

SHORT COMMUNICATION

Manabu Futamura · Hiroyuki Nishimori
Takayuki Shiratsuchi · Shigetoyo Saji · Yusuke Nakamura
Takashi Tokino

Molecular cloning, mapping, and characterization of a novel human gene, *MTA1-L1*, showing homology to a metastasis-associated gene, *MTA1*

Received: June 19, 1998 / Accepted: August 5, 1998

Abstract Through large-scale sequencing of clones randomly selected from libraries of human cDNAs, we have isolated a novel human gene encoding a product with 59.6% identity in amino acid sequence to human *MTA1*, a protein associated with tumor invasion and metastasis. This cDNA, named *MTA1-L1* (*MTA1 like 1*), consists of 2736 nucleotides with an open reading frame encoding 668 amino acids. A single 3.0-kb transcript of *MTA1-L1* was expressed ubiquitously on Northern blots. Structural analysis of the *MTA1-L1* gene revealed 18 exons spanning 8.1 kb of genomic DNA. We assigned the *MTA1-L1* locus to chromosomal band 11q12–13.1 by fluorescence in situ hybridization.

Key words Human genome project · cDNA library screening · Cancer · Metastasis · *MTA1*

Introduction

A metastasis-associated gene, *MTA1*, was originally isolated by differential screening of a cDNA library using a rat mammary adenocarcinoma metastatic system (Toh et al. 1994, 1995). To evaluate the relevance of the human homologue of *MTA1* in progression of carcinoma in humans, Toh et al. (1997) examined levels of *MTA1* mRNA in colorectal and gastric carcinomas and showed that overexpression of the *MTA1* gene correlated with tumor invasion and the presence of metastases. They suggested that an increase in *MTA1* mRNA might serve as an indica-

tor for assessing the malignant potential of colorectal and gastric carcinomas.

As part of our human genome project, we have been determining nucleotide sequences of randomly selected cDNA clones and comparing them with a public database to identify novel genes that are likely to possess biologically important functions and/or might be associated with human diseases (Isomura et al. 1996; Tanaka et al. 1996). Here we describe the isolation, mapping, and characterization of a novel gene, *MTA1-L1*, whose product shows significant homology to *MTA1*.

Materials and methods

Isolation of *MTA1-L1* cDNA

The 5' portions of cDNA clones randomly selected from a human adult-heart cDNA library were sequenced as part of the human genome project (Sudo et al. 1994, and unpublished data). Using FASTA (Pearson and Lipman 1988) and Basic Local Alignment Search Tool (BLAST, NCBI database) programs against a public database, we identified a cDNA fragment highly homologous to *MTA1*. To isolate its full-length cDNA, we screened the same library using the fragment as a probe, and determined nucleotide sequences of positive clones with an ABI Prism 377 DNA sequencer (Applied Biosystems, Foster City, CA, USA). Computer-assisted analysis of the deduced amino acid sequence was performed using MotifFinder (Kyoto University, Japan) and PSORT (Osaka University, Japan) software programs.

Northern blot analysis

Northern blots containing poly(A)+ RNA from 16 normal human tissues were purchased from Clontech (Palo Alto, CA, USA). The blots were hybridized with the random-primed, ³²P-labeled cDNA probe according to the supplier's recommendations. The blots were washed with 0.1 × stan-

M. Futamura · H. Nishimori · T. Shiratsuchi · Y. Nakamura · T. Tokino (✉)
Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan
Tel. +81-3-5449-5372; Fax +81-3-5449-5433
e-mail: tokinta@ims.u-tokyo.ac.jp

