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*Not*I linking/jumping clones of human chromosome 3: mapping of the TFRC, RAB7 and HAUSP genes to regions rearranged in leukemia and deleted in solid tumors

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Abstract By applying the 'recognition mask' strategy to 300 mammalian sequences containing *Not*I sites we demonstrated that 5′ ends of genes are highly enriched in *Not*I sites. A *Not*I linking clone NL2-252 (D3S1678) containing transferrin receptor (TFRC) gene was used as an initial point for chromosomal jumping. One of the jumping clones, J21-045 traverses 210 kbp and links NL2-252 to NL26 (D3S1632), a *Not*I linking clone containing highly polymorphic sequences. The TFRC gene was mapped to 3q29, close to the telomeric marker D3S2344, by linkage analysis, a panel of hybrid cell lines, GeneBridge 4 panel and FISH. Clone NLM-007 (D3S4302) was found to contain *ras*-homologous gene RAB7. By FISH and a panel of hybrid cell lines this gene was mapped to 3q21. This region is of particular interest due to frequent rearrangements in different types of leukemia. Clone L2-081 (D3S4283) containing new member of ubiquitin-specific proteases (HAUSP gene) was localized in 3p21 inspiring further investigation of involvement of this gene in development of lung and renal carcinomas.

Key words: Gene mapping; Cancer related gene; *Not*I linking clone; *Not*I jumping clone; (Human chromosome 3)

1. Introduction

Rare-cutting restriction endonucleases like *Not*I are very useful tools for physical and functional mapping of complex genomes. One of the most powerful techniques exploring the advantages of rare-cutting enzymes is based on combined application of linking and jumping clones [1,2]. In linking clones *Not*I site remains in its natural surroundings as in intact genome, while in jumping clones left and right flanks of a restriction site belong to two different *Not*I sites neighboring each other in the genome. Preparation of genomic libraries containing *Not*I sites has been improved and representative *Not*I linking and jumping libraries have been constructed covering the whole human genome or the individual chromosomes [3,4].

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At present, *Not*I linking clones have become not only important landmarks in low-resolution physical mapping of the human genome but they also highlight the regions of the genome where genes are located. Their usefulness in constructing *Not*I restriction maps for the entire chromosomes or large chromosomal regions has been demonstrated [1].

Their versatility makes them an indispensable tool for joining physical, transcriptional and genetic maps, for ordering YAC and cosmid clones into contigs, for locating CpG islands and providing DNA fragments for the isolation of regularly spaced microsatellite markers [5–7].

The *Not*I linking clones are also good markers for expressed genes [8–10]. Random sequencing of the *Not*I linking and jumping clones is suitable to establish their order in the genome [11]. Here, we demonstrate the effectiveness of the *Not*I linking and jumping libraries in identifying and mapping of transcribed sequences in general and in particular for localization of cancer-related genes.

2. Materials and methods

2.1. DNA

DNA isolation, Southern blotting, and other standard procedures were performed according to the text-book protocols [12,13]. PFGE was done as described earlier [11].

2.2. Construction of NotI linking and NotI jumping libraries

MCH 903.1 is a mouse-human microcell hybrid containing a single copy of human chromosome 3, derived from a normal human diploid fibroblast cell line HFDC [3]. DNA isolated from this cell line was used for constructing the following libraries: *Not*I linking libraries NLM and NL2 [3,4] and *Not*I jumping libraries J21 and J22 [14]. Construction of the *Not*I linking and jumping libraries was described elsewhere [4,14].

