2, chromosome analysis demonstrated the same chromosome rearrangement between 8 and 16 in all 20 cells. In addition, 11 of these cells showed an extra chromosome segment attached to chromosome 14 (Fig. 1b). The karyotypes in patient 2 was described as 46, XX, t(8;16)(p11.2;p13.3), add(14)(p11.2)[11]/46,XY[9]. Negative FISH result for t(15;17)(q24;q21)/*PML-RARA* further ruled out the diagnosis of APL (data not shown). Metaphase FISH analysis confirmed t(8;16)(p11.2;p13.3)/*KAT6A-CREBBP* fusion and demonstrated a part of chromosome 1 on chromosome 14 (Fig. 2a and 2b). In addition to characterize the extra chromosomal 1 material, aCGH was carried out. aCGH confirmed the FISH findings and detected a 46.7Mb gain of chromosome 1 at bands q32.1q44 (201,304,064-248,102,389bp, GRCh36/hg18, USCS Genome Browser) (Fig. 3a).

In case 3, t(8;16)(p11.2;p13.3) with gain of a similar chromosome segment on the long arm of chromosome 3 was detected in 18 of 20 cells by karyotyping analysis (Fig. 1c). FISH confirmed *KAT6A-CREBBP* fusion and revealed the additional chromosome 1 material (Fig. 2c and 2d). Loss of the end portion of chromosome 3 long arm was not found by FISH (Fig. 3e). aCGH further detected gain of

chromosome 1 at bands 1q32.1q44 (201,408,592-251,323,872bp, GRCh37/hg19, UCSC Genome Browser) (Fig. 3b). The molecular size was 49.9 Mb.

# Discussion

AML is one of the most common diseases characterized by proliferation of blast cells in bone marrow or peripheral blood, which accounts for approximately 30% of leukemia adult cases. As reported previously, common chromosomal translocations such as t(8;21)/*RUNX1-RUNX1T1*, t(15;17)/*PML-RARA*, and inv(16)/*CBFB-MYH11* are frequently observed, and numerous uncommon chromosomal aberrations also exist in AML [12]. The detection of these fusion transcripts is important for the diagnosis and progression monitoring of AML patients[21].

In previous large studies, approximately 160 AML cases with t(8;16)(p11.2;p13.3) have been reported[13-20]. Among them, 9 cases showed a gain of 1q in variable sizes[13-15,19]. As an uncommon entity, t(8;16) accounts for 0.2 to 0.4% of all cases of AML[13-20]. In our study, three cases with t(8;16)(p11.2;p13.3) were identified: one man, two women. The two women were both diagnosed as AML (subtype M5) and detected an extra copy of 1q at the same bands q32.1q44 which were different from the reported nine cases. The clinical features and cytogenetic data of the 11 cases of AML with t(8;16)(p11.2;p13.3) and 1q duplication are summarized in Table 1. To the best of our knowledge, this is the first study of delineation of 1q duplication by aCGH in AML patients with t(8;16)(p11.2;p13.3).