M. Futamura · S. Saji
Second Department of Surgery, Gifu University, Gifu, Japan

1	CCCAACGACTAGTGGGACTCCGCGGGGGCGGGGTAGCTGGAGCCTGGCTCTGGCCTGGCAGGAGCCGAGCTTGTTCGGGAAGAAGCCGAGCGGACGGGG	100
101	GCCAGCCTCAGCGTCCCGGGAGTGAGGCGATAGCTGCGGGCGGCAGCAGCGCGGGCCGGATGAACCCGCGACGGCTGAGGCAGCGGAGGTGCCGCTGCCG	200
201	GGCCCCAGTGAAGACTCCCTCGAAGCGGCAGCCACCCTTCGGGGCTTTGCCCTCGAGCCGAGCCCTGCCCCGCGAGCCTCCCGGACCCCTTTGTGCGGC	300
301	CGGAGGCGGCGGGGGAACCGCCATGGCGGCAACATGTACCGGGTGGGAGATTACGTCTATTTTTGAAGTCTTCCAGCAATCCTTACCTGGTTAGACG	400
	M A A N M Y <u>R V G D Y V Y</u> F E N S S S N P Y L V R R	26
	T Y K	
401	GATTGAGGAGCTCAACAAGACTGCAAAATGGAAATGTGGAGGCAAAGGTGTCTGTCTTTCCGGCGCAGGGACATTTCTAGTAGCCTCAACAGCCTGGCT	500
27	I E E L N K T A N G N V E A K V V C L F R R R D I S S S L N <u>S L A</u>	59
	CK 2	
501	GATAGTAATGCCAGGAGTTTGAAGAGGAATCAAAGCAGCCAGGGATGTCTGAGCAGCAGCCATCAACTGAAGCACCAGGAACTTTTCTTTCTCGGC	600
60	<u>D S N A R E F E E E S K Q P G M S E Q Q R H Q L K H R E L F L S R Q</u>	93
601	AATTTGAATCATTACCAGCCACCCACATACGGGGAAATGCAGTGTGACCCCTTTGAATGAGACAGATATCTTGAGCCAGTACCTGGAAAAGGAGGACTG	700
94	F E S L P A T H I R G K C S V T L L N E T D I L S Q Y L E K E D C	126
701	CTTTTTTACTCACTGGTGTGTGACCCCGTGCAGAAGACACTTCTCGTGATCAGGGCGAGATTAGAGTTGGTTGCAAATACCAAGCTGAGATCCAGAT	800
127	F F Y S L V F D P V Q K T L L A D Q G E I R V G C K Y Q A E I P D	159
801	CGCTAGTAGAGGGAGAACTCTGATAATCGGAACCAGCAGAAGATGGAGATGAAGTCTGGGACCCAGACAACCCCTCTCAGACCCGCGAGATCGACCACT	900
160	R L V E G E S D N R N Q Q K M E M K V W D P D N P L <u>T D R</u> Q I D Q F	193
	P K C	
901	TTCTTGTGGTGGCCCGAGCTGTGGGAACCTTTGCAAGAGCCCTAGATTGTAGCAGCTCCATTTCGGCAGCCAAGCTTGCACATGAGTGCAGCTGCTGCCTC	1000
194	L V V A R A V G T F A R A L D C S S <u>S I R</u> Q P S L H M S A A A A S	226
	P K C	
1001	CCGAGATATCACTCTGTTTTCACGCCATGGATACCTTGCAAAGGAACGGTACGACCTGGCTAAGGCCATGTGACCCCTGGTACCCCGAGGAGCCCGGTG	1100
227	R D I T <u>L F H A M D T L Q R N G Y D L A K A M S T L</u> V P Q G G P V	259
	L E U	
1101	CTGTGTCGGGATGAGATGGAGGAATGGTCAGCCTCAGAGGCCATGCTATTGAGGAGGCCCTAGAGAAGTATGGGAAGGACTTCAATGATATTCGCCAGG	1200
260	L C R D E M E E W <u>S A S E A M L F E E A L E K Y G K D F N D I R Q D</u>	293
	CK 2	
1201	ATTTTCTACCTGGAAGTCACTTCCAGCATAGTCCAGTTTATTACATGTGAAAAACCAGACCCGGTATATTTCAGCAGAAAAGGTGAAAGCTGCTGA	1300
294	F L P W K S L A S I V Q F Y Y M W K T <u>T D R</u> Y I Q Q K R L K A A E	326
	P K C	
1301	AGCAGACAGCAAACTGAAACAGGTCTACATTCCACCTACACTAAGCCAAACCCCTAACAGATCATTTCTGTGGGTTCAAACCTGGCATGAATGGGGCT	1400
