Mol Genet Genomics (2001) 266: 239–245
DOI 10.1007/s004380100549

ORIGINAL PAPER

E.V. Pankratova · I.E. Deyev · S.V. Zhenilo
O.L. Polanovsky

Tissue-specific isoforms of the ubiquitous transcription factor Oct-1

Received: 9 April 2001 / Accepted: 28 June 2001 / Published online: 31 July 2001
© Springer-Verlag 2001

Abstract The ubiquitously expressed transcription factor Oct-1 is a member of the POU protein family. It is involved in the activation of snRNA promoters and some mRNA promoters (e.g., promoters and enhancers of genes for histone H2B and immunoglobulins). In this work we have cloned and sequenced a new Oct-1 isoform, named Oct-1L. Both *Oct-1L* mRNA and *Oct-1R* mRNA (cloned earlier) are expressed in lymphocytes, but not in any other cell line tested. This is the first report of tissue-specific *Oct-1* gene expression. Both these forms differ from the ubiquitously expressed Oct-1 isoforms in the N-termini. They are probably generated by alternative splicing and/or alternative initiation of transcription. The latter is confirmed by the localization of transcription start points upstream of exons 1L (lymphocyte-specific) and 1U (ubiquitously expressed). We assume that tissue-specific expression of Oct-1L and Oct-1R in lymphocytes and their structural differences from the ubiquitously expressed Oct-1 isoforms may be related to B and T cell differentiation and/or expression of the immunoglobulin genes.

Keywords *Oct-1* gene · Tissue-specific isoforms · *Oct-1L* and *Oct-1R* isoforms · Tissue-specific expression

Communicated by G. P. Georgiev

E.V. Pankratova · I.E. Deyev · S.V. Zhenilo
O.L. Polanovsky (✉)
Engelhardt Institute of Molecular Biology,
Russian Academy of Sciences, Vavilov St. 32,
Moscow, 117984, Russia
E-mail: pol@genome.eimb.relarn.ru
Tel.: +7-095-1359903
Fax: +7-095-1351405

E.V. Pankratova
Centre for Medical Studies, University of Oslo,
Moscow, Russia

I.E. Deyev · S.V. Zhenilo
Moscow Institute of Physics and Technology,
Institutskii Per. 9, Dolgoprudny,
Moscow Region, 141700, Russia

Introduction

The Oct proteins contain the conserved DNA-binding POU domain, which is common to the POU family of transcription factors (Verrijzer and Van der Vliet 1993; Ryan and Rosenfeld 1997). Oct-1 is known as a ubiquitous nuclear protein expressed in all eukaryotic cells. It plays multiple roles in the cell, acting as either a positive or a negative regulator of gene transcription and DNA replication (Verrijzer and Van der Vliet 1993; Ryan and Rosenfeld 1997); it is also involved in the anchoring of chromatin loops to the nuclear matrix (Kim et al. 1996; Imai et al. 1997) and in apoptosis (Veenstra et al. 1998). The gene encoding Oct-1 is one of the first genes to be expressed in the embryo (Veenstra et al. 1997). The pleiotropic effects of Oct-1 result from the expression of the many genes that are under its control. Thus, Oct-1 is involved in the regulation of some housekeeping genes, e.g., those encoding histone H2B (Fletcher et al. 1987), replacement histone H3B (Witt et al. 1997), as well as U2, U6, and 7SK snRNAs (Ryan and Rosenfeld 1997). Being a ubiquitous transcription factor, Oct-1 also takes part in the regulation of tissue-specific gene expression. Target genes controlled by Oct-1 include those encoding the light and heavy chains of immunoglobulins (Ig) (Luo and Roeder 1995; Shah et al. 1997), interleukin-2 (IL-2) (Ullman et al. 1991; Delhase et al. 1996), IL-8 (Wu et al. 1997), IL-3, IL-5, granulocyte/macrophage colony stimulating factor (GM-CSF) (Kaushansky et al. 1994), and Pit-1 (Delhase et al. 1996).

