Ectopic Expression of MAFB Gene in Human Myeloma Cells Carrying (14;20)(q32;q11) Chromosomal Translocations

Ichiro Hanamura,1,2 Shinsuke Iida,1,8 Yumiko Akano,1 Yoshihito Hayami,1,2 Miyuki Kato,1 Kazuhsia Miura,1 Shinsuke Harada,1 Shogo Banno,1 Atsushi Wakita,1 Hitoshi Kiyoi,4 Tomoki Naoe,4 Shirou Shimizu,3 Shin-ichi Sonta,6 Masafumi Tanikawa1 and Ryuzo Ueda1

1Second Department of Internal Medicine, Nagoya City University Medical School, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467-8601, 2Aichi Blood Disease Research Foundation, 13-2 Machikita, Moriyama-ku, Nagoya 463-0074, 3Third Department of Internal Medicine, Kyoku Prefectural University of Medicine, 456 Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-0841, 4Department of Infectious Diseases, Nagoya University School of Medicine, 65 Tsuruma-cho, Showa-ku, Nagoya 466-8560, 5Shimane Prefectural Central Hospital, 116 Inaichi-cho, Izumo, Shimane 693-8555, 6Department of Genetics, Institute for Developmental Research, Aichi Human Service Center, 713-8 Kamiya-cho, Kasugai, Aichi 480-0392 and 7Second Department of Internal Medicine, Aichi Medical University, 21 Karimata, Nagakute-cho, Aichi-gun, Aichi 480-1195

Chromosome 14q+, which represents a chromosomal rearrangement involving the immunoglobulin heavy chain gene (IgH) locus, is a genetic hallmark of human multiple myeloma (MM). Here, we report the identification of (14;20)(q32;q11) chromosomal translocations found in MM cells. Double color fluorescence in situ hybridization analyses pinpointed the breakpoints at the 20q11 locus in two MM cell lines within a length of at most 680 kb between the KIAA0823 and MAFB gene loci. Among the transcribed sequences in the vicinity of the breakpoints, an ectopic expression of the MAFB gene, which is located at 450–680 kb telomeric to one of the breakpoints and encodes a member of the MAF family basic region/leucine zipper transcription factor, was demonstrated to be associated with t(14;20). This finding, together with that of a previous study describing its transforming activity, suggests that the MAFB gene may be one of the targets deregulated by regulatory elements of the IgH gene as a result of t(14;20).

Key words: Multiple myeloma — t(14;20)(q32;q11) — MAFB — Ectopic expression

Complex chromosomal rearrangements represent genetic aberrations involved in the multistep oncogenesis of human multiple myeloma (MM).1–3) In particular, the importance of the chromosomal translocations involving immunoglobulin (Ig) gene loci, such as IgH on 14q32 (14q+ chromosome) and Igλ on 22q11, has been well documented.1–4) Consequently, the specific protooncogenes located at donor chromosomal loci such as 11q13, 8q24, 6p25, 4p16 and 16q24, harboring respectively the CyclinD1, c-MYC, MUM1, FGFR3 and c-MAF genes, are deregulated by the effect of regulatory elements of the Ig genes.2,3,5–10) Each chromosomal translocation seems to have a distinct role in the development of MM. For instance, t(11;14)(q13;q32) arises during the early phase of plasma cell dyscrasia, which is clinically represented by monoclonal gammapathy of undetermined significance (MGUS), in contrast to t(8;14)(q24;q32) and t(4;14)(p16;q32), which are assumed to accelerate the progression from MGUS through MM.11,12) However, not all of the responsible genes activated on the 14q+ chromosomes in MM have been identified. This prompted us to focus on the remaining partner chromosomes of the IgH loci in an attempt to ascertain new elements associated with MM development.

This is the first report to clarify, by means of fluorescence in situ hybridization (FISH) analysis, the detailed locations of the two 20q11 breakpoints involved in t(14;20)(q32;q11). We also found that this specific genetic alteration resulted in an ectopic expression of the MAFB protooncogene, which is a member of the MAF family basic region/leucine zipper transcription factor and is located at 450–680 kb telomeric to one of the breakpoints, probably due to the influence of the 3′α enhancers of the IgH gene.

