Complex rearranged small supernumerary marker chromosomes (sSMC), three new cases; evidence for an underestimated entity?

Vladimir Trifonov1,2, Simon Fluri3, Franz Binkert4, Adayapalam Nandini5, Jasen Anderson6, Laura Rodriguez7, Madeleine Gross2, Nadezda Kosyakova2, Hasmik Mkrtchyan2, Elisabeth Ewers2, Daniela Reich2, Anja Weise2 and Thomas Liehr*2

Address: 1Department of Clinical Veterinary Medicine, Madingley Road, Cambridge, CB3 OES, UK, 2Institut für Humangenetik und Anthropologie, Kollegienasse 10, D-07743 Jena, Germany, 3Universitätskinderklinik, Inselspital, CH-3010 Bern, Switzerland, 4MCL Medizinische Laboratorien, Freiburgstr 634, 3127 Niederwangen, Switzerland, 5Department of Cytogenetics, Queensland Health Pathology Services, Herston QLD 4029, Queensland, Australia, 6Department of Cytogenetics, Sullivan Nicolaides Pathology, Taringa QLD, Australia and 7Estudio Colaborativo Español de Malformaciones Congénitas (ECEMC) del Centro de Investigación sobre Anomalías Congénitas (CIAC), Instituto de Salud Carlos III, Ministerio de Sanidad y Consumo, Madrid, Spain

Email: Vladimir Trifonov - vlad@bionet.nsc.ru; Simon Fluri - bif@mcl.ch; Franz Binkert - bif@mcl.ch; Adayapalam Nandini - Adayapalam_Nandini@health.qld.gov.au; Jasen Anderson - Jasen_Anderson@snp.com.au; Laura Rodriguez - laura@isciii.es; Madeleine Gross - mgross@mti.uni-jena.de; Nadezda Kosyakova - Nadezda.Kosyakova@mti.uni-jena.de; Hasmik Mkrtchyan - Hasmik.Mkrtchyan@mti.uni-jena.de; Elisabeth Ewers - Elisabeth.Ewers@mti.uni-jena.de; Daniela Reich - Daniela.Reich@mti.uni-jena.de; Anja Weise - aweise@mti.uni-jena.de; Thomas Liehr* - i8lith@mti.uni-jena.de

* Corresponding author

Abstract

Background: Small supernumerary marker chromosomes (sSMC) are present ~2.6 × 10^6 human worldwide. sSMC are a heterogeneous group of derivative chromosomes concerning their clinical consequences as well as their chromosomal origin and shape. Besides the sSMC present in Emanuel syndrome, i.e. der(22)t(11;22)(q23;q11), only few so-called complex sSMC are reported.

Results: Here we report three new cases of unique complex sSMC. One was a de novo case with a dic(13 or 21;22) and two were maternally derived: a der(18)t(8;18) and a der(13 or 21)t(13 or 21;18). Thus, in summary, now 22 cases of unique complex sSMC are available in the literature. However, this special kind of sSMC might be under-diagnosed among sSMC-carriers.

Conclusion: More comprehensive characterization of sSMC and approaches like reverse fluorescence in situ hybridization (FISH) or array based comparative genomic hybridization (array-CGH) might identify them to be more frequent than only ~0.9% among all sSMC.

Background

Small supernumerary marker chromosomes (sSMC) are a major problem in cytogenetic diagnostics and genetic counseling. sSMC are structurally abnormal chromosomes that cannot be identified or characterized unambiguously by conventional banding cytogenetics alone, and are generally about the size of or smaller than a chromosome 20 in the same metaphase spread. Molecular cytogenetic techniques are necessary for comprehensive sSMC characterization [1]. Cases with a de novo sSMC, par-
particularly those that are prenatally ascertained, are not easy
to correlate with a clinical outcome [2]. It has been estab-
lished that substantial parts of sSMC lead to four specific
syndromes, i.e. Pallister-Killian [= i(12p)], isochrom-
some 18p [i(18p)], cat-eye [i(22p-q)], and Emanuel or
derivative chromosome 22 [der(22)t(11;22)] syndromes
[1]. Moreover, for the remaining ones, recently a first step
towards a genotype-phenotype correlation was reported
[2]. In general, the risk for an abnormal phenotype in pre-
natally ascertained de novo cases with sSMC is considered
to be ~13% [3]. This has been refined to 7% (for sSMC
from chromosome 13, 14, 21 or 22) and 28% (for all non-
acrocentric autosomes) [4] and has now been suggested to
be 30% [5]. Also generally speaking, sSMC transmitted by
normal sSMC carriers to their progeny are not correlated
with clinical problems [6], although exceptions have been
described [7].