Comparative analysis of Oct-1 isoforms and structural study of the human locus *OTF-1* that encodes Oct-1 (Sturm et al. 1993) suggest that *Oct-1* pre-mRNA may be spliced in several ways, resulting in the synthesis of protein isoforms that may differ functionally. Two splice variants of human Oct-1 have been described (Das and Herr 1993): Oct-1A and Oct-1B. These alternative splice forms were found in all cell lines tested. Oct-1B displayed a greater ability to activate the human histone H2B promoter than Oct-1A (Das and Herr 1993).

Murine *Oct-1* mRNA isoforms – *Oct-1a*, *Oct-1b*, *Oct-1c* – have also been described, but show ubiquitous expression (Suzuki et al. 1993).

The aim of this work was to study the tissue-specific isoforms of Oct-1, named Oct-1L and Oct-1R. The mRNA for Oct-1L has a short 5′-terminal exon (1L) similar to that in the Oct-1R messenger (Stepchenko 1992a), but differs from it in that the rest of the Oct-1L mRNA is homologous to the murine *Oct-1b* message. We show here that expression of the *Oct-1L* and the previously described *Oct-1R* (Stepchenko 1992a) mRNAs is tissue-specific. We suggest that these tissue-specific isoforms arise by alternative splicing and/or transcription initiation from two alternative promoters.

Materials and methods

Cell lines and culture conditions

The murine cell lines used were myeloma NS/0, neuroblastoma NB41A3, teratocarcinoma F9, mouse fibroblasts 10(1), the haemopoietic progenitor cell line FDCP-2, and thymoma EL-4. They were maintained in DMEM containing 10% fetal calf serum and 40 μg/ml gentamycin.

RNA isolation

RNA was isolated from cell lines and from lymph nodes, spleen, bone marrow, and thymus cells of C57BL/6 mice, using guanidine thiocyanate as described by Chomczynski and Sacchi (1987).

Oligonucleotides

The following synthetic oligonucleotides were used as primers for various purposes (see below). α1L (5′-GTCACTGCAGTC-CAGCATGGC-3′) is specific for exon 1L of the *Oct-1R* mRNA; α1U (5′-CTCATCTTGACTCGCTGCTC-3′) for exon 1U; ex2 (5′-GGTTTCTGATGGATTATTCATTC-3′) for exon 2; 1L 5′-GCC-ATGCTGGACTGCAGTGAC-3′) for exon 1L; 1U (5′-GAGCA-GCGAGTCAAGATGAG-3′) for exon 1U; and 5′-1L (5′-ACTAAGCTTCTCTTCCCACCCTTGTT-3′) for the 5′-untranslated region (UTR) upstream of exon 1L. The oligonucleotide 1A (5′-TAGCCAGCCTATCACCCTGTAGT-3′) is specific for the 3′ end of *Oct-1a,b,c* mRNAs; 1R (5′-ATA-GGATCCTTAAGTGCAAACCCATCT-3′) for the 3′ end of *Oct-1R* mRNA; T13 (5′-GGGAGGCCCTTTTTTTTTTTTT-3′) was used to prime the synthesis of full-length *oct-1* cDNAs.

Reverse transcription (RT)

The reaction was carried out with total RNA (3–5 μg) and M-MuLV reverse transcriptase according to the manufacturer's instructions. The products of alternative splicing were analyzed using the oligonucleotide ex2, which is specific for the second exon. Full-length *oct-1* cDNAs were generated using oligonucleotide T13. Transcription start points were localized by primer extension analysis using oligo α1L for the 5′-terminal exon of *oct-1R* cDNA or oligo α1U for the 5′-terminal exon of *oct-1a,b,c* cDNA. The reaction products were analyzed on 6% polyacrylamide gels containing 8 M urea. The known 5′-UTR sequence of the *oct-1* gene was used as a marker.