MATERIALS AND METHODS

A total of 16 MM cell lines (U266, SK-MM-1, ODA, AMO1, NCU-MM-1, XG-7, FR4, NOP-1, KM-4, KM-5, KM-7, SACHI, JIN3, ILKM-2, ILKM-3 and ILKM-8) were used.7,9,13) These cell lines have been characterized previously except for SACHI, which was established from the pericardial fluid of a 47-year-old female patient with plasma cell leukemia (PCL) generating IgG-λ type M-protein. G-Banding analysis revealed its complex karyotype.

8To whom correspondence should be addressed.
E-mail: iida@med.nagoya-cu.ac.jp
sequences were reported by Wang et al.1) Twenty-two patients with t(14;20)(q32;q11) in SK-MM-1 was demonstrated by spectral karyotyping analysis.2) Total RNA was isolated with the guanidine isothiocyanate/cesium chloride ultracentrifugation method. Human MAFB clones were amplified from the PAC RPCI4-644L1 by PCR, as this gene has no intron, by using a primer pair, F5′ (5′-GACGCTTCTCCGACGACA-3′) and R6′ (5′-CCCTCTCGCTCAAGTCAAAC-3′), whose sequences were reported by Wang et al.3) The size of the probe was 479 bp. Expressed sequenced tag (EST) clones, mapped telomeric to SACHI’s breakpoint, were purchased from Research Genetics Inc. and their inserts were used as probes. The quality and amount of each RNA were assessed by subsequent hybridization with β-ACTIN probe.

RESULTS AND DISCUSSION

The chromosome 20q11 locus is known to be rearranged or deleted in various types of human malignancies. It has attracted the attention mainly of hematologists because a region extending from 20q11.2 to 20q12 is commonly deleted in myeloid leukemias, suggesting the existence of an as yet unidentified tumor suppressor gene within this region.4,5) Accordingly, YAC contigs have already been constructed by several groups and were available when we focused on t(14;20), which is occasionally encountered in human MM. In order to determine the approximate locations of the 20q11 breakpoints of SK-MM-1 and SACHI cell lines, we decided to use DCFISH analysis. In brief, two Mega-YACs’ DNAs located between loci D20S884 and D20S96 were labeled (Fig. 1A), one with Spectrum Green and the other with Spectrum Orange, and hybridized to metaphase spreads of the two cell lines. When the green and red signals were split onto different chromosomes, we could determine the locations of the breakpoints between the two YACs, which were used as probes. This strategy resulted in the eventual confirmation of SK-MM-1’s breakpoint within y953C12 itself and that of SACHI between y953C12 and y808C5 (Fig. 1, A, B and Fig. 2, A, B). These YACs were then mapped at the 20q11.2–12 locus. To narrow down the breakpoints, PAC/BAC contigs encompassing the region between the D20S174 and PLC1 gene loci, whose locations were mapped to centromeric and telomeric ends of y953C12 and y808C5, respectively, were constructed based on the sequence information provided by Sanger Centre Human Genome Data Base. As for the PAC/BAC clones whose complete sequences were not available, we confirmed each overlap by means of Southern hybridization analyses using PAC/BAC-end probes obtained with the bubble-PCR method, as shown open circles in Fig. 1. Further FISH analyses using PAC/BAC probes could narrow down the locations of these two breakpoints to within PACs 600E6 for SK-MM-1 and 191L6 for SACHI cells, as shown in Fig. 1. This means that the distance between the breakpoints was no more than 680 kb (460–680 kb), as estimated from the PAC/BAC data with respect to size and sequence.

In an attempt to make sure that these 20q11 breakpoints were juxtaposed to the IgH gene at the chromosome 14q32 locus as a result of t(14;20), we next employed DCFISH using either y808C5 or PAC644L1, which were mapped
telomeric to SACHI's breakpoint, and BAC417P24 probes spanning the IgH constant region at 14q32, as shown in Fig. 2C. The reason for this strategy was that the protooncogenes, dysregulated by the 3′α enhancers of IgH as a result of the presence of 14q+ chromosomes in MM, were reported generally to be located telomeric to chromosomal breakpoints. In SK-MM-1 cells, signals derived from y808C5/PAC644L1 moved to chromosome 14q32 and fused to BAC417P24, indicating that the telomeric tip to its breakpoint at 20q11 was juxtaposed to the constant region of the IgH gene (Fig. 2D). In a SACHI cell, two fused signals between y808C5/PAC644L1 and BAC417P24 were observed in a metaphase spread, while they were mapped onto two marker chromosomes, whose derivations originated from neither chromosome 14 nor 20 (Fig. 2E).