2.3. Primer design and PCR

PCR primers were designed using the PRIMER program (http://www.bmb.psu.edu/597A/stdnts96/ducker/primer.htm). PCR conditions for amplification of sequences adjacent to the *Not*I site were 2.0–3.0 mM $MgCl_2$; 10 mM Tris-HCl, pH 8.8; 50 mM KCl; 0.2 mM of each dNTP; 100 nM of each primer; 96°C for 5 min, 30–35 cycles of 96°C for 30 s, annealing at 58°C for 20 s, extension at 72°C for 1 min, and final extension at 72°C for 5 min. PCR products were analyzed on 1.5–2% agarose gels. Sequences of primers used for PCR amplification of TFRC gene: (i) 5′ AGGAAGTGACGCACAGCC 3′;

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(ii) 5′ AGGGAGGACACGAGGGTC 3′; of NRL-094: (i) 5′ ACGTGTCTGTTCAGGTGTGC 3′; (ii) 5′ AATTACGGCATTTT-GACATGC 3′.

2.4. FISH

Preparation of metaphase spreads, labeling of probes and hybridization were essentially the same as described earlier [15]. The R-banding FISH was based on the known procedures [16]. The slides were analyzed with Olympus microscope equipped with a Cohu CCD camera and the signals were processed by Cyto Vision Ultra software system from Applied Imaging.

3. Results and discussion

3.1. NotI sites are mainly located at 5′ ends of the genes

Our work on short-gun sequencing approach to construct *Not*I restriction map of human chromosome 3 led to production of more than 300 unique sequences containing *Not*I sites [10]. Using this set of DNA fragments it became possible to verify the hypothesis that *Not*I sites are located mainly at 5′ ends of the genes [8]. To achieve this aim, we have used a 'recognition mask' strategy [17,18]. This procedure allowed us to analyze the oligonucleotide composition of a selected sequence or set of sequences. The degree of similarity (F) of the given set of sequences may be evaluated by comparison of oligonucleotide frequency distribution of F for new set with the distribution for the 'training' set (S) and for the random set. If the frequency distribution for the given set of sequences overlaps with the pattern for one of the training sets or with the pattern for random sequences, it indicates, respectively, the similarity or dissimilarity of the analyzed and the training sequences.

Approximately 300 *Not*I site-flanking sequences with an average length of about 250–500 bp were compared with two training sets containing 2100 5′-flanking and 2400 3′-flanking regions (300 bp for each sequence) of human genes from the EMBL database (Release 30). EMBL accession numbers of *Not*I-flanks were from Z22238 to Z22509 and from X87544 to X87575.

Comparisons were made with oligonucleotides shorter than octamers. The same procedure for comparison of the *Not*I-flanking sequences with the 5′- and the 3′-regions demonstrated a profoundly different pattern: *Not*I sequences differ from the 3′-flanking regions as the random sequences do (Fig.