One of the smallest subgroup of sSMC is constituted by
the so-called complex marker chromosomes. 'Complex'
are such sSMC which consist of chromosomal material
derived from more than one chromosome [1]. Thus,
besides the aforementioned larger group of Emanuel- or
derivative chromosome 22- [der(22)t(11;22)-] syndrome
cases, up to now only 19 unique complex sSMC were
described (see Tab. 1). Here we report three more such
cases of unique complex sSMC and provide a review of the
literature. Moreover, it is discussed if this kind of sSMC is
under-diagnosed due to lack of appropriate screening
techniques.

Results and discussion
Case reports
Case A (= #13 in Tab. 1)
A 13 months old boy was studied cytogenetically because
of failure to thrive and psychomotor development delay.
The patient was the product of the fourth pregnancy of a
non-consanguineous couple. At birth, the mother was 31
and the father 55 years old. The pregnancy was compi-
lcated by hyperemesis gravidarum treated with metoclopr-
amid; additionally, there was a mild exposure to tobacco
(3 cigarettes a day) and to alcohol (1 unit per month).
Sonography was normal during whole pregnancy. The
patient was born by normal vaginal delivery at 41 1/7
weeks of gestation with a birth weight of 2150 g (10th cen-
tile), a length of 52 cm (50th to 90th centile) and a head cir-
cumference of 34 cm (10th centile). Neonatal adaptation
was good with an APGAR-score of 9/10/10 and no appar-
ent congenital abnormalities were noticed. During the
first year of live, the patient showed an increasing refusal
to eat with insufficient growth (weight -3.6 SDS, length
2.4 SDS, head circumference 3.8 SDS at the age of 13
months). At 13 months, psychomotor development was
markedly delayed with a Griffith General Intelligence
Quotient of 63. The neurological examination revealed

slight muscular hypotonia but otherwise no abnormali-
ties. MRI of the brain was normal. Laboratory analyses
were not suggestive for any metabolic disorder.

For family history: the mother was treated for attention-
deficit/hyperactivity problems during her adolescence
and her IQ was borderline. The father presented no med-
ical problems. The patient’s 6 year old brother was born
with diaphragmatic hernia and is at present treated for
attention-deficit disorder. The 4 years old brother showed
a delayed speech development with first words at the age
of 3 years but to date his linguistic performance was nor-
amal. A fourth child was lost in the 12th week of gesta-
tion due to unknown reasons. A neuropsychological de-
velopment therapy was initiated.

Banding cytogenetics revealed a karyotype 47,XY,+mar-
mat [100%]. cenM-FISH uncovered a derivative chromo-
some 18 (result not shown), which was further charac-
terized to include the entire short arm of chromosome 18.
The subtelomeric probe for 18pter (Fig. 1d), the centro-
mere-near probe RP11-411B10 in 18p11.21 and the cen-
trомерic probe D18Z1 (Fig. 1e) were present on the
sSMC. MCB applying a probe set for chromosome 18 did
stain the whole sSMC without leaving any region
unstained (Fig. 1f). Surprisingly, flow sorting and reverse
FISH of the sSMC revealed the presence of additional
material on the derivative chromosome 18, which orig-
nated from chromosome 8pter (Fig. 1b). This result was
confirmed by a centromeric probe for chromosome 18
applied in combination with a subtelomeric one for chro-
mosome 8pter (Fig. 1c). Thus, a partial trisomy 18p plus
8pter was present in case A and his mother due to an
sSMC der(18)t(8;18)(8p23.2~23.1;18q11.1).

Case B (= case #16 in Tab. 1)
A newborn male, born at 42 weeks of gestation by normal
vaginal delivery, was product of the first pregnancy of a
healthy and not consanguineous couple. At birth the
mother was 23 years old and the father 38. During whole
pregnancy an exposure to tobacco (3 cigarettes a day) was
present. Sonography performed in 6th month of preg-
nancy revealed an atrial septal defect (ASD) and a club
foot on the right side. Pregnancy was continued and birth
weight was 2,760 g (3rd to 25th centile) with a length 49
cm (25th to 50th centile) and an occipito-frontal circum-
cference (OFC) of 33 cm (25th centile). The prenatally
observed findings were confirmed, but no other congeni-
tal defects reported. At present the child is two years old,
and his development is normal without any delay. The
parents are phenotypically normal, even though the
mother seems to have a borderline IQ.