327	A D S K L K Q V Y I P T Y T K P N P N Q I I S V G S K P G M N G A	359
1401	GGATTTGAGAAGGGCCTGACTTGTGAGAGTGGCCACACCACACAGTCTGCTCAGTGGTATGCCTGGGGCCACCTAACATGCAGTGGCCCTCTGTGCTT	1500
360	G F Q K G L T <u>C E S C H T T O S A O W Y A W G P P N M O C E R L C A S</u>	393
	Z I N	
1501	CCTGTTGGATCTACTGGAAGAAGTATGGGGACTGAAGACCCCACTCAGCTTGGAGGGGCCACTCGGGGCCACCAGGACCCACTCAAGGGGTCAATTT	1600
394	<u>C W I Y W K K Y G G L K T P T Q L E G A T R G T T E P H S R G H L</u>	426
	CK 2	
1601	ATCCAGACCTGAAGCTCAAAGTCTCTCTCCTTACACAACCAGCGCCAACAGGGCCAAAGCTACTGGCTAAGAACAGACAAACTTTCTGCTTCAGACCACA	1700
427	<u>S R P E A Q S L S P Y T T S A N R A K L L A K N R Q T F L L Q T T</u>	459
	CK 2	
	P K C	
1701	AAGCTGACCCGCTTGGCAGACGCATGTGCAGGGACCTATTACAGCCAAGGAGGGCCCGCCGACGGCCCTTATGCTCCTATCAATGCCAATGCCATCAAAG	1800
460	<u>K L T R L A R R M C R D L L Q P R R A A R R P Y A P I N A N A I K A</u>	493
1801	CAGAGTGTCCATTCGACTTCCCTAAGCCGCCAAGACTCCATTGAAGATTACCCCTCTGGTGGGCTGCCCTGGCAACTATCGTCAAAGATCTGGTGGC	1900
494	E C <u>S I E</u> L P K A A K T P L K I H P L V R L P L A T I V K D L V A	526
	P K C	
1901	CCAGGCACCCCTGAAACCAAAAACCTCGGGGTACCAAGACACCGATCAACAGAAACCAGCTGTCCAGAACCCGGGACTGGGGGCATTATGGTGAAA	2000
527	Q A P L K P K <u>T P R</u> G T K T P I N R N Q L S Q N R G L G G I M V K	559
	P K C	
2001	CGGGCCTATGAGACTATGGCAGGGGCGGGGTTCCCTTCTCTGCCAATGGAAGGCCCTCTGGCTTCAGGGATTCTGTTCAAGCTCACAGCCAGCAGCCAAGC	2100
560	R A Y E T M A G A G V P F S A N G R P L A S G I R S S S Q P A A K R	593
2101	GTCAGAACTAAACCCAGCTGATGCCCCCAATCTGTGGTGTGTTGTGGCCACAAGGATACCCAGGGCCCTACGGAAGGCTCTGACCCATCTGGAATGCG	2200
594	Q K L N P A D A P N P V V F V A T K D T R A L R K A L <u>T H L E M R</u>	626
	CK 2	
2201	GCGAGCTGCTCGCCGACCCAACTTGCCCTGAAGGTGAAGCCAACGCTGATTGCAGTGGCGCCCTGTCCCTCTACCTGCACCCTCACATCTGCCAGC	2300
627	R A A R R P N L P L K V K P T L I A V R P P V P L P A P S H P A <u>S</u>	659
2301	ACCAATGAGCCTATTGTCTGGAGACTGAGCACTGTGGGAAGGGAGGTGGGCTGAGAGGTAGAGGTGGATGCCAGGGCACCCAAACCTCCCTTCC	2400
660	<u>T N E P I V L E D</u> *	668
	CK 2	
2401	CTTTCGTGTCGAAGGGAGTGAGGAGTGAATTAAGGAAGAGAGCAAGTGAGTGTGTGTCCTGGAGGGGTGGGCGCCCTCTGGTGTACCACCTCGAGAC	2500
2501	TTGTCTCATGCCTCCATGCTTGGCCGATGGAGGACAGACTGCAGGAACCTGGCCCATGTGGAAACCTAGCCCTGTTTGGGGGTAGGACCCACAGATGTCT	2600
2601	TGGACAGTTTGGGGGAGGGTTTTAAATTTTAAAGTTTTCCTCCCTTTGTGAAAGGGGATGGGGAGGGGAAG <u>AGTAA</u> ACAGATAACAGGTGGT	2700
2701	GTACCTGGTTGGGGGAGGGGGCGTGCACCTGCATG	2736