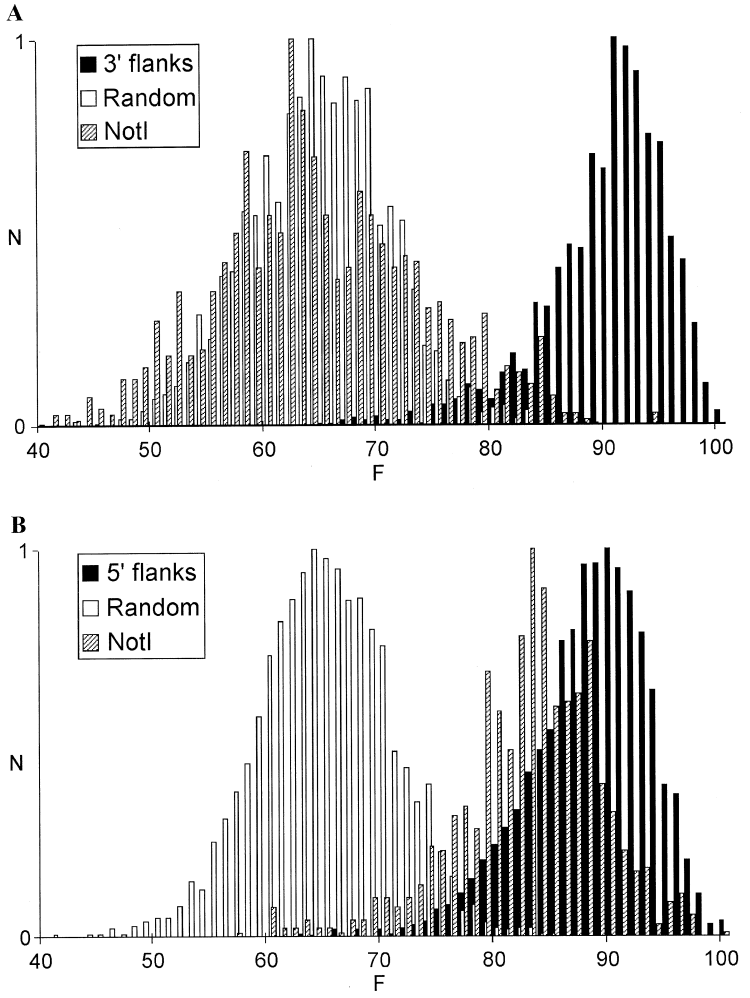
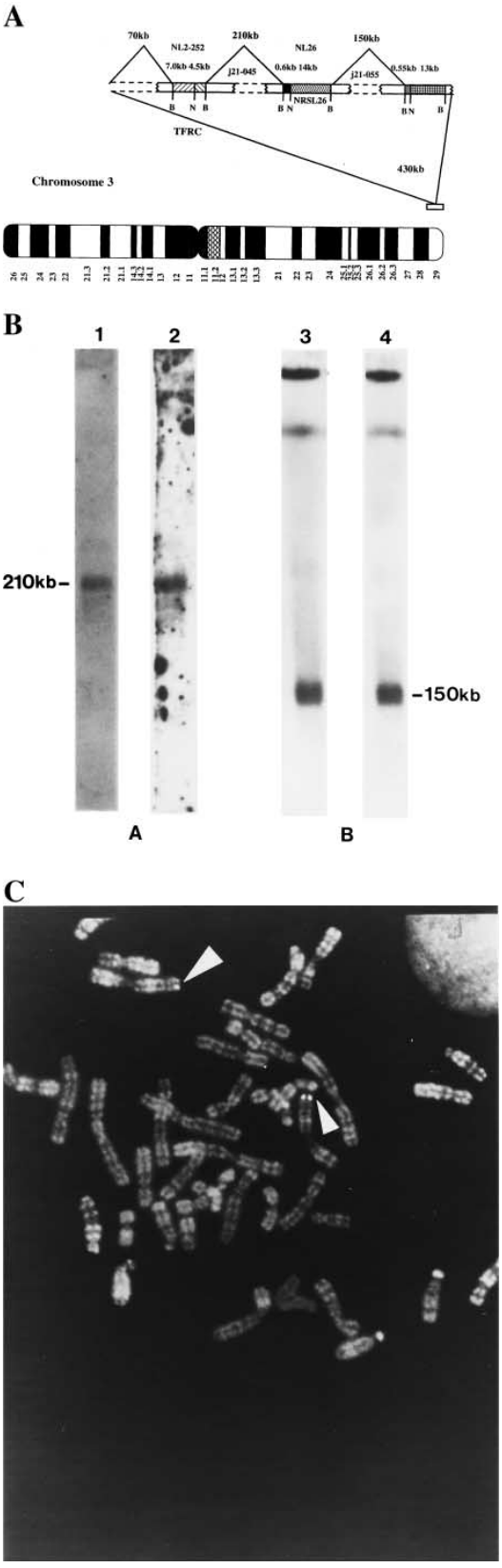


Fig. 1. Comparison of the oligonucleotide compositions for two sets of sequences estimated by the distributions of F values. For each sequence of each set the measure of similarity F is calculated. The height of the column indicates the number of sequences of one set with the same F. All heights are normalized to have the equal maximum values for each set. A: Distribution of the 3′-flanking regions, random and *Not*I sequences drawn using 3′-flanking regions as a training set. The F values of the *Not*I-flanks are remote from the F values of the 3′-flanking sequences. B: Distribution of the 5′-flanking regions, random and *Not*I sequences drawn using 5′-flanking regions as a training set. The histogram of the *Not*I-flanks is very similar to the histogram of the 5′-flanks.