PCR

PCRs were performed using 1/5 of the single-stranded cDNA generated by reverse transcription. The products of alternative splicing were analyzed using ^{32}P-labeled oligo ex2 together with (5′-1L), 1L, or 1U. The PCR products were analyzed in denaturing polyacrylamide gels using the known 5′-UTR sequence of the *oct-1* gene as a marker. Full-length *oct-1* cDNAs were obtained by PCR using two different primer pairs: 5′-1L and 1A or 5′-1L and 1R (Fig. 1). Control reactions were carried out using the 1U-1A pair. The PCR products were analyzed using Southern hybridization with a ^{32}P-labeled DNA probe corresponding to the Oct-1 POU-specific domain.

The mixtures of PCR products were separated on a 1% agarose gel. The bands with molecular weights corresponding to *oct-1L* or *oct-1R* cDNA were cut out and the DNA was eluted from the gel; these fragments were cloned into the vector pUC18 and sequenced.

Nucleotide sequences

The nucleotide sequence data reported in this paper appears in the EMBL database under the Accession No. AJ296212.

Results

A new isoform of transcription factor Oct-1

A new isoform of *oct-1* cDNA, termed *oct-1L*, was isolated from a myeloma cell line NS/0. This cDNA has a 5′-terminal sequence similar to that of the cDNA encoding the isoform Oct-1R cloned earlier from the same myeloma cell line (Stepchenko 1992a), while the remainder of the molecule is homologous to the cDNA encoding the isoform Oct-1b (Suzuki et al. 1993). The 5′-terminal regions of *oct-1R* and *oct-1L* cDNAs are identical to the exon 1L previously identified in the murine locus *otf-1* (Pankratova and Polanovsky 1998), and different from the 5′-terminal regions of the other ubiquitously expressed human and murine full-length *oct-1* isoforms: *oct-1A,B* (Das and Herr 1993) and *oct-1a,b,c*, (Suzuki et al. 1993) (Fig. 1).

The 5′-terminal exon of the *oct-1R* and *oct-1L* cDNAs encodes 10 amino acid residues, while the 5′-terminal exon of the human isoform *oct-1A* encodes 21 N-terminal amino acid residues of the protein (Table 1).

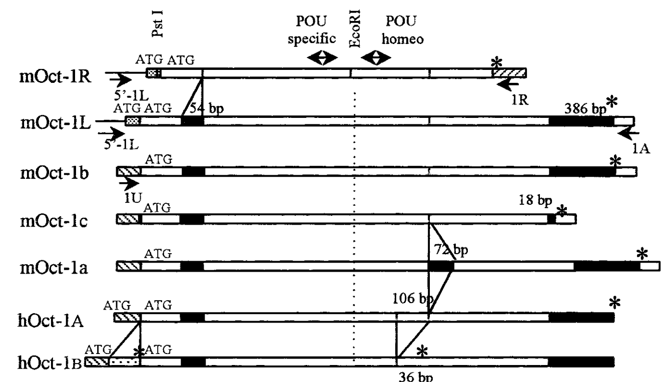

Fig. 1 Schematic representation of *oct-1* cDNA isoforms. The *arrows* indicate the positions of the oligonucleotides used to obtain the full-length *oct-1* cDNAs. The POU-specific and POU homeo domains are marked. Alternatively spliced exons are shown as *filled boxes*. Termination codons are indicated by *asterisks*

Table 1 Comparison of predicted N-terminal amino acid sequences of murine Oct-1L and Oct-1R with those of other known murine (m) and human (h) Oct-1 and Oct-2 isoforms

Isoform	Amino acid sequence	Reference
mOct-1L,R	MLDCSDCVLDSRMNNPSETNKSSMES...	Pankratova and Polanovsky (1998)
mOct-1, exon 1L	MLDCSDCVLD	Stepchenko et al. (1992a)
hOct-2, exon1	MVHSSMGAPD	Sturm et al. (1993)
hOct-1, exon 1U	MADGGAASQDESSAAAAAAAD	Sturm et al. (1993)
mOct-1a,b,c	GGAASQDESSAAAAAAADSRMNNPSETNKSSMES...	Suzuki et al. (1993)
hOct-1A	MADGGAASQDESSAAAAAAADSRMNNPSETNKSSMES...	Das and Herr (1993)
hOct-1B	MNNPSETNKSSNES....	Das and Herr (1993)

We named these exons 1L and 1U, respectively. Murine cDNAs encoding Oct-1a, b and c (Suzuki et al. 1993) appear also to contain exon 1U except that 9 nt, corresponding to the first three codons of the human sequence, are missing.