**Table 1. The previously reported AML cases with t(8;16)(p11.2;p13.3) and 1q duplication**

| | Sex | Age (years) | FAB type | Karyotype | 1q Bands | Outcome (years) | Last state |
|---|---|---|---|---|---|---|---|
| Case 2 | F | 28 | M5 | 46,XX,t(8;16)(p11.2;p13.3), add(14)(p11.2)[11]/46,XX[9] | 1q32.1q44 | CR after induction Relapsed 3 months later | Alive |
| Case 3 | F | 69 | M5 | 46,XX,t(8;16)(p11.2;p13.3) [2]/46,idem,add(3)(q?27)[18] | 1q32.1q44 | spontaneous regression | Died |
| Haferlach et al. | F | 39 | M5a | 45,XX,t(8;16) (p11;p13),der(10;13) (q10;q10) [10]/46,XX,der(7)t(1;7) (q21;q35),t(8;16)(p11;p13) [2]/46,XX [1] | 1q21 | NA | NA |
| Diab et al. | M | 14,5 | M4 | 46,XY,+1,del(1)(p22),t(8;16) (p11;p13),-10,der(14)t(10;14) (q11.2;p11.2)[8]/ 47,XY,del(1) (q11),+der(1)t(1;8) (p11;q11.2)x2,+i(5) (p10),-8,-10,der(14)t(10;14) (q11.2;p11.2),der(16)t(8;16) | Partial 1q gain | CR for 10.5 | Dead |
| Diab et al. | F | 14,2 | M4/5 | 5,XX,t(8;16) (p11;p13),-18,der(21)t(1;21) (q12;p13)[4]/46,XX[16] | 1q12 | CR for 5 | Alive |
| Diab et al. Diab et al. | F | 1,2 | M4 | 46,XX,t(8;16)(p11;p13) [3]/46,idem,der(10)t(1;10) (q11;p11)[5]/ 46,idem,add(7) (p21),der(10)t(1;10) (q11;p11)[2]/46,idem,add(7) (p21)[2]/46,XX[2} | 1q11 | CR for 0.6 | Died |
| Diab et al. | F | 14,1 | M4 | 46,XY,t(8;16) (p11;p13),der(14)t(1;14) (q31;p11)[20]* | 1q31 | CR for 11.5 | Alive |
| Diab et al. | F | 7,3 | M5 | 46,X,der(X)t(X;1) (q26;q23),t(8;16) (p11;p13),der(11)t(11;11) (p11;q13) | 1q23 | NA | NA |
| Xie et al. | M | 28 | M4 | 46,XY,der(3)t(3;8) (q27,q13),del(6)(p22),t(8;16) (p11.2;p13.3),del(10) (q21q25),add(13) (p11.2),del(16)(p12),del(20) (p11.2),del(20)(q11.2q13.3) [4]/46,idem,del(1) (p35p36.3),del(15) (q23),add(19)(p13.1)[2]/ 46,XY,t(8;16) (q27;q13),del(12) (q21q24.1),del(13) (q21q31),-16,der(19)t(1;19) (q32;p13.3),+mar[3]/ 46,XY,del(6)(p22),t(8;16) (p11.2;p13.3)[cp2]/46,XY[9] | 1q32 | CR for 7 months | Dead |
| Brown et al. | M | 71 | M4 | 47,X,der(Y)t(Y;1)(q12;q21), +6,t(8;16) (p11;p13) [6] /47,idem,del(13)(q3q3) [checked with CAD data] | 1q21 | No CR | Died 1 month after treatment |
| Brown et al. | F | 1,2 | M4 | 46,XX,t(8;16)(p11;p13)[3] /46,idem,der(10)t(1;10) (q11;p11)[5] /46,idem,add(7) (p21),der(10)t(1;10) (q11;p11) [2] /46,idem,add(7)(p21) [2]/46,XX [2] | 1q11 | early remission after course 1. Relapsed at 5 months and 7 months | Died |

| | | | | | | | | after diagnosis |
|---|---|---|---|---|---|---|---|---|

AML, acute myeloid leukemia;FAB, French–American–Britishh; M, male; F, female; NA, not available; CR, compelete remssion.

AML patients with this abnormality often shows unique clinical and biological characteristics [22]. Compared to current categories t(15;17), t(8;21), inv(16), and t(11q23) in AML, t(8;16) is clustered close to t(11q23) sharing commonly expressed genes [15]. Xie et al. reported 15 adult AML cases with t(8;16)(p11.2;p13.3), indicating that t(8;16)(p11.2;p13.3) commonly exhibits monoblastic or myelomonocytic differentiation, and arises in patients with a history of cytotoxic-treated cancer. Patients with *de novo* AML with t(8;16) or treatment-related AML with t(8;16) without adverse prognostic factors have a good outcome [14]. Identifying adverse prognostic factors was of significance to the chosen of therapies and evaluation of survivals in AML patients with t(8;16).