1A). Distribution mean values for the *Not*I-flanks, 3′-flanks and random sequences are 0.6, 0.9 and 0.65, respectively. The degree of overlapping for the *Not*I- and 3′-flanks is as low as 5%. At the same time there is a non-random correlation between oligo compositions of *Not*I sequences and 5′-flanking regions (Fig. 1B). The mean values of frequency distribution are 0.82, 0.98 and 0.65 for the *Not*I-flanks, 5′-flanks and random sequences, respectively. Most of the *Not*I-flanks possess the same degree of similarity with the recognizing mask as the 5′-flanks themselves. The difference between the *Not*I-flanks and 3′-flanks was even greater than the difference between the latter and the random sequences. It implies that at a high level of significance the *Not*I sites were virtually never located at the 3′-flanks of the genes. On the other hand, there is a high level of coincidence of the *Not*I sites and the 5′-flanks of human genes. Taken this pattern into account would simplify searching the homology between known sequences and newly sequenced *Not*I-flanks. Our conclusion is consistent with the observation that *Not*I clones containing portions of the genes, revealed identities to the 5′ ends of the genes [10,15].



Interestingly, several genes, which might be important for the carcinogenesis, were identified by *Not*I linking clones. Human melanoma NCK protein gene (NL2-270), human aminoacylase ACY gene (NL1-245), human arginine-rich ARP gene (NL1-216) and others were localized previously [10,15] and here we present additional data on use of *Not*I linking clones for identification and mapping of genes important for growth and differentiation control.

3.2. Localization of the TFRC gene

The NL2-252 clone sequence (EMBL accession number Z22395), a 237 bp segment, was completely identical to the 5′ part of the TFRC gene [10,19]. This gene has been shown previously to be important for growth/differentiation and probably is involved in the development of leukemia [20,21]. Due to the absence of informative polymorphic markers in the vicinity of the TFRC gene, it had not been precisely localized on the genetic map of the chromosome 3 [22,23]. For this reason, we decided to map this gene more precisely.

Both *Bam*HI-*Not*I halves of the insert from the NL2-252 clone (D3S1678) were used as probes to isolate the corresponding *Not*I jumping clones from the J21 and J22 libraries (Fig. 2A). One jumping clone, named J21-045, covered about 210 kb as detected by PFGE (Fig. 2B). Using the 0.6 kbp *Bam*HI-*Not*I fragment from the J21-045 clone as a probe, the overlapping *Not*I linking clone NL26 (D3S1632) was identified. The 14 kb *Bam*HI-*Not*I fragment of this clone was used to identify another overlapping jumping clone J21-055 (Fig. 2A). Using these two clones we have established a *Not*I restriction map near TFRC gene encompassing about 0.5 mbp (Fig. 2A, B). Clones NL2-252 and NL26 were mapped by FISH (Fig. 2C) and using the panel of hybrid cell lines [24] to 3q29. All DNAs from the NL26 contig were sequenced around *Not*I sites, the average sequence length was about 1000 bp [11]. Search of the GENBANK database using

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Fig. 2. Mapping of the 3q29 region with linking and jumping clones. A: Schematic map of NL26 contig. Orientation of the contig towards telomere is unknown. B: PFGE analysis of NL26 contig. B.A, B.B: Hybridization with PFGE filter no. 1 and no. 2 respectively. Human DNA was digested with *Not*I. Hybridizations were performed with: 1, NL2-252, 4.5 kb *Not*I-*Bam*HI fragment; 2, NL26, 0.6 kb *Not*I-*Bam*HI fragment; 3, NL26, 14 kb *Not*I-*Bam*HI fragment; 4, J21-055, 0.55 kb *Not*I-*Bam*HI fragment. C: Chromosomal localization of NL26 DNA by FISH; positive signals are shown by arrows (3q29).