Alternative splicing of 5′-terminal exons of the *Oct-1* gene

Alternative splicing of 5′-terminal exons of the gene encoding the transcription factor Oct-1 was studied using various cell lines and tissues. In order to detect mRNA containing murine exon 1U we used a pair of oligonucleotides, 1U and ^{32}P-labeled ex2. A 77-bp PCR product corresponding to the 5′ end of the mature *Oct-1a,b,c* mRNAs was found in all tissues and cell lines studied: neuroblastoma NB41A3, teratocarcinoma F9, fibroblasts 10(1), myeloma NS/0, thymoma EL-4, and also in the cells of murine myeloid progenitor cell line FDCP2, bone marrow, spleen, lymph nodes, and thymus (Fig. 2A, B). Exon 1L-containing *Oct-1* mRNA was detected by RT-PCR using two different primer pairs: ^{32}P-labeled oligo ex2 and oligo 1L, or oligo ex 2 and oligo 5′-1L (Fig. 2). As also seen in Fig. 2, Oct-1L mRNA contains the UTR identified earlier in the murine *otf-1* locus (Pankratova and Polanovsky 1998). Unlike the *Oct-1a,b,c* mRNAs, the *Oct-1* mRNA containing exon 1L proved to be expressed only in lymphoid cells: strongly in the B cell line myeloma NS/0, spleen cells, bone marrow cells, and in lymph nodes; and weakly in T cells: thymocytes (immature T lymphocytes) and T-lymphoma EL-4 (corresponds to mature T cells). It should be noted that in T cells the signal was detected only after long exposure. No expression of these mature *Oct-1* mRNAs was found in any other cell line under study. Based on these data, we suggest that positioning of the 1L exon at the 5′ end of the mature *Oct-1* mRNA results from tissue-specific alternative splicing.

In order to check whether any mature form of *Oct-1* mRNA might contain both 1L and 1U exons, we performed PCRs on the same DNA with oligonucleotide pairs complementary to these exons: 1U-α1L and 1L-α1U. No *Oct-1* mRNAs containing both correctly spliced 1L and 1U exons were found (data not shown).

Expression of *Oct-1L* and *Oct-1R* mRNAs in B and T lymphocytes

To study the expression of *Oct-1* mRNAs containing the 5′-terminal exon 1L, we generated full-length *oct-1* cDNA using RT-PCR with primer 5′-1L and either 1R or 1A. The reaction products were separated on a 1% agarose gel and then analyzed using Southern hybridization with a ^{32}P-labelled probe for the Oct-1 POU-specific domain (Fig. 3). Two different isoforms of *Oct-1* mRNA were detected. They had identical 5′-terminal exons 1L, but differed in their 3′-terminal sequences and were identified as *Oct-1L* and *Oct-1R*. The *Oct-1L* mRNA isoform is expressed in both B and T lymphocytes; however, in the T-cell line EL-4 the *Oct-1L* mRNA is a minor transcript and can be detected only after long exposure. The other lymphoid-specific isoform of *Oct-1* mRNA, *Oct-1R* is expressed only in the B-cell line myeloma NS/0, spleen, and lymph nodes; no expression of *Oct-1R* was detected in thymocytes or EL-4 cells. The ubiquitous *Oct-1a,b* were expressed to much the same extent in all these cell lines.

Transcription start sites of the *oct-1* gene

Reverse transcription using oligonucleotides complementary to exons 1L and 1U (oligos α1L and α1U, respectively) allowed us to detect two transcription starts upstream of each of these exons (Fig. 4). For exon 1L the proximal start is the A at position –159 (5′-TAGTTT-3′) and the distal one is T at –307 (5′-TTGTTT-3′); there is no canonical TATA box in the promoter upstream of exon 1L. The transcription start points for exon 1U are at positions –160 (proximal) and –384 (distal) from the ATG codon.