A maternally derived, NOR-positive sSMC was detected in
this case in all studied cells. By application of commer-

cially available centromeric probes for the acrocentric chromosomes a derivative chromosome 13 or 21 was characterized. As well-known, centromeres of chromosomes 13 and 21 harbor identical repetitive elements – thus, one cannot decide for a heterochromatic sSMC from which of the both chromosomes the sSMC derives. Centromere-near probes for chromosomes 13 and 21 were not indicative for euchromatic material on the sSMC (Fig. 3a). However, a big part of the sSMC remained unstained by whole chromosome painting probes for chromosome 13 or 21 (results not shown). Thus, glass needle based microdissection of the sSMC followed by reverse FISH were done, which demonstrated that the yet unstained part of the derivative chromosome 13 or 21 was derived

| Case acc. to | GTG-karyotype | sSMC acc. to FISH | abnormal clinical outcome |
|-------------|----------------|------------------|--------------------------|
| 1 07-U-1    | 47,XX,+mar [100%] | der(7)(X;5:7)(p22.l:q35.p13q21) | +                        |
| 2 13/21-U27 | 47,XY,+mar [100%] | der(13 or 21)(t(13 or 21;18)(13 or 21pter->13 or 21q11:18p11.21->18p12) | +                        |
| 3 13/21-U-8 | 47,XX,+mar [100%] | der(13 or 21)(t(13 or 21)q11.12) | ?                        |
| 4 14-O-q11.2/1-1 15-O-q11.1/4-1 | 47,XY,+mar [100%] | dic(14:15)(14pter->14q11.2->15q11.1->15p13) | -                        |
| 5 15-CW-3   | 47,XX,+mar [100%] | der(15)(t(15;22)(q11:q22)) | +                        |
| 6 15-U-6 22-U-4 | 47,XY,+mar [100%] | der(15)(t(Y;15)(q12q22)) | ?                        |
| 7 15-U-10   | 47,XY,+mar [100%] | der(15)(t(Y;15)(q12q22)) | ?                        |
| 8 17-W-p13.3/1-1 | 47,XYq,+mar [100%] | der(17)(t(17acro)(q11.p11.2)) | +                        |
| 9 22-U-18   | 47,XY,+mar [100%] | der(22)(t(12;22)(p12q11.2->12q11.2)) | +                        |
| 11 15-CO-1 0Y-CO-2 | 47,XX,+mar [100%] | dic(Y;15) presence of 2 alpha-cepY and cep15 signals; PCR prove of Yq11 euchromatic region (AZF1); absence of SRY region | -                        |
| 12 21-O-q11.1/1-1 22-O-q11.1/3-1 | 46,5q,t(21:22).+mar [100%] | der(21)(t(21:22)(q11.1:p11.2)) | -                        |
| 13 18-U-10  | 47,XY,+mar [100%] | der(18)(t(8;18)(8q23.2-23.1:18p11.1)) | +                        |
| 14 13/21-O-q10/4-1 | 47,XX,+mar [87%]/46,XX [13%] | dic(13 or 21:14)(q10q10) | -                        |
| 15 13/21-O-q10/5-1 15-O-q10/4-1 | 47,XX,+mar [100%] | dic(13 or 21:15)(q10q10) | -                        |
| 16 13/21-U-28 | 47,XY,+mar [100%] | der(13 or 21)(t(13 or 21;18)(13 or 21pter->13 or 21q11:18p11.21->18pter)) | +                        |
| 17 12-U-6   | 47,+mar [100%] | der(12)(t(4;12)(p16q11)mat | +                        |
| 18 13-U-8   | 47,XY,+mar [100%] | der(13)(t(8;13)(p23.2q12.2)mat | +                        |
| 19 15-O-q11.2/5-1 | 47,XY,+mar [100%] | der(15)(t(9;15)(p24q11.2)mat | -                        |
| 20 15-U-15  | 47,XY,+mar [100%] | der(15)(t(15;16)(q13p3.2)mat | +                        |
| 21 18-CW-2  | 47,XX,+mar [100%] | der(18)(t(18:21 or 22)mat | +                        |
| 22 22-U-11  | 47,XY,+mar [100%] | der(22)(t(22;22)(q24.1q11.2)mat | +                        |

All cases with unique complex sSMC reported in the literature according to [10]; the case numbering scheme is explained also in Ref. 10. GTG-karyotype, sSMC as characterized after FISH and information on the clinical outcome are provided. The three new cases reported here are marked by asterisks.