Since the IgH 3′α enhancer has been reported to influence the transcription of specific protooncogenes over sev-

---

**Fig. 1.** Relationship of chromosomal breakpoints identified in two MM cell lines to MAEB gene. A. A YAC contig spanning 20q11–12 locus. YACs are shown as bold lines, the length of which reflects the number of included STSs (sequenced tagged sites), not the actual size. The physical distances between adjacent STSs have not been determined directly. Information for YACs was obtained through the web site of the MIT Whitehead Institute. B. A PAC/BAC contig at the 20q11.2–12 locus encompassing two chromosomal breakpoints identified in MM cell lines and the MAEB gene is shown. Closed circles represent STS and open circles PAC-end derived markers. Solid boxes show the locations of known genes and open boxes those of EST markers. Approximate locations of the chromosomal breakpoints confirmed in SK-MM-1 and SACHI cell lines are indicated along the top. All PAC/BAC clones between PACs 616B8 and 644L1 are linked based on the sequence overlap and on the hybridization results with PAC-end probes shown as open circles. Cen., centromeric side; Tel., telomeric side.
eral hundred kilobases in MM cells,\textsuperscript{2,5,18} we hypothesized the presence of the common target protooncogene(s) in these two cell lines, specifically at a location telomeric to the 20q11 breakpoints. We then surveyed transcripts mapped telomeric to the breakpoints of both cell lines at the 20q11 locus according to the sequence data and gene profile of the PAC/BAC clones obtained from the Sanger Centre Human Genome Data Base in addition to the exon trapping analyses of PAC155H19, whose genomic sequences had not been fully completed. This region showed a relatively low gene density. Only three ESTs and two known genes, \textit{BPI} (bactericidal/permeability-increasing protein) and \textit{MAFB}, have been reported between the SACHI’s breakpoint and PAC644L1, which are located at no more than 800 kb downstream to the breakpoint, as shown in Fig. 1. For the purpose of identifying candidate gene(s) dysregulated by t(14;20), we examined the expression of each of their cDNAs by means of northern blot analyses of MM cell lines including SK-MM-1 and SACHI cells. The mRNA expression of ESTs R98337, SG53189 and \textit{BPI} was not detected in the MM cell lines we used (data not shown). This was supposed to be due to either the high fidelity of promoter functions, which were shut down in the plasma cell stage, or the low sensitivity of our northern analyses. But, EST SG30600 was expressed as a 4.0 kb message at similar levels in all MM cell lines, as well as in various hematopoietic cell lines including those consistent with the mature B cell stage (data not shown). Interestingly, the \textit{MAFB} gene mapped at 450–680 kb telomeric to the SACHI’s breakpoint was expressed in both SK-MM-1 and SACHI cells (Fig. 3). In our panel of 16 MM cell lines, three cell lines, SK-MM-1, SACHI and KM-5, expressed 3.0 kb transcripts as shown in Fig. 3A (some data omitted). In particular, remarkable overexpression of both 3.0 kb mRNA and 1.8 kb mRNA of an alternatively transcribed form was observed in the SACHI cells when compared to that in SK-MM-1 and KM-5. Since the expression of the \textit{MAFB} gene is restricted to immature myeloid/monocytic lineages in hematopoietic cells, mRNA expression in these three MM cell lines is ectopic.\textsuperscript{15,19,20} We also analyzed various hematopoietic cell lines including B-lymphoid lines, ranging from pro-B to mature B cell stages, for \textit{MAFB} expression, but no expression was seen (Fig. 3B). We next attempted to clarify by means of DCFISH analyses the mechanisms underlying the ectopic \textit{MAFB} expression in KM-5 cells. However, the \textit{MAFB} locus did not fuse to any other Ig gene loci, including the \textit{IgH}, \textit{Igλ} and \textit{Igκ} loci, in this cell line, nor could any amplification of the gene be found when Southern blot analysis was used (data not shown), so the responsible mechanism in this cell line remains to be clarified.