Fig. 1 Characterization of full-length *MTA1-L1* cDNA. Nucleotide sequence of the *MTA1-L1* cDNA (accession number AB016591) and the deduced amino acid sequence of the MTA1-L1 protein (one-letter code) are shown. Polyadenylation signal (AGTAAA) is *underlined*, and termination codon (TGA) is indicated by an *asterisk*. Possible phosphorylation sites for tyrosine kinase (TYK), protein kinase C (PKC), and casein kinase 2 (CK 2) are indicated, as well as a putative leucine zipper (LEU) and a zinc-finger (ZIN) DNA-binding motif

dard saline citrate (SSC), 0.1% sodium dodecylsulfate (SDS) at 65°C, and exposed for autoradiography at -80°C for 72 h.

Structural analysis of the MTA1-L1 gene

A genomic cosmid clone (cosMTA1-L1) was isolated by screening a human cosmid library with a clone of *MTA1-L1* cDNA (Sambrook et al. 1989). Sequencing of the human insert confirmed the cDNA sequence and determined the structure of the entire *MTA1-L1* gene, including the promoter region and the introns.

Fluorescence in situ hybridization (FISH)

We performed FISH using the cosmid clone as a probe, as previously described (Inazawa et al. 1993). For denaturation of the G-banding pattern, we prepared metaphase

chromosomes by thymidine synchronization and bromodeoxyuridine release. Before hybridization, metaphase cells were stained with Hoechst 33258 (Sigma, St. Louis, USA) and irradiated with ultraviolet light. The probe was labeled with biotin-16-2'-deoxy-uridine-5'-triphosphate (dUTP) (Boehringer, Mannheim, Germany) by nick translation and hybridized to the denatured chromosomes. Hybridization signals were detected with FITC-avidin (Boehringer). Precise assignments of the signals were determined by visualization of the replicated G-bands.

Results and discussion

Among the cDNA clones randomly selected from an adult-heart cDNA library, one revealed significant homology to the human *MTA1* gene. To isolate a full-length cDNA, we screened the same cDNA library (1×10^6 clones) using the

Fig. 2 **A** Multiple-tissue Northern blot of *MTA1-L1* mRNA. **B** Chromosomal localization of the *MTA1-L1* gene. Metaphase chromosomes were stained with propidium iodide, showing doublet signals (arrowheads)