| Case acc. to | GTG-karyotype | sSMC acc. to FISH | abnormal clinical outcome |
|-------------|----------------|------------------|--------------------------|
| de novo     |                |                  |                          |
|            |                |                  |                          |
| Unclear origin |                |                  |                          |
|            |                |                  |                          |
| sSMC from mother |                |                  |                          |
|            |                |                  |                          |
| Parental balanced translocation |                |                  |                          |
|            |                |                  |                          |
from the short arm of chromosome 18 (results not shown). While the centromere-near probe RP11-411B10 in 18p11.21 was present (Fig. 2b), the centromeric probe D18Z1 was absent on the sSMC (results not shown) with the karyotype der(13 or 21)(13 or 21pter->13 or 21q11.2::18p11.21->18pter).

**Case C (= case #10 in Tab. 1)**

A 14 month old female with significant developmental delay, cardiac anomalies, preauricular tags, dysmorphism, polypsena, extrahepatic biliary atresia, intestinal malrotation and hearing loss in right ear was referred to cytogenetic analysis in connection with thrombocytopenia following liver transplant. Clinically a cat eye syndrome was suggested. Bone marrow showed complete replacement with chronic lymphocytic leukemia and marked reduction in erythroid precursors (pure red cell aplasia). Following bone marrow transplant the patient remained in remission. The parents were phenotypically normal. A *de novo* sSMC was present in all studied cells of this case. The NOR-positive sSMC was initially characterized as a derivative of chromosome 13 or 21 by application of the corresponding commercially available centromeric probes for #13/21 (D13/21Z1 – green) and a probe specific for all acrocentric *p*-arms (midi54 – blue) were present on the marker. However, no centromere-near material, neither from chromosome 13 nor 21 was detectable on the marker (pink and red probes). Three-color-FISH using partial chromosome painting (pcp) probe for the short (green) and the long arm of chromosome 18 (blue) together with a probe for the centromere-near region of 18p11.2 (red) revealed that the whole short arm was present on the sSMC.
or21q11::22q11.1~11.2->22q11.21~11.22::22q11.21~11.22->22pter) was characterized.

Discussion
Here we report three new cases of patients with unique complex sSMC. Two of the sSMC are maternally derived (cases A and B) and one is de novo (case C). The two maternally derived sSMC both lead to partial trisomies of the short arm of chromosome 18 and interestingly two similar cases are already reported in the literature [8,9] (cases 2 and 3 in Tab. 1). Compared to cases with partial trisomy of the short arm of chromosome 18 (overview on 140 cases reported in the literature see [10]), those four cases with partial trisomy 18p present with surprisingly mild clinical signs and symptoms.

The third case reported here (Case C) is a child with a cat eye syndrome which is carrier of a dicentric sSMC leading to a partial tetrasomy of 22q11.21. However, it is the first cat eye syndrome associated sSMC with centromeres derived from two different chromosomes, i.e. 13 or 21 and 14 or 22, even though 132 cases are already reported [10]. It is suggested that acrocentric derived dicentric inverted duplicated sSMC are formed due to an U-type exchange during meiosis [1]. Thus, the most likely explanation for this unusual sSMC in case C is, that one of the original chromosomes 22 already had a polymorphic centromeric region with D13/21Z1 instead of D14/22Z1 sequences in its centromeric region. A similar polymorphic behavior for the sequence D15Z1 was recently reported to be present in 17.6% of the acrocentric chromosomes [11]. An alike mode of formation could be suggested for cases 4, 6, 12, 14 and 15 of Tab. 1.

Overall, now 22 complex sSMC are reported in the literature (see Tab. 1). According to Fig. 4 it can be reckoned that in principle all chromosomes can be involved in their formation; examples for chromosomes #1, #2, #3, #6, #10, #11, #19 and #20 will be detected, when more unique complex sSMC are reported. Nonetheless, Fig. 4 also indicates, that some chromosomes might be involved more often in complex sSMC than others, i.e. #13/21, #15, #18 and #22, possibly also #8. Due to low case number it can only be speculated if, similar to the formation of the der(22)t(11;22), specific DNA-sequences are causative for their formation [12]. At least this could be speculated for cases 13 and 18 from Tab. 1, where the breakpoint in chromosome 8 was 8p23.2. Here it is known that low copy repeats co-mediate recurrent rearrangements consisting of triplication at 8p23.2 [13].