At present, we cannot exclude the possibility of other target gene(s) existing besides \textit{MAFB}, because the ectopic

Fig. 2. DCFISH analyses showing the location of 20q11 breakpoints and fusion signals from the telomeric region to the breakpoints and \textit{IgH} loci. A. SK-MM-1 has its 20q11 breakpoint within y953C12. YAC-DNAs derived from y953C12 and y808C5 were labeled with Spectrum Green and Spectrum Orange, respectively. A part of the green signals remains on chromosome 20 as indicated by the arrowhead, while the other part fused with a red signal (a yellow signal) moved to 14q as indicated by the arrowhead, while the other

---

\textit{MAFB} in t(14;20) Myeloma
expression pattern found in MM cells carrying t(14;20) is obviously aberrant, thus indicating the possibility of MAFB being one of the target genes of this chromosomal aberration. As is often the case with IgH rearrangements with c-MAF and CyclinD1 loci reported in MM cells, the distance between the SACHI’s breakpoint and the MAFB gene is not far for the IgH 3′α enhancer to have an effect, either.5, 8) The MAFB gene, also known as KRML, belongs to the MAF family basic region/leucine zipper (bZip) transcription factors.21) Like other large MAF proteins such as c-MAF involved in MM with t(14;16),8) it has both a carboxy-terminal bZip domain, which mediates DNA binding and dimer formation, and an amino-terminal acidic domain associated with transactivating capability.15, 21) MAFB proteins have dual functions in the transcription of downstream genes and whether they function as transactivator or transrepressor depends on the target sequences of MAF-responsive elements (MARE) and the interacting proteins, such as c-Fos and Ets-1. MAFB seems to be ubiquitously expressed in various tissues, while its expression in hematopoietic cells is restricted to myelomonocytic lineage and macrophages. It has recently been demonstrated to play crucial roles in the proliferation of myelomonocytic progenitors and subsequently the promotion of differentiation into the monocytic lineage, and in the prevention of erythroid differentiation in myeloid progenitors.19, 20) Although we have not yet fully sequenced the MAFB cDNAs derived from SK-MM-1 and SACHI cells, transcripts with aberrant sizes were not observed, at least in northern analysis. However, wild-type MAFB itself has been shown to transform chicken embryonic fibroblasts when it is artificially overexpressed,21) indicating that it acts as an oncogene under certain circumstances. We conclude that the ectopic MAFB expression in plasma cells as a result of t(14;20) may disturb physiological process of proliferation and differentiation of B lymphocytes, depending on the presence of interacting proteins, and may eventually lead to unlimited proliferation. In our experiments, it has been difficult to find any correlation between expression level of the MAFB gene in three MM cell lines and specific malignant phenotypes, because these cell lines carry not only t(14;20) but also other 14q+ chromosomes, which lead to the deregulated expression of various protooncogenes such as c-MYC and MUM1.7) Accordingly, the effect of MAFB expression in B cell lineage remains to be clarified through further transfection and transgenic studies.

By means of DCFISH using PAC644L1 and BAC417P24 probes, we further explored the frequency of the fusion between MAFB and IgH loci in human MM. Although metaphase spreads were prepared and analyzed for the 14 MM cell lines other than SK-MM-1 and SACHI, no cell lines harboring MAFB/IgH fusions were found, thus indicating a 12.5% frequency of t(14;20) in MM cell lines. Because of the low mitotic index of the MM cells, interphase DCFISH was used to analyze fresh MM samples, as it was effective in the case of SK-MM-1 and SACHI, as shown in Fig. 2F. The fusion signals evalu-

Fig. 3. Ectopic MAFB gene expression in MM cell lines carrying t(14;20). MAFB expression in a panel of human MM cell lines (A) and in various hematopoietic tumor-derived cell lines (B). MAFB mRNA expression was evaluated by means of northern analysis using a 479 bp MAFB cDNA probe. Note that 3.0 kb MAFB mRNA is detected only in SACHI, KM-5 and SK-MM-1 cell lines as indicated by arrows. A spliced variant of 1.8 kb MAFB mRNA is faintly observed only in SACHI cell line. BALL-1, Pre-B cell line; P3HR-1 and KIS-1, mature B cell lines; HUT-102, mature T cell line; HL-60, myeloid line; THP-1, monocytic line. The expression level of β-ACTIN mRNA is shown below. Ten micrograms of total RNA was loaded onto each lane. Dashes on the left indicate 28S and 18S ribosomal RNA markers.
ated in controls accounted for 7.40±2.07% (mean±1 SD). Of the 22 cases analyzed, none possessed MAFB/IgH fusions in statistically significant fractions (mean±3 SD) of the total nuclei. Accordingly, t(14;20) seems to be a nonrandom but relatively rare chromosomal alteration in human MM, although further studies covering a large number of MM cases are need to clarify the significance of this alteration, especially in association with clinical and biological behaviors, as it has been suggested that some specific 14q+ markers may be relevant to certain clinical phenotypes.2,3,10