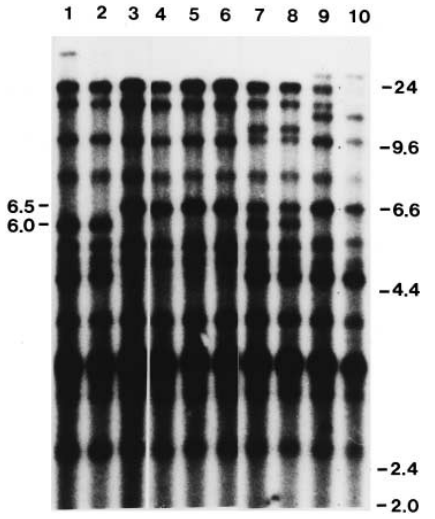

Fig. 3. *Taq*I polymorphism of NL26 DNA. Lanes 1–10: Human genomic DNA isolated from various individuals and digested with *Taq*I. Two polymorphic alleles used for linkage analysis are marked on the left side. Size markers are indicated on the right side.

BLAST program [25] revealed no significant sequence similarity for clones NL26 and J21-055 with any sequence in the databank. The *Not*I linking clone NL26 exhibited restriction fragment length polymorphism (RFLP, Fig. 3). A RFLP detected by *Taq*I restriction endonuclease was used to localize NL26 DNA by linkage mapping. The two alleles of 6.5 and 6 kbp have a frequency of heterozygotes of 0.48. Human genomic DNA samples for the reference families were provided by CEPH. The procedures for genotyping and linkage analysis were performed as described earlier [26]. The two-point linkage analysis was performed on a VAX/VMS mainframe computer using the CRI-MAP linkage program. Genotype data for the reference markers were obtained from the CEPH database 6. Two-point linkage data indicated 10; 10 and 9 cm genetic distances from the most telomeric D3S1311 (lod: 3.5), D3S1265 (lod: 5.04) and D3S42 (lod: 17.06) markers respectively. Multipoint linkage analysis failed to position NL26 DNA uniquely (lods > 3) on the reference map [27].

To localize the TFRC gene precisely, we generated PCR primers specifically for this gene (near NL2-252, see Section 2). CEPH megaYAC pools A and B (Research Genetics) were screened and only one positive YAC clone was identified, 827c9. However, this YAC clone appeared to be useless due to its chimeric nature.

We mapped NRL-094 (D3S3870) about 1 mbp telomeric to NL2-252 (our unpublished data), to the very telomeric region of human chromosome 3, 4.8 cR from D3S3954 (WI-9695) and 1.6 cR from D3S2344 using radiation hybrid panel GeneBridge 4 (Research Genetics).

In summary, our results demonstrated that the TFRC gene is located close to the D3S2344 marker, telomeric to the D3S3669 and D3S1601 markers, and centromeric to the D3S1311 marker.

3.3. Localization of the RAB7 gene

FASTA analysis of sequences from another *Not*I linking clone, NLM-007 (D3S4302, EMBL Z22474) revealed that this clone contained sequences virtually identical (97.4% over 151 bp) to the 5′ end of human *ras*-homologous gene RAB7 [28].

The non-identity was due to two mismatches and two deletions. All of them were located in GC-rich regions where most of the sequence errors occur due to compression of the bands during electrophoresis. Therefore we assume that these four non-identities were caused by sequencing errors either in the initial RAB7 sequence, or in NLM-007 DNA, or in both fragments.