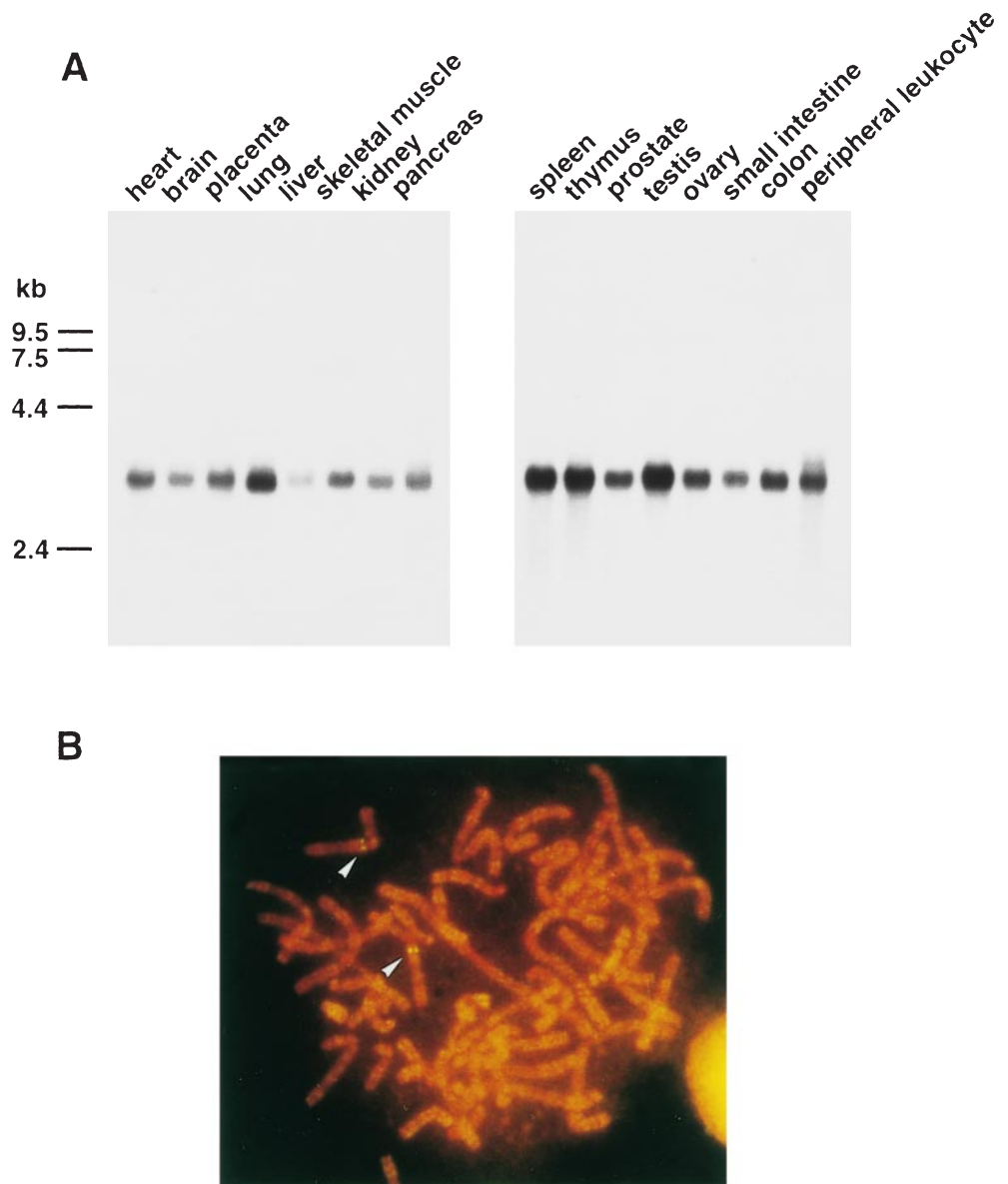


Fig. 3 Comparison of MTA1-L1 amino acid sequence with human (accession number U35113) and rat (accession number U02522) MTA1 proteins, with *Xenopus* ER1 (accession number AF015454), and with the similar-to-MTA1 protein of *Caenorhabditis elegans* (accession number U41264). Identities are indicated in *black*; gaps introduced for maximal alignment are marked with *dashes*