Analysis of nucleotide sequences from the Human Genome Data Bank (AL136984) has located exon 1L about 4 kb upstream of exon 2 within the locus *OTF-1*, and exon 1U more than 80 kb upstream of exon 2: 1U is a 5′-terminal exon. Comparison of a DNA fragment of the murine *otf-1* locus (Pankratova and Polanovsky 1998) containing the 1L exon (2.2 kb) with the human *OTF-1* locus shows almost complete identity in the region of exon 1L (there is one nucleotide substitution that does not affect the reading frame) and very high (87%) homology in a 1-kb 5′-UTR and the 5′ segment (about

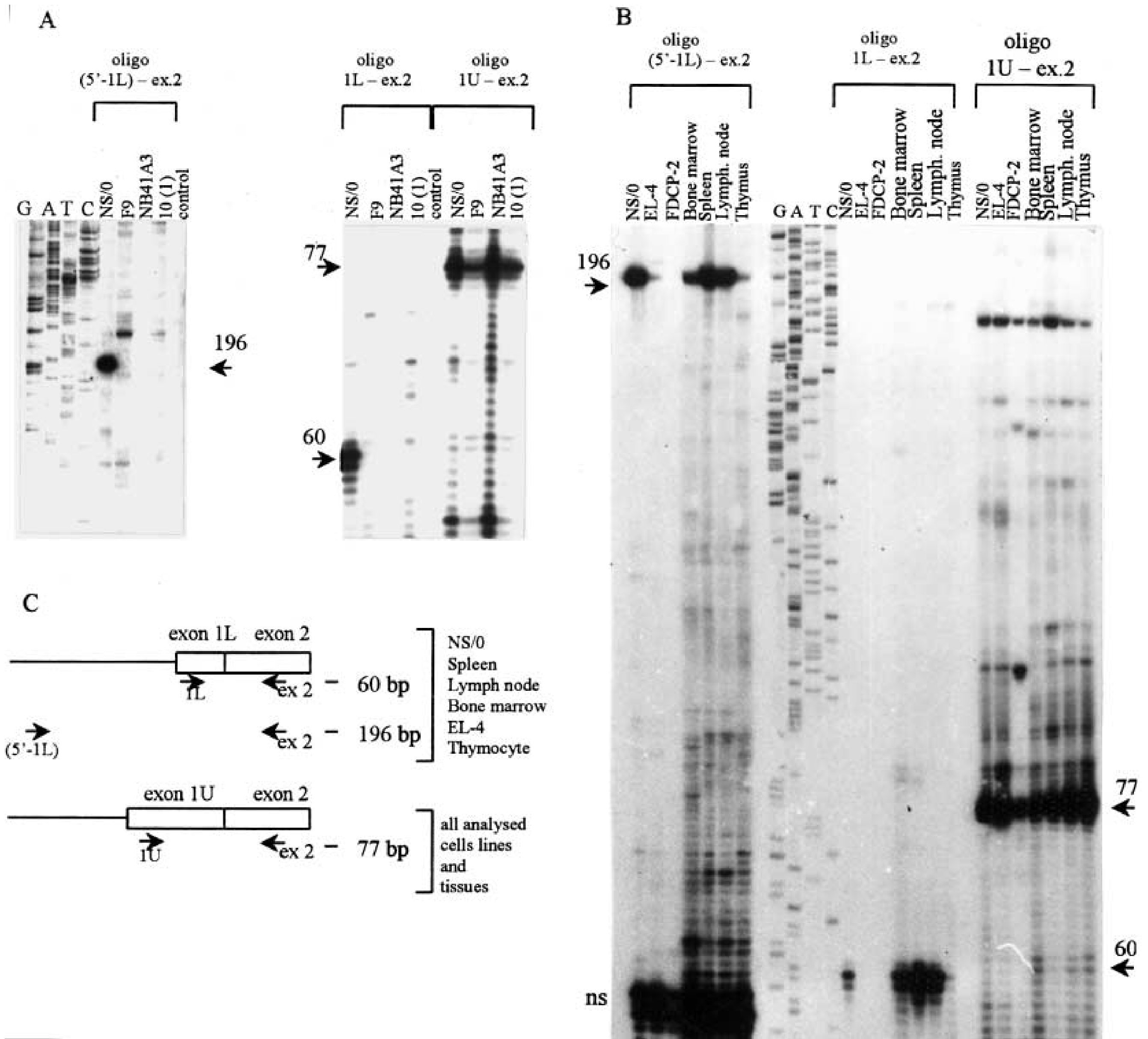

Fig. 2A–C Alternative splicing of *Oct-1* 5′-exons. **A** Products of RT-PCR from the myeloma cell line NS/0 and non-lymphoid cell lines. **B** Products of RT-PCR from lymphoid tissues and cell lines. **C**. Strategy used for RT-PCR. The *arrows* indicate the positions of the primers

200 bp) of the intron (Fig. 4C). In murine DNA, regions upstream and downstream of exon 1L contained canonical oct sites known to bind Oct proteins with maximal affinity, non-canonical oct sites, Sp1, and CCAAT sites. All these *cis*-acting elements are present in the homologous region of the human *oct-1* gene. We previously found A/T-rich clusters with TAAT core sites in this 5′-terminal region. These sites are known