RAB7 protein belongs to a superfamily of small molecular weight GTPases known to be associated with early and late endosomes [29]. The RAB7 function is not required for early internalization events, but is crucial in downstream degradative events [28]. Chromosomal localization of the RAB7 gene could be important for various reasons. However, mapping of genes which possess many structurally homologous members becomes a difficult task if cDNA clones are applied. Our *Not*I linking clones contain in average about 8 kb insert that should be sufficient for mapping. *Not*I fragment of NLM-007 clone (about 6 kb) was applied for mapping using panel of hybrid cell lines [24] and FISH. The results from both types of experiments were in good agreement and mapped NLM-007 to 3q21.

It should be noticed that this region is especially interesting due to its frequent involvement in different types of leukemia and myelodisplastic syndrome [30,31]. The 3q21-q26 rearrangements include translocations, inversions, deletions, and duplications. No genes important for the development of leukemia have been identified in this locus so far. The potential importance of RAB7 gene in development of these malignancies should be examined in future.

3.4. Localization of new ubiquitin-specific protease gene in 3p21

Clone L2-081 (D3S4283, EMBL Z94768) displayed 90.4% identity over 197 bp to recently discovered new ubiquitin-specific protease gene HAUSP [32]. Considering the accuracy of our sequences [10,11] we can be confident that these matches mean that L2-081 contain 5′ end of the HAUSP gene. HAUSP gene codes for a cellular 135 kDa protein. The function of this protein is presently unknown but it was shown that it binds herpes simplex virus type 1 (HSV1) immediate early protein Vmw110. This binding stimulates expression of viral genes [32]. We have localized this gene in 3p21 region.

This region has been regarded as the tentative site for at least one or probably more tumor suppressor genes (TSG) due to the frequent occurrence of deletions in tumors. Many studies have shown abnormalities of the short arm of chromosome 3 in kidney, lung, breast, ovary, cervix, testis and nasopharyngeal carcinomas giving reason to focus on 3p in the search for a candidate TSG or group of them [33].

It was also shown that 3p21 is a breakpoint in myelodisplastic syndrome and acute myeloid leukemia [34]. The ubiquitin-dependent proteolysis plays a role in diverse cellular processes, including cell cycle control, DNA repair, stress response and selective protein degradation [35,36]. Alteration in ubiquitin pathway may result in cancer and different members of this pathway could have oncogene or TSG activity [37,38]. Indeed, it was found that TRE oncogene is a member of ubiquitin-specific proteases [39] and expression of ubiquitin-activating enzyme E1 (UBEL1) is greatly reduced in almost all lung tumor cell lines [35]. Since UBEL1 was localized in 3p21 it was suggested as candidate TSG but no prove for this

function was presented so far. Since we mapped the HAUSP gene also in 3p21 it raises the question if this gene itself or in cooperation with UBEL1 plays a role in development of lung, renal and other solid tumors and inspire further investigations.

In conclusion, in these experiments we have demonstrated the usefulness of *Not*I linking clones for localization of genes probably involved in growth/differentiation control in normal and malignant cells. Obviously, using the similar strategies, the same approach might be easily extended to *Not*I linking and jumping libraries specific for other chromosomes.