ACKNOWLEDGMENTS

We wish to thank Miss C. Fukuyama, K. Sanuki and M. Aoyama for their skillful technical assistance, and K. Okumura for her secretarial work. We are also grateful to S. Tagawa (Osaka City University), M. Ogura (Aichi Cancer Center), B. Klein (University of Montpellier, France) and R. S. K. Chaganti (Memorial Sloan Kettering Cancer Center, New York) for providing us with cell lines derived from patients with MM and to Kirin Brewery Corporation (Tokyo) for providing us with human recombinant interleukin-6 (IL-6) used for the culture of IL-6-dependent MM cell lines. This work was supported in part by Grants-in-Aid for S. Iida, M. Taniwaki and R. Ueda from the Ministry of Education, Science, Sports and Culture, and for A. Wakita and R. Ueda from the Ministry of Health and Welfare, Japan and by a Grant-in-Aid for Research in Nagoya City University for S. Iida.

(RECEIVED FEBRUARY 5, 2001/REVISED MARCH 27, 2001/ACCEPTED APRIL 13, 2001)

REFERENCES

1) Rao, P. H., Cigudosa, J. C., Ning, Y., Calasanz, M. J., Iida, S., Tagawa, S., Danieli, J., Klein, B., Dalla-Favera, R., Jhanswar, S. C., Ried, T. and Chaganti, R. S. K. Multicolor spectral karyotyping identifies new recurring breakpoints and translocations in multiple myeloma. Blood, 92, 1743–1748 (1998).
2) Iida, S. and Dalla-Favera, R. Molecular pathogenesis of multiple myeloma. Rev. Clin. Exp. Hematol., 3, 60–70 (1997).
3) Hallek, M., Bergsagel, P. L. and Anderson, K. C. Multiple myeloma: increasing evidence for a multistep transformation process. Blood, 91, 3–21 (1998).
4) Yoshida, S., Nakazawa, N., Iida, S., Hayami, Y., Sato, S., Nakazawa, N., Ueda, Y., Ueda, T., Matsuda, F., Kashima, K. and Taniwaki, M. The Ig heavy chain gene is frequently involved in chromosomal translocations in multiple myeloma and plasma cell leukemia as detected by in situ hybridization. Blood, 90, 526–534 (1997).
5) Ronchetti, D., Finelli, P., Richelda, R., Baldini, L., Rocchi, M., Viggiano, L., Cuneo, A., Bogni, S., Fabris, S., Lombardi, L., Maiolo, A. T. and Neri, A. Molecular analysis of 11q13 breakpoints in multiple myeloma. Blood, 93, 1330–1337 (1999).
6) Chesi, M., Nardini, E., Brents, L. A., Schrock, E., Ried, T., Kuehl, W. M. and Bergsagel, P. L. Frequent translocation t(4;14)(p16.3;q32.3) in multiple myeloma is associated with increased expression and activating mutations of fibroblast growth factor receptor 3. Nat. Genet., 16, 260–264 (1997).
7) Iida, S., Rao, P. H., Butler, M., Corradini, P., Boccadoro, M., Klein, B., Chaganti, R. S. K. and Dalla-Favera, R. Deregulation of the MUM1/IRF4 gene by chromosomal translocation in multiple myeloma. Nat. Genet., 17, 226–230 (1997).
8) Chesi, M., Bergsagel, P. L., Shonukan, O. O., Martelli, M. L., Brents, L. A., Chen, T., Schrock, E., Ried, T. and Kuehl, W. M. Frequent dysregulation of the c-maf proto-oncogene at 16q23 by translocation to Ig locus in multiple myeloma. Blood, 91, 4457–4463 (1998).
9) Yoshida, S., Nakazawa, N., Iida, S., Hayami, Y., Sato, S., Wakita, A., Shimizu, S., Taniwaki, M. and Ueda, R. Detection of MUM1/IRF4-IgH fusion in multiple myeloma. Leukemia, 13, 1812–1816 (1999).
10) Nakazawa, N., Ishida, K., Taniwaki, M., Kobayashi, M., Iwai, T., Horikke, S., Nishigaki, H., Otoku, T., Tomiyama, Y., Fuji, H., Kashima, K. and Taniwaki, M. Interphase detection of t(4;14)(p16.3q32.3) by in situ hybridization and FGFR3 overexpression in plasma cell malignancies. Cancer Genet. Cytogenet., 117, 89–96 (2000).
11) Aver-Loiseau, H., Facon, T., Daviet, A., Godon, C., Rapp, M.-J., Harousseau, J.-L., Grosbois, B. and Bataille, R. 14q32 translocations and monosomy 13 observed in monoclonal gammapathy of undetermined significance delineate a multistep process for the oncogenesis of multiple myeloma. Cancer Res., 59, 4546–4550 (1999).
12) Shou, Y., Martelli, M. L., Gabrea, A., Qi, Y., Brents, L. A., Roschke, A., Dewald, G., Kirsh, I. R., Bergsagel, P. L. and Kuehl, W. M. Diverse karyotypic abnormalities of the c-myc locus associated with c-myc dysregulation and tumor progression in multiple myeloma. Proc. Natl. Acad. Sci. USA, 97, 228–233 (2000).
13) Iida, S., Hanamura, I., Suzuki, T., Kamiya, T., Kato, M., Hayami, Y., Miura, K., Harada, S., Tsuboi, K., Gawkata, A., Akano, Y., Taniwaki, M., Nitta, M. and Ueda, R. A novel human multiple myeloma-derived cell line, NCU-MM-1, carrying t(2;11)(p11;q23) and t(8;22)(q24;q11) chromosomal translocations with overexpression of c-Myc protein. Int. J. Hematol., 72, 85–91 (2000).
14) Iida, S., Rao, P. H., Nallasivam, P., Hishboosh, H., Butler, M., Louie, D. C., Dyomin, V., Ohno, H., Chaganti, R. S. K. and Dalla-Favera, R. The t(9;14)(p13;q32) chromosomal translocation associated with lymphoplasmacytoid lymphoma involves the PAX-5 gene. Blood, 88, 4110–4117
15) Wang, P. W., Eisenhart, J. D., Cordes, S. P., Barsh, G. S., Stoffel, M. and Le Beau, M. M. Human KRML (MAFB): cDNA cloning, genomic structure, and evaluation as a candidate tumor suppressor gene in myeloid leukemias. *Genomics*, 59, 275–281 (1999).