to bind Oct-1 and Oct-2 proteins (Verrijzer et al. 1992; Stepchenko 1992b, 1994; Stepchenko et al. 1997a, 1997b; Pankratova and Polanovsky 1998). Most of these TAAT core sites were also found in human DNA. The high degree of homology of these *oct-1* gene regions upstream and downstream of exon 1L and the identity of regulatory sites indicate an important role for this region in the regulation of *oct-1* gene expression. The structure of the 5′-UTR of the murine exon 1U remains unknown. However, analysis of human DNA (GenBank Accesion No. AC025991, AL136984) has shown that the 5′-UTR of exon 1U contains a canonical TATA box, but no oct sites or TAAT core sites.

Discussion

As follows from the results of this work, transcription of the *oct-1* gene is initiated in all tested cell lines from two transcription start sites located upstream of exons 1L and 1U. The promoter located upstream of exon 1L has no TATA box, contains "octamer" sites, and is

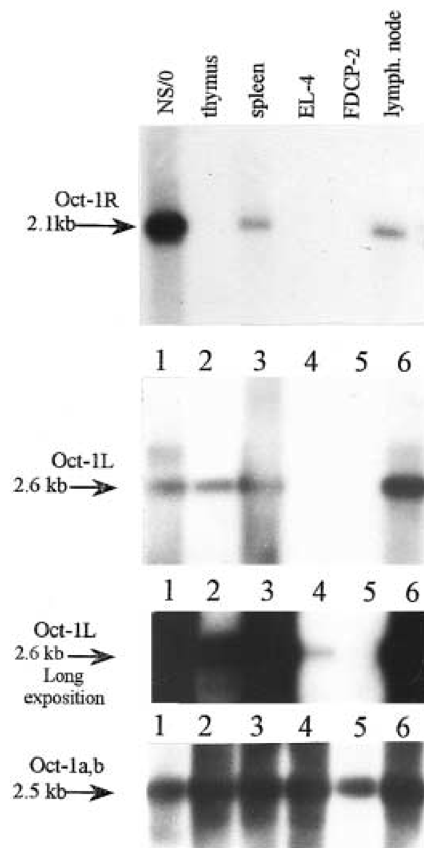

Fig. 3 Southern analysis of products of RT-PCR showing the expression pattern of *oct-1* splicing products. *Oct-1* isoforms were obtained by PCR using the following pairs of oligonucleotides as primers: for *oct-1R*, 5′-1L and 1R; for *oct-1L*, 5′-1L and 1A; and for *oct-1a,b*, 1U and 1A

probably autoregulated (Pankratova and