According to Tab. 1 and summarized in Fig. 5 only 50% of unique complex sSMC are de novo. The remainder 50% are parentally derived: 20% of the patients inherited the sSMC directly – here only maternal inheritance is reported yet. In the remainder 30% of the cases the unique complex sSMC was part of a balanced translocation in one parent. The latter resembles to the mode of formation of the most frequent complex sSMC, the der(22)t(11;22) [12].

In 19/22 cases summarized in Tab. 1 the clinical outcome was reported. In ~1/3 of the cases a normal phenotype and in the rest an in parts severely abnormal clinical outcome was present (Fig. 6).

Conclusion
Among ~2500 reported sSMC cases studied for their chromosomal origin and subsequently reported, by now 22 cases with unique complex sSMC were detected [10]. I.e. unique complex sSMC are to be expected in at least 0.9% of patients with an sSMC. However, the question is, if the percentage of this specific kind of sSMC is not underestimated. Unique complex sSMC are easy to be missed if, in case of acrocentric chromosome derived sSMC not all centromeric probes are applied, and/or if no flow sorting or microdissection followed by reverse FISH or array-CGH [14] is performed. Thus, for cases similar to cases 2, 3, 9,
10, 15 and 16 from table 1 one may suggest there is no euchromatin on the sSMC after its origin from an acrocentric chromosome was revealed by a centromeric probe. Or, as in case 13, if already a (relatively large) euchromatic imbalance was detected, which could explain the clinical symptoms of the specific patient, a very small part of another chromosomal origin is very unlikely to be detected. This can be problematic especially in prenatal diagnostics, but also concerning genotype-phenotype correlations of sSMC.

In conclusion, a really comprehensive characterization of all sSMC by different probes, probe sets and approaches could enhance the detection rate of unique complex sSMC. Unique complex sSMC are especially to be expected in cases with a 'heterochromatic sSMC', no uniparental disomy in connection with the sSMC and, nonetheless, clinical symptoms. Here a reverse FISH or array-CGH experiment of the sSMC should be performed and might show additional chromosomal imbalances.

**Methods**

**Cytogenetics and molecular cytogenetics**

Banding cytogenetics (GTG-banding and NOR-staining) was done on metaphase cells derived from peripheral blood of the three aforementioned patients and their parents according to standard procedures. 25 cells were analyzed per case.

The sSMC were characterized in more detail by commercially available centromeric probes or centromere-specific multicolor fluorescence in situ hybridization (cenM-FISH) [15], subcentromere-near [16] (#13, #18, 21, #22) and commercially available subtelomeric FISH-probes (#8 and #18, Vysis) and/or home made partial chromosome painting probes for the long and the short arm of chromosome 18 [16] plus the short arm of all acrocentric chromosomes (probe midi54 [17]). Additionally, the multicolor banding (MCB) probe set for chromosome 18 [18] was applied in case A. In case C the probes RP11-172D7 and RP11-81B3 in 22q11.21 plus RP11-1058B20 in 22q11.22 were used to characterize the size of the cat...
eye syndrome specific tetrasomy. In case A and B also chromosome flow sorting [19] or glass needle based microdissection of the sSMC were done [2], respectively, followed by reverse FISH. All aforementioned molecular cytogenetic approaches are standard techniques of (multicolor) FISH and were repeatedly described before in detail.

Review of the literature
The sSMC-related literature is collected from [10]. The database was searched for complex sSMC cases, which were included in Table 1.

Competing interests
The author(s) declare that they have no competing interests.

Authors’ contributions
VT and MG performed chromosome flow sorting and FISH analysis; SF, AN and LR performed the clinical cases and description, FB, JA and LR performed banding cytogenetic analyses and detected the sSMC, MG, HM, EE and DR did molecular cytogenetic studies, NK performed microdissection and reverse FISH, AW, TL have been involved in drafting the manuscript and revising it critically for important intellectual content. All authors read and approved the final manuscript.