MAT1-L1	MAANMYRVGDYVVFENSSSNPYLVRRRIEELNKTANGNVEAKVVC	60
MTA1 (human)	MAANMYRVGDYVVFENSSSNPYLVRRRIEELNKTANGNVEAKVVC	
MTA1 (rat)	MAANMYRVGDYVVFENSSSNPYLVRRRIEELNKTANGNVEAKVVC	
MAT1-L1	SNAR-----EFEEESKQEGM---SEQQRHQLKHLRELFLSRQFESLPAT	100
MTA1 (human)	KHATLSVCYKAGPGADNGEEGETIEEEMENPEMVDLPBKLKHQLRHLRELFLSRQFESLPAT	
MTA1 (rat)	KHATLSVCYRAGPGADTGEEGETVEEVENPEMVDLPBKLKHQLRHLRELFLSRQFESLPAT	
MAT1-L1	HIRGKCSVTLLNETDIIISQYLEKEDCFYSLVFDVQKTLADQGEIRVGCCKYQAEIPDR	160
MTA1 (human)	HIRGKCSVTLLNETESIKSYLEREDFFYSLVYDFQKTLADKGEIRVGNRYQADITIDL	
MTA1 (rat)	HIRGKCSVTLLNETESIKSYLEREDFFYSLVYDFQKTLADKGEIRVGNRYQADITIDL	
ER1 (xenopus)	ETMVGSMFQAEIPVVG	
MAT1-L1	LVEGESDNRNQQKMMKVVNDEDNPLTDRQIDQFLVVARAVGTFARALDCSSSIROP SLHM	220
MTA1 (human)	LKGEEDGRDQSRLETQVWEAHNPLTDKQIDQFLVVARAVGTFARALDCSSSVROP SLHM	
MTA1 (rat)	LKDGEEEDGRDQSKLETQVWEAHNPLVDKQIDQFLVVARAVGTFARALDCSSSVROP SLHM	
ER1 (xenopus)	ICKYRETEKVEYENDDQLLWNEEYVMEERVID	
MAT1-L1	SAAAASRDITLPHAMDTLQRNICYDLAKAMSTLVPOGGPVLCRDEMEEWSASEANLFEERAL	279
MTA1 (human)	SAAAASRDITLPHAMDTLHKNIYDISKATISALVPOGGPVLCRDEMEEWSASEANLFEERAL	
MTA1 (rat)	SAAAASRDITLPHAMDTLHKNIYDISKATISALVPOGGPVLCRDEMEEWSASEANLFEERAL	
ER1 (xenopus)	REELSVWTEEECRNFEQGL	
C. elegans	RSDALGFDBSEAKAFEEESI	
MAT1-L1	EKYGKDFNDIRQDFLPWKSLSASTVQFYMWKTTDRYVQOKRLKAAEADSKLKQVYTPYNYT	339
MTA1 (human)	EKYGKDFNDIQDFLPWKSLSISTIEYVYMWKTTDRYVQOKRLKAAEASKLLKQVYTPYNYN	
MTA1 (rat)	EKYGKDFNDIQDFLPWKSLSISTIEYVYMWKTTDRYVQOKRLKAAEASKLLKQVYTPYNYN	
ER1 (xenopus)	KAYGKDFHLIQANKVTRTSVGECAVAFYMWKKSERY	
C. elegans	ELYGKDFSLIRLRLLPYRKYVGELEIYYVQWKLTPGY	
MAT1-L1	KPNPNQITISVGS-KPEGM-NGACF--Q---KGLTCESEHTTQSAQWYAWGPPNMQCRLCAS	393
MTA1 (human)	KPNPNQI-SVNNVKAQVINGTCAPGQSPGAGRACESCYYTTSQSYQWYSWGPPNMQCRLCAS	
MTA1 (rat)	KPNPNQI-SVNSVKAQVINGTCPTGQSPGAGRACESCYYTTSQSYQWYSWGPPNMQCRLCAS	
MAT1-L1	CWLYWKYGGGLKIPTRLDGEGATRGITTEPHSRGHLRSRPEAQSLSPYTTSANRAKLLAKNRQT	453
MTA1 (human)	CWLYWKYGGGLKMPTRLDGERPCPNRNNMSPH-GLEPARSSGSP-----KFAFKTRQA	
MTA1 (rat)	CWLYWKYGGGLKMPTRLDGERPCPNRNNMSPH-GLEPARSSGSP-----KFAFKTRQA	
MAT1-L1	FLLQTTKLTRLIARRMCRDLICPERRAARRPYAPINANA IKAECTSIRLPEAKAAPTPLKIHPLV	513
MTA1 (human)	FYLHTTKLTRLIARRICREILRFPWHAARNPYLPINSAA IKAECTARLPEASQSPVLKQAV	
MTA1 (rat)	FYLHTTKLTRLIARRICREILRFPWHAARHPYMPINSAA IKAECTARLPEASQSPVLKQAV	
MAT1-L1	RLPLATIVKDLVAQA-PLKPK-----TP-----RGTK-----TPINRNQ	546
MTA1 (human)	RKPLEAVLRYLETHPRPEKPDVVKSVSSVLSSTIPAKVAPVINNGSP-----TILGKRS	
MTA1 (rat)	RKPLEAVLRYLETHPRPEKPD-----FV-----KSSSSVLSSTIPAKSAP	
MAT1-L1	LSQNRGLGGIMVKR-----AYETMAGA-GV-----E---FSANGRPLAS	581
MTA1 (human)	YEQHNGVDGNMKRLLMPSRGLANHGQTRHMCP-SR-----N---LLLNKGSYPT	
MTA1 (rat)	VINN-GSPTILGKR-----SYEQHNGVDGLANHGQTRHMCP-SRNLNLLNKGYSYPT	
MAT1-L1	G---IRSSSQFAAKRQKLNPA DAPNPVVFV-ATKDTRALRKAITHLIEMRRAARRENLEFLK	637
MTA1 (human)	KVRLIRGGSLEPVKRRRMNWDAPGD-VFYMPKEETRKIRKLLSSSETKRAARREYKFLA	
MTA1 (rat)	KVRLIRGGSLEPVKRRRMNWDAPDD-VFYMATTEETRKIRKLLSSSETKRAARREYKFLA	
MAT1-L1	VKPTLIAV--RPPVPPAPSHPASTN-EPIVLED	668
MTA1 (human)	LRQSQ-ALPPRPP-PPAP-----VNDEPIVIED	
MTA1 (rat)	LRQSQ-ALPLRPP-PPAP-----VNDEPIVIED	