Over the past 15 years, cytogenetic and molecular technologies have largely promoted the efficiency of identification and characterization of this disease [5].Compared to the conventional cytogenetic analysis and FISH method, aCGH is an attractive method for the investigation of cancer genomes [23]. aCGH has higher resolution, simplicity, high reproducibility, shorter turnaround time and precise mapping of aberrations. Most importantly, it avoids the need for cell culture and dividing cells [24-26]. Furthermore, aCGH chromosomal analysis facilitates rapid detection and duplication of cytogenetic abnormalities previously undetectable by conventional cytogenetics [27]. In our investigation, we applied aCGH to characterize the additional chromosome 1 materials in case 2 and 3, and interestingly found that the two cases revealed same extra copy of 1q at bands q32.1q44. Patients with 1q duplication have also demonstrated a wide range of multiple malformations such as mental retardation, macrocephaly, large fontanels, prominent forehead, broad flat nasal bridge, high-arched palate, retrognathia, low-set ears, and cardiac defects [28,29]. More recent studies manifest that 1q gain is also related to a slice of solid tumors. For instance, the gain of 1q is well known as a poor prognostic biomarker of Wilms tumor [30], it plays an important role in predicting poor clinical outcome in patients with thyroid carcinoma as well[31]. Besides, patients with 1q duplication showed worse survival and high risk in acute leukemias, Burkitt lymphoma, and myeloproliferative neoplasms [32-36]. The outcomes of 1q duplication in nine reported AML patients with t(8;16)(p11.2;p13.3) were summarized (table 1). Seven patients' data were available. All seven patients (two adult and five pediatric) received induction chemotherapy, and six achieved CR. At the time of last follow-up, two adult patients and three of five pediatric patients died. Only two pediatric patients were alive. Two adult cases we reported here, case 2 achieved CR but relapsed 3 months later, case 3 had a

spontaneous regression and died two years after diagnosis. Taken together, the findings suggest that 1q duplication might be associated with adverse outcome in AML patients with t(8;16)(p11.2;p13.3). Whereas, the significance of 1q duplication in AML with t(8;16) needs to be further investigated. Since such changes were seldom reported, the pathogenic effects of 1q duplication in AML patients with t(8;16)(p11.2;p13.3) need more studies to delineate.

# Conclusion

Three patients were detected with t(8;16)(p11.2;p13.3) from an 1824 AML patients' database. Two female patients of them were identified with 1q duplication by FISH and aCGH analyses. Combining our investigation with the findings of published studies, we conclude that 1q duplication is a recurrent finding in AML patients with t(8;16). Our data also suggest that 1q duplication might be associated with unfavorable prognosis in these cases. The understandings of cytogenetic data would contribute to the diagnosis and treatment evaluation of AML.

# List Of Abbreviations

AML: Acute myeloid leukemia

aCGH: Array comparative genomic hybridization

FISH: Fluorescence in situ hybridization

APL: Acute promyelocytic leukemia

WCP: Whole chromosome painting

CR: Complete Remission

# Declarations

### Ethics approval and consent to participate

This study was approved by University of Oklahoma Institutional Review Board for the Protection of Human Subjects.

### Consent for publication

Not applicable.

### Availability of data and materials

All data generated or analyzed during this study are included in this published article.

### Competing interests

The authors declare that they have no competing interests.


### Funding

This study has received no funding support.


### Authors' contributions

M Liu and YR gathered clinical information and drafted the manuscript. YR, YK and M Liu performed routine cytogenetic analysis and participated in the interpretation of the results. M Li performed FISH analysis and participated in the interpretation of the results. XL supervised the FISH analysis and helped draft the manuscript. XW performed CGH array analysis and helped draft the manuscript. LZ and SL conceived the study, participated in its design, and extensively reviewed and revised the manuscript. All authors have read and approved the final manuscript.


### Acknowledgements

We thank Sherrill Marble for her editorial help on the manuscript.