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References

[1] Ichikawa, H., Hosoda, F., Arai, Y., Shimizu, K., Ohira, M. and Ohki, M. (1993) Nature Genet. 4, 361–366.
[2] Wang, D. and Smith, C.L. (1994) Genomics 20, 441–451.
[3] Zabarovsky, E.R., Boldog, F., Thompson, T., Scanlon, D., Winberg, G., Marcsek, Z., Erlandsson, R., Stanbridge, E.J., Klein, G. and Sumegi, J. (1990) Nucleic Acids Res. 18, 6319–6324.
[4] Zabarovsky, E.R., Allikmets, R., Kholodnyuk, I., Zabarovska, V.I., Paulsson, N., Bannikov, V.M., Kashuba, V.I., Dean, M., Kisselev, L.L. and Klein, G. (1994) Genomics 20, 312–316.
[5] Weber, J.L. (1990) Genomics 7, 524–530.
[6] Smith, C.L., Lawrance, S.K., Gillespie, G.A., Cantor, C.R., Weissman, S.M. and Collins, F.S. (1987) in: Methods in Enzymology (Gottesman, M.M., Ed.) Vol. 151, pp. 461–489, Academic Press, San Diego.
[7] Gemmill, R.M., Chumakov, I., Scott, P., Waggoner, B., Rigault, P., Cypser, J., Chen, Q., Weissenbach, J., Gardiner, K., Wang, H., Pekarsky, Y., Le Gal, I., Le Paslier, D., Guillou, S., Li, E., Robinson, L., Hahner, L., Todd, S., Cohen, D. and Drabkin, H.A. (1995) Nature 377, 299–319.
[8] Bird, A.P. (1987) Trends Genet. 3, 342–347.
[9] Larsen, F., Gundersen, G., Lopez, R. and Prydz, H. (1992) Genomics 13, 1095–1107.
[10] Allikmets, R.L., Kashuba, V.I., Pettersson, B., Gizatullin, R., Lebedeva, T., Kholodnyuk, I.D., Bannikov, V.M., Petrov, N., Zakharyev, V.M., Winberg, G., Modi, W., Dean, M., Uhlen, M., Kisselev, L.L., Klein, G. and Zabarovsky, E.R. (1994) Genomics 19, 303–309.
[11] Zabarovsky, E.R., Kashuba, V.I., Pettersson, B., Petrov, N., Zakharyev, V., Gizatullin, R., Lebedeva, T., Bannikov, V., Pokrovskaya, E.S., Zabarovska, V.I., Allikmets, R.L., Erlandsson, R., Domninsky, D., Sumegi, J., Stanbridge, E.J., Winberg, G., Uhlen, M., Kisselev, L.L. and Klein, G. (1994) Genomics 21, 495–500.
[12] Ausubel, F.M., Brent, R., Kingston, R.E., More, D.D., Seidman, J.G., Smith, J.A. and Struhl, K. (1987) Current Protocols in Molecular Biology, Wiley, New York.
[13] Sambrook, J., Fritsch, E.F. and Maniatis, T. (1989) Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.
[14] Zabarovsky, E.R., Boldog, F., Erlandson, R., Kashuba, V.I., Allikmets, R.L., Marcsek, Z., Kisselev, L.L., Stanbridge, E., Klein, G., Sumegi, J. and Winberg, G. (1991) Genomics 11, 1030–1039.
[15] Protopopov, A.I., Gizatullin, R.Z., Vorobieva, N.V., Protopopova, M.V., Kiss, C., Kashuba, V.I., Klein, G., Kisselev, L.L., Graphodatsky, A.S. and Zabarovsky, E.R. (1996) Chromosome Res. 4, 443–447.
[16] Lemieux, N., Dutrillaux, B. and Viegas-Pequignot, E. (1992) Cytogenet. Cell Genet. 59, 311–312.
[17] Korolev, S.V., Solovyev, V.V. and Tumanyan, V.G. (1992) Biophysics 37, 733–742.
[18] Solovyev, V.V., Korolev, S.V. and Lim, H.A. (1992) Int. J. Genome Res. 1, 109–128.
[19] Miskimins, W.K., McClelland, A., Roberts, M.P. and Ruddle, F.H. (1986) J. Cell Biol. 103, 1781–1788.