cDNA fragment as a probe, and isolated ten cDNA clones. Alignment of overlapping clones revealed that the cDNA, which we named *MTA1-L1* (*MTA1 like 1*), consisted of 2736 nucleotides whose open reading frame (2004 nucleotides) encoded a 668-amino acid protein (Fig. 1). Since Northern-blot analysis with a *MTA1-L1* cDNA probe identified a single 3.0-kb transcript in all the adult human tissues examined (Fig. 2A), we estimated that the nucleotide sequence for *MTA1-L1* shown in Fig. 1 encompassed almost the full-length cDNA. The expression pattern of this novel gene was ubiquitous and strong not only in testis but also in lung, spleen, and thymus in the human tissues, in contrast to that of *MTA1* in the rat, in which expression is strong in the testis but weak in other normal tissues, including brain, heart, lung, liver, and kidney. The functions of *MTA1* and *MTA1-L1* are probably redundant, but these two genes may be expressed in a cell-specific manner.

From a human genomic cosmid library we obtained one cosmid (cosMTA1-L1) containing the *MTA1-L1* gene. Sequencing of the human insert revealed that the *MTA1-L1* gene spanned approximately 8.1 kb of genomic DNA and consisted of 18 exons (database accession number for the entire genomic sequence, AB012922). Using cosMTA1-L1 as a probe, we performed FISH to determine the chromosomal location of *MTA1-L1*. Specific doublet signals were observed on both copies of chromosome 11 at band q12-13.1 (Fig. 2B).