### Contributor Information


Meng Liu, Email: liulinxi0210@163.com

Yuan Ren, Email: renyuancmu@163.com

Xianfu Wang, Email: Xianfu-Wang@ouhsc.edu

Xianglan Lu, Email: Xianglan-Lu@ouhsc.edu

Ming Li, Email: 99127157@qq.com

Young Mi Kim, Email: Young-Kim@ouhsc.edu

Shibo Li, Email: Shibo-Li@ouhsc.edu

Lijun Zhang, Email: lzhang202003@163.com

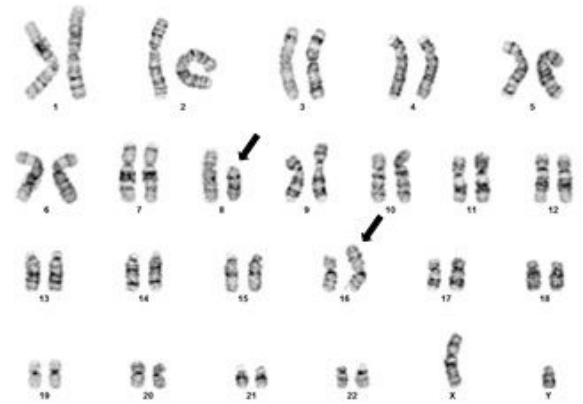

## References


1. Braess J. Acute myeloid leukemia. Dtsch Med Wochenschr. 2016;141:1748-51.
2. Luppi M, Fabbiano F, Visani G, Martinelli G, Venditti A. Novel agents for acute myeloid leukemia. Cancers (Basel). 2018;10:429.
3. Cancer Research UK. Acute myeloid leukaemia (AML) incidence statistics. 2018. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-aml/incidence. Accessed 31 August 2018.

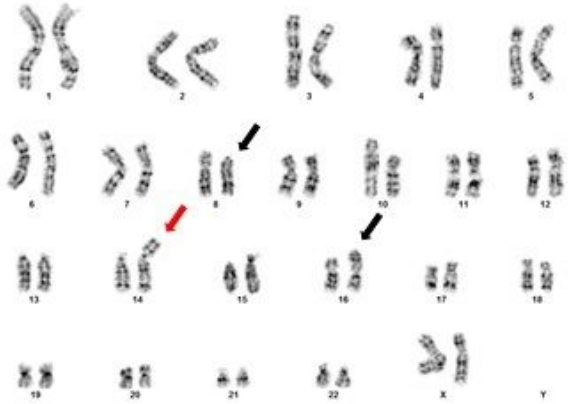
4. Jung J, Cho BS, Kim HJ, Han E, Jang W, Han K, Lee JW, Chung NG, Cho B, Kim M, Kim Y. Reclassification of acute myeloid leukemia according to the 2016 WHO classification. Ann Lab Med. 2019;39:311-6.
5. Murphy T and Yee KWL. Cytarabine and daunorubicin for the treatment of acute myeloid leukemia. Expert Opin Pharmacother. 2017;18:1765-80.
6. Byrd JC, Mrózek K, Dodge RK, et al. Pretreatment cytogenetic abnormalities are predictive of induction success, cumulative incidence of relapse, and overall survival in adult patients with de novo acute myeloid leukemia: results from Cancer and Leukemia Group B (CALGB 8461). Blood. 2002;100:4325-36.
7. Lindsley RC, Mar BG, Mazzola E, et al. Acute myeloid leukemia ontogeny is defined by distinct somatic mutations. Blood. 2015;125:1367-76.
8. Vardiman JW, Thiele J, Arber DA, et al. The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: Rationale and important changes. Blood. 2009;114:937-51.
9. Saultz JN and Garzon R. Acute myeloid leukemia: A concise review. J Clin Med. 2016;5:33.
10. Döhner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. N Engl J Med. 2015;373:1136-52.
11. Strickland SA, Shaver AC, Byrne M, et al. Genotypic and clinical heterogeneity within NCCN favorable-risk acute myeloid leukemia. Leuk Res. 2018;65:67-73.
12. Yang JJ, Park TS, Wan TSK. Recurrent cytogenetic abnormalities in acute myeloid leukemia. Methods Mol Biol. 2017;1541:223-45.
13. Coenen EA, Zwaan CM, Reinhardt D, et al. Pediatric acute myeloid leukemia with t(8;16)(p11;p13), a distinct clinical and biological entity: a collaborative study by the International-Berlin-Frankfurt-Munster AML-study group. 2013;122:2704-13.
14. Xie W, Hu S, Xu J, Chen Z, Medeiros LJ, Tang G. Acute myeloid leukemia with t(8;16)(p11.2;p13.3)/KAT6A-CREBBP in adults. Ann Hematol. 2019;98:1149-57.
15. Haferlach T, Kohlmann A, Klein HU, et al. AML with translocation t(8;16)(p11;p13) demonstrates unique cytomorphological, cytogenetic, molecular and prognostic features. Leukemia. 2009;23:934-43.
16. Gervais C, Murati A, Helias C, et al. Acute myeloid leukaemia with 8p11 (MYST3) rearrangement: An integrated cytologic, cytogenetic and molecular study by the groupe francophone de cytogénétique hématologique. 2008;22:1567-75.
17. Diab A, Zickl L, Abdel-Wahab O, et al. Acute myeloid leukemia with translocation t(8;16) presents with features which mimic acute promyelocytic leukemia and is associated with poor prognosis. Leuk Res. 2013;37:32-6.
18. Schouten TJ, Hustinx TW, Scheres JM, Holland R, de Vaan GA. Malignant histiocytosis. Clinical and cytogenetic studies in a newborn and a child. Cancer. 1983;52:1229-36.
19. Brown T, Swansbury J, Taj MM. Prognosis of patients with t(8;16)(p11;p13) acute myeloid leukemia. Leuk Lymphoma. 2012;53:338-41.