[20] Valentini, M., Gregorini, A., Bartolucci, M., Porcellini, A. and Papa, S. (1994) Eur. J. Histochem. 38, (Suppl. 1) 61–68.
[21] Zolotukhin, A.S., Harford, J.B. and Felber, B.K. (1994) Nucleic Acids Res. 22, 4725–4732.
[22] Naylor, S.L., Buys, C.H. and Carritt, B. (1994) Cytogenet. Cell Genet. 65, 1–50.
[23] Naylor, S.L., Carritt, B., Boileau, C., Beroud, C., Alexander, C., Allderdice, P., Alimov, A., Ashworth, T., Bonifas, J., Bugert, P., Buys, C.H., Chipperfield, M.A., Deng, G., Drabkin, H., Gemmill, R.M., Grompe, M., Joensuu, T., Jonasdottir, A., Gizatullin, R., Krols, L., Leach, R.J., Lott, S.T., Killary, A., Martinsson, T., Messiaen, L., O'Connell, P., Opalka, B., Plaetke, R., Sankila, E.-M., Smith, D.I., Strachen, T., van den Berg, A. and Zabarovsky, E. (1996) Cytogenet. Cell Genet. 72, 255–270.
[24] Wang, J.Y., Zabarovsky, E.R., Talmadge, C., Berglund, P., Chan, K.W., Pokrovskaya, E.S., Kashuba, V.I., Zhen, D.K., Boldog, F., Zabarovskaya, V.I., Kisselev, L.L., Stanbridge, E.J., Klein, G. and Sumegi, J. (1994) Genomics 20, 105–113.
[25] Altschul, S.F., Gish, W., Miller, W., Myers, E.W. and Lipman, D.J. (1990) J. Mol. Biol. 215, 403–410.
[26] Tory, K., Latif, F., Modi, W., Schmidt, L., Wei, M.H., Li, H., Cobler, P., Orcutt, M.L., Delisio, J., Geil, L., Zbar, B. and Lerman, M. (1992) Genomics 13, 275–286.
[27] Dib, C., Faure, S., Fizames, C., Samson, D., Drouot, N., Vignal, A., Millasseau, P., Marc, S., Hazan, J., Seboun, E., Lathrop, M., Gyapay, G., Morissette, J. and Weissenbach, J.A. (1996) Nature 380, A28–A29.
[28] Feng, Y., Press, B. and Wandinger-Ness, A. (1995) J. Cell Biol. 131, 1435–1452.
[29] Rousseau-Merck, M.F., Zahraoui, A., Touchot, N., Tavitian, A. and Berger, R. (1991) Hum. Genet. 86, 350–354.
[30] Mitelman, F., Mertens, F. and Johansson, B. (1997) Nature Genet. 15, 417–474.
[31] Jotterand Bellomo, M., Parlier, V., Muhlematter, D., Grob, J.P. and Beris, P. (1992) Cancer Genet. Cytogenet. 59, 138–160.
[32] Everett, R.D., Meredith, M., Orr, A., Cross, A., Kathoria, M. and Parkinson, J. (1997) EMBO J. 16, 1519–1530.
[33] Kok, K., Naylor, S.L. and Buys, C.H. (1997) Adv. Cancer Res. 71, 27–92.
[34] Shi, G., Weh, H.J., Martensen, S., Seeger, D. and Hossfeld, D.K. (1996) Cytogenet. Cell Genet. 74, 295–299.
[35] Kok, K., Hofstra, R., Pilz, A., van den Berg, A., Terpstra, P., Buys, C.H. and Carritt, B.A. (1993) Proc. Natl. Acad. Sci. USA 90, 6071–6075.
[36] Huang, Y. and Fischer-Vize, J.A. (1996) Development 122, 3207–3216.
[37] Zhu, Y., Carroll, M., Papa, F.R., Hochstrasser, M. and D'Andrea, A.D. (1996) Proc. Natl. Acad. Sci. USA 93, 3275–3279.
[38] Zhu, Y., Lambert, K., Corless, C., Copeland, N.G., Gilbert, D.J., Jenkins, N.A. and D'Andrea, A.D. (1997) J. Biol. Chem. 272, 51–57.
[39] Xiao, W., Fontanie, T. and Tang, M. (1994) Yeast 10, 1497–1502.