16) Bench, A. J., Aldred, M. A., Humphray, S. J., Champion, K. M., Gilbert, J. G. R., Asimakopoulos, F. A., Deloukas, P., Gwilliam, R., Bentley, D. R. and Green, A. R. A detailed physical and transcriptional map of the region of chromosome 20 that is deleted in myeloproliferative disorders and refinement of the common deleted region. *Genomics*, 49, 351–362 (1998).

17) Wang, P. W., Iannantuoni, K., Davis, E. M., Espinosa, R., III, Stoffel, M. and Le Beau, M. M. Refinement of the commonly deleted segment in myeloid leukemias with a del(20q). *Genes Chromosom. Cancer*, 21, 75–81 (1998).

18) Madisen, L. and Groudine, M. Identification of a locus control region in the immunoglobulin heavy-chain locus that deregulates c-myc expression in plasmacytoma and Burkitt’s lymphoma cells. *Genes Dev.*, 8, 2212–2226 (1994).

19) Sieweke, M. H., Tekotte, H., Frampton, J. and Graf, T. MafB is an interaction partner and repressor of ets-1 that inhibits erythroid differentiation. *Cell*, 85, 49–60 (1996).

20) Kelly, L. M., Englmeier, U., Lafon, I., Sieweke, M. H. and Graf, T. MafB is an inducer of monocytic differentiation. *EMBO J.*, 19, 1987–1997 (2000).

21) Kataoka, K., Fujiiwara, K. T., Noda, M. and Nishizawa, M. MafB, a new maf family transcription activator that can associate with maf and fos but not with jun. *Mol. Cell. Biol.*, 14, 7581–7591 (1994).