20. Barrett R, Morash B, Roback D, et al. FISH identifies a KAT6A/CREBBP fusion caused by a cryptic insertional t(8;16) in a case of spontaneously remitting congenital acute myeloid leukemia with a normal karyotype. Pediatr Blood Cancer. 2017;64:10.
21. Schumacher J, Szankasi P, Kelley TW. Detection and quantification of acute myeloid leukemia-associated fusion transcripts. Methods Mol Biol. 2017;1633:151-61.
22. Díaz-Beyá M, Navarro A, Ferrer G, et al. Acute myeloid leukemia with translocation (8;16)(p11;p13) and MYST3-CREBBP rearrangement harbors a distinctive microRNA signature targeting RET proto-oncogene. 2013;27:595-603.
23. Veigaard C, Nørgaard JM, Kjeldsen E. Genomic profiling in high hyperdiploid acute myeloid leukemia: a retrospective study of 19 cases. Cancer Genet. 2011;204:516-21.
24. Yasar D, Karadogan I, Alanoglu G, et al. Array comparative genomic hybridization analysis of adult acute leukemia patients. Cancer Genet Cytogenet. 2010;197:122-9.
25. van der Veken LT, Buijs A. Array CGH in human leukemia: From somatics to genetics. Cytogenet Genome Res. 2011;135:260-70.
26. Laskowska J, Szczepanek J, Styczyński J, Tretyn A. Array comparative genomic hybridization in pediatric acute leukemias. Pediatr Hematol Oncol. 2013;30 :677-87.
27. Mehrotra M, Luthra R, Ravandi F, et al. Identification of clinically important chromosomal aberrations in acute myeloid leukemia by array-based comparative genomic hybridization. Leuk Lymphoma. 2014;55:2538-48.
28. Kulikowski LD, Bellucco FTS, Nogueira SI, et al. Pure duplication 1q41-qter: further delineation of trisomy 1q syndromes. Am J Med Genet A. 2008;146A:2663-7.
29. Nowaczyk MJM , Bayani J, Freeman V, Watts J, Squire J, Xu J. De novo 1q32q44 duplication and distal 1q trisomy syndrome. Am J Med Genet A. 2003;120A:229-33.
30. Cone EB, Dalton SS, Van Noord M, Tracy ET, Rice HE, Routh JC. Biomarkers for Wilms Tumor: A Systematic Review. J Urol. 2016;196:1530–5.
31. Xu B, Ghossein R. Genomic Landscape of poorly Differentiated and Anaplastic Thyroid Carcinoma. Endocr Pathol. 2016;27:205–12.
32. Fournier A, Florin A, Lefebvre C, Solly F, Leroux D, Callanan MB. Genetics and epigenetics of 1q rearrangements in hematological malignancies. Cytogenet Genome Res. 2007;118:320–7.
33. Lancman G, Tremblay D, Barley K, et al. The effect of novel therapies in high-molecular-risk multiple myeloma. Clin Adv Hematol Oncol. 2017;15:870–9.
34. Bacher U, Schnittger S, Grüneisen A, Haferlach T, Kern W, Haferlach C. Inverted duplication dup(1)(q32q21) as sole aberration in lymphoid and myeloid malignancies. Cancer Genet Cytogenet. 2009;188:108–11.
35. Marcellino BK, Hoffman R, Tripodi J, et al. Advanced forms of MPNs are accompanied by chromosomal abnormalities that lead to dysregulation of TP53. Blood Adv. 2018;2:3581–9.
36. Beach DF, Barnoski BL, Aviv H, et al. Duplication of chromosome 1 [dup(1)(q21q32)] as the sole cytogenetic abnormality in a patient previously treated for AML. Cancer Genet. 2012;205:665–8.