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References
1. Liehr T, Claussen U, Starke H: Small supernumerary marker chromosomes (sSMC) in humans. Cytogenet Genome Res 2004, 107:55-67.
2. Liehr T, Mrasek K, Weise A, Dufke A, Rodriguez L, Martinez Guardia N, Sanchis A, Vermeesch JR, Camel C, Polickyo A, Haas OA, Anderson J, Claussen U, von Egelling F, Starke H: Small supernumerary marker chromosomes—progress towards a genotype-phenotype correlation. Cytogenet Genome Res 2006, 112:23-34.
3. Warburton D: De novo balanced chromosome rearrangements and extra marker chromosomes identified at prenatal diagnosis: clinical significance and distribution of breakpoints. Am J Hum Genet 1991, 49:995-1013.
4. Croll JA: FISH and molecular studies of autosomal supernumerary marker chromosomes excluding those derived from chromosome 15: II. Review of the literature. Am J Med Genet 1998, 75:367-381.
5. Liehr T, Weise A: Frequency of small supernumerary marker chromosomes in prenatal, newborn, developmentally retarded and infertility diagnostics. Int J Mol Med 2007, 19:719-731.
6. Brondum-Nielsen K, Mikkelsen M. A 10-year survey, 1980–of prenatally diagnosed small supernumerary marker chromosomes, identified by FISH analysis. Outcome and follow-up of 14 cases diagnosed in a series of 12,699 prenatal samples. Prenat Diagn 1990, 10(7):615-619.
7. Anderlid BM, Sahlen S, Schoumans J, Holmberg E, Ahgren I, Mortier G, Speleman F, Blenow E: Detailed characterization of 12 supernumerary ring chromosomes using micro-FISH and search for uniparental disomy. Am J Med Genet 2001, 99:223-233.
8. Mabboux P, Brisset S, Aboura A, Pineau D, Koubi V, Joannidis S, Labrune P, Tachdjian G: Pure and complete trisomy 18p due to a supernumerary marker chromosome associated with moderate mental retardation. Am J Med Genet A 2007, 143:727-733.
9. Abstract of Minelli E, Müller-Navia J, Mazzola D, Mny P, Bronz L, Uhr M: Characterization of a marker chromosome with FISH and microdissection in prenatal diagnosis on the 4th European Cytogenetics Conference, Sept, Bologna. 2003 [http://web.hec.bologna.it/13_31.html].
10. The sSMC homepage by T Liehr [http://www.med.uni-jena.de/fish/ssMC/005START.htm].
11. Cockwell AE, Jacobs FA, Crolla JA: Distribution of the D15Z1 copy number polymorphism. Eur J Hum Genet 2007, 15:441-445.
12. Kurahashi H, Inagaki H, Yamada K, Ohye T, Taniguchi M, Emanuel BS, Toda T: Cruciform DNA structure underlies the etiology for palindrome-mediated human chromosomal translocations. J Biol Chem 2004, 279:35377-35383.
13. Giorda R, Ciccone R, Gimelli G, Pramparo T, Beri S, Bonaglia MC, Giglio S, Guarnardi M, Argento J, Rocchi M, Zuffardi O: Two classes of low-copy repeats mediate a new recurrent rearrangement consisting of duplication at 8p23.1 and triplication at 8p21.2. Hum Mutat 2007, 28:459-468.
14. Baclo L, Van Esch H, Melotte C, Kosyakova N, Starke H, Frijns JP, Liehr T, Vermeesch JR: Array painting using multicolor digoxigenin-labeled DNA probes for the detection of supernumerary marker chromosomes (sSMCs). Cytogenet Genome Res 2008, 114:51-67.
15. Starke H, Nietszel A, Weise A, Keller A, Mrasek K, Belitz B, Kelbova S, Volkleth M, Albrecht B, Mitulla B, Trappe R, Barletts I, Adolph S, Dufke A, Singer S, Stumm M, Wegner RD, Seidel J, Schmidt A, Kuechler A, Schreyer I, Claussen U, von Eggeling F, Liehr T: Small supernumerary marker chromosomes (SMMCs): genotype-phenotype correlation and classification. Hum Genet 2003, 114:51-67.
16. Starke H, Seidel J, Henn W, Reichardt S, Wolleth M, Stumm M, Behrend C, Sandig KR, Kelbova C, Senger G, Albrecht B, Hansmann I, Heiler A, Claussen U, Liehr T: Homologous sequences at human chromosome 9 bands p12 and q13-21.1 are involved in different patterns of pericentric rearrangements. Eur J Hum Genet 2002, 10:790-800.
17. Liehr T, Heiler A, Starke H, Rubcov S, Trifonov V, Mrasek K, Weise A, Kuechler A, Claussen U: Microdissection-based high resolution multicolor banding for all 24 human chromosomes. Int J Mol Med 2002, 9:335-339.
18. Telenius H, Pelmeir AR, Tuanacilffe A, Carter NP, Behnel A, Ferguson-Smith MA, Norsendjoeld M, Pfrang R, Ponder BA: Cytogenetic analysis by chromosome painting using DOP-PCR amplified flow-sorted chromosomes. Genes Chromosomes Cancer 1992, 4:257-263.