Computer-assisted analysis of the amino acid sequence predicted that *MTA1-L1* would contain neither an N-terminal signal sequence for transfer into the endoplasmic reticulum nor a hydrophobic domain characteristic of transmembrane proteins (Kyte and Doolittle 1982). However, several potential phosphorylation sites were present (Fig. 1). A data-base homology search revealed the similarity of predicted amino acid sequences of the *MTA1-L1* gene product to the *MTA1* proteins of rat (58.6% identity) and human (59.6%) (Fig. 3). The deduced *MTA1-L1* protein contains 13 dispersed cysteine residues that may be capable of forming intra- and/or inter-molecular disulfide bonds to stabilize the protein structure; 11 of these cysteine residues are conserved in rat and human *MTA1*. The potential phosphorylation sites and a zinc-finger domain as a DNA-binding motif (amino acid residues 367-394) are imperfectly conserved between *MTA1* and *MTA1-L1*. However, a putative leucine-zipper motif in *MTA1-L1* (amino acid residues 231-252) is not present in *MTA1* (Fig. 1).

The *MTA1-L1* product also contains a region (amino acid residues 146-191) showing 40% homology to the *Xenopus* ER1 (early response 1) protein, and another re-

gion (amino acid residues 262-316) with 30% similarity to ER1 and to the *Caenorhabditis elegans* *MTA1*-like sequence (Fig. 3). *ER1* had been isolated as a novel gene whose expression increased in *Xenopus* embryo explants during mesoderm development induced by fibroblast growth factor (Paterno et al. 1997). *ER1* is thought to function as a transcription factor; as its essential region for transactivation is conserved in *MTA1-L1* (Fig. 3), *MTA1-L1* may also be a transcription factor. In any event, the data reported here suggest that *MTA1-L1* is a member of a conserved multi-gene family and that it could play a role in cancer invasion and metastasis.

Acknowledgements We thank Keiko Okui for technical assistance.

This work was supported in part by a special Grant for Strategic Advanced Research on Cancer from the Ministry of Education, Culture, Sports, and Science of Japan.

References

- Inazawa J, Saito H, Ariyama T, Nakamura Y (1993) High resolution cytogenetic mapping of 342 new cosmid markers including 43 RFLP markers on human chromosome 17 by fluorescence in situ hybridization. *Genomics* 17: 153-162
- Isomura M, Okui K, Fujiwara T, Shin S, Nakamura Y (1996) Isolation and mapping of RAB2L, a human cDNA that encodes a protein homologous to RalGDS. *Cytogenet Cell Genet* 74: 263-265
- Kyte J, Doolittle RE (1982) A simple method for displaying the hydropathic character of a protein. *J Mol Biol* 157: 105-132
- Paterno GD, Li Y, Luchman HA, Ryan PJ, Gillespie LL (1997) cDNA cloning of a novel, developmentally regulated immediate early gene activated by fibroblast growth factor and encoding a nuclear protein. *J Biol Chem* 272: 25519-25595
- Pearson WR, Lipman DJ (1988) Improved tools for biological sequence comparison. *Proc Natl Acad Sci USA* 85: 2444-2448
- Sambrook J, Fritsch EF, Maniatis T (1989) *Molecular cloning: A laboratory manual*, 2nd ed. Cold Spring Harbor Laboratory, Cold Spring Harbor, New York
- Sudo K, Chinen K, Nakamura Y (1994) 2058 expressed sequence tags (ESTs) from a human fetal lung cDNA library. *Genomics* 24: 276-279
- Tanaka T, Inazawa J, Nakamura Y (1996) Molecular cloning of a human cDNA encoding putative cysteine protease (PRSC1) and its chromosome assignment to 14q32.1. *Cytogenet Cell Genet* 74: 120-123
- Toh Y, Pencil SD, Nicolson GL (1994) A novel candidate metastasis-associated gene, *mta1*, differentially expressed in highly metastatic mammary adenocarcinoma cell lines. *J Biol Chem* 269: 22958-22963
- Toh Y, Pencil SD, Nicolson G (1995) Analysis of the complete sequence of the novel metastasis-associated candidate gene, *mta1*, differentially expressed in mammary adenocarcinoma and breast cancer cell lines. *Gene* 159: 97-104
- Toh Y, Oki E, Tokunaga E, Ohno S, Maehara Y, Nicolson GL, Sugimachi K (1997) Overexpression of the *mta1* gene in gastrointestinal carcinomas: Correlation with invasion and metastasis. *Int J Cancer* 74: 459-463