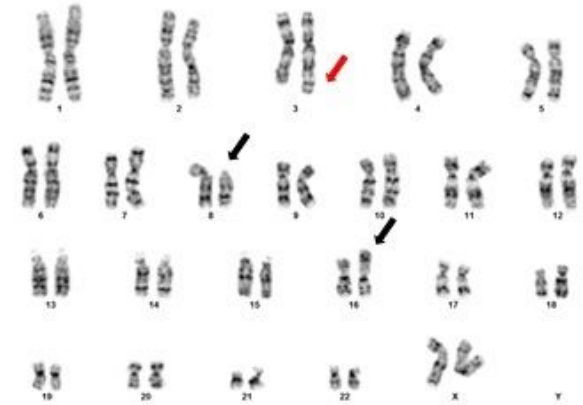
# Figures



a. Patient 1



b. Patient 2

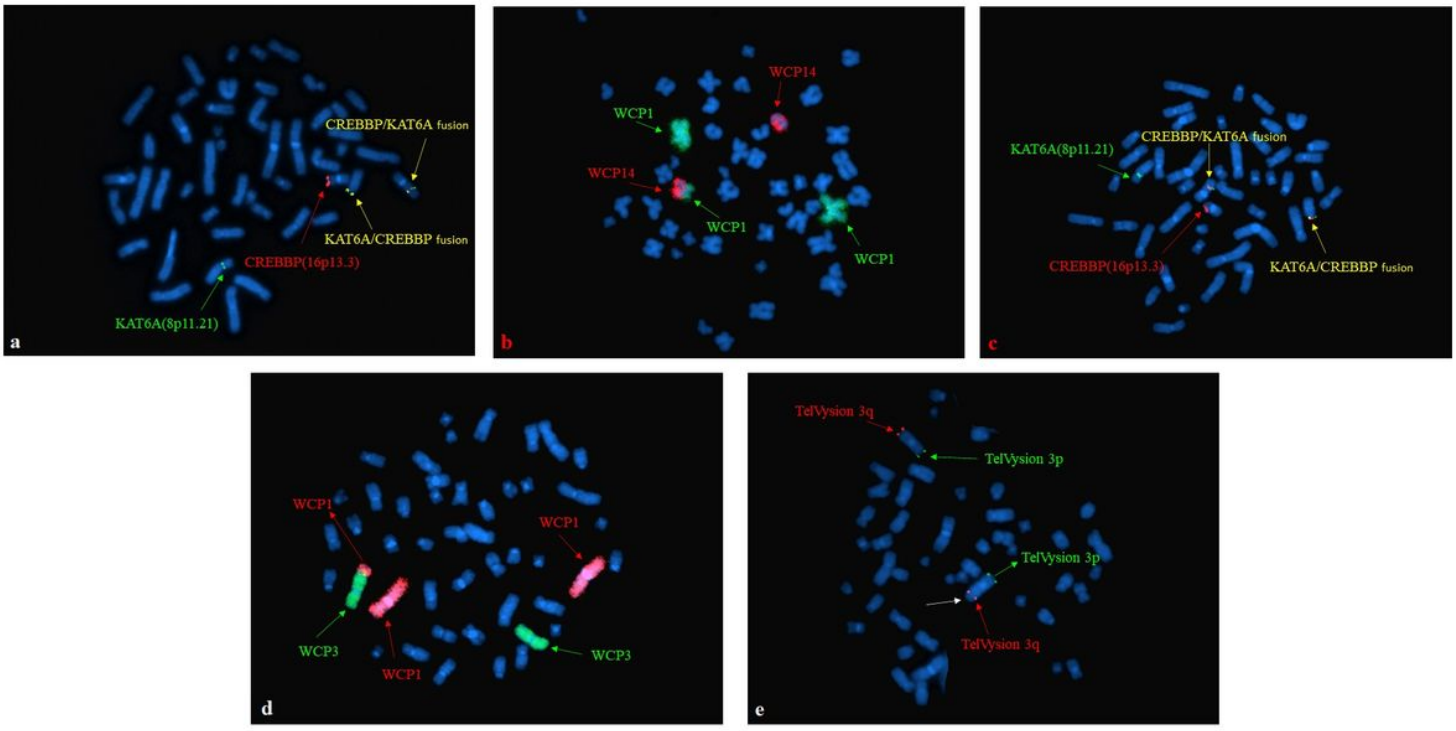


c. Patient 3

## Figure 1

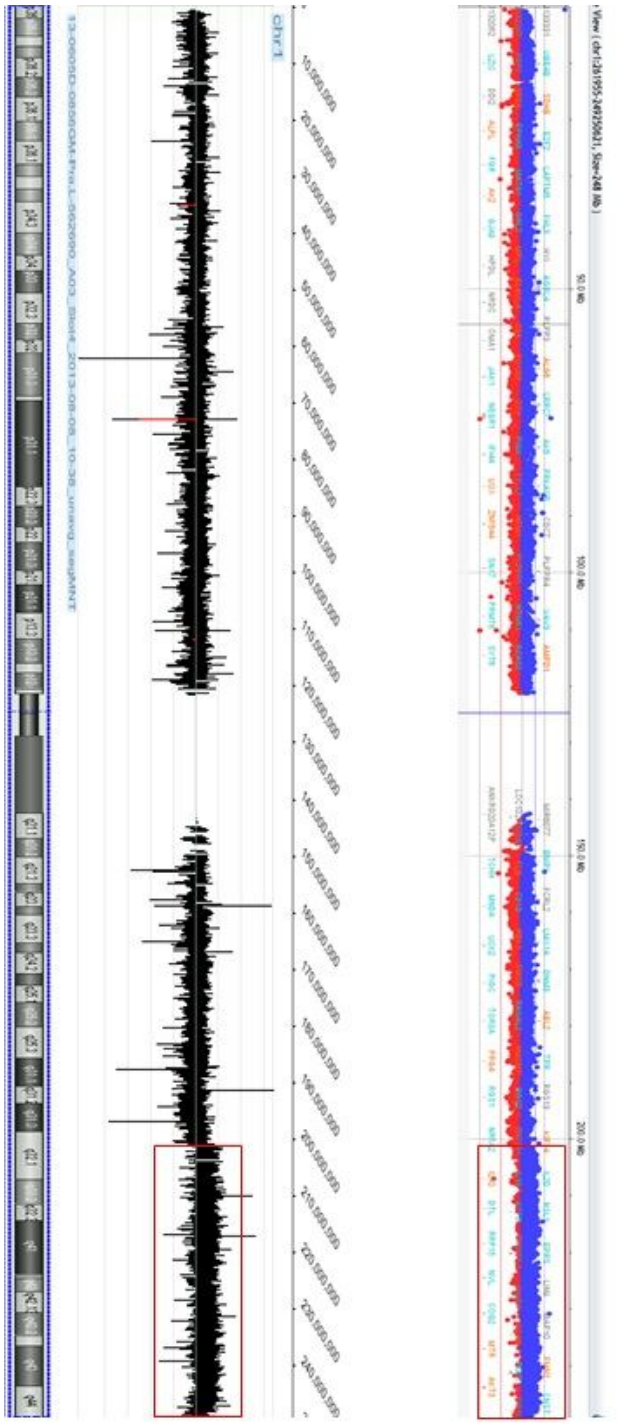
Representative abnormal karyotypes of three patients with t(8;16)(p11.2;p13.3). (a) Karyotype of patient No.1 showing 46,XY,t(8;16)(p11.2;p13.3) as a sole abnormality; (b) and (c) Karyotypes of patient No.2 and No.3 showing 46,XX,t(8;16)(p11.2;p13.3) and an additional chromosome segment attached to the short

arm of chromosome 14 and the long arm of chromosome 3, respectively. Translocated derivatives 8 and 16 were indicated by black arrows, derivatives 14 and 3 were indicated by red arrows.




## Figure 2

Metaphase FISH of patient No.2 (a) and No.3(c) showing KAT6A/CREBBP fusion signals. WCP FISH indicating the extra chromosomal materials on chromosome 14 and chromosome 3 both from chromosome 1 (b and d). No loss of the end portion of chromosome 3 long arm was indicated (e).



a. Patient 2 b. Patient 3

## Figure 3

aCGH results of patient 2 and patient 3 showing partial 1q gain; duplicated 1q regions were indicated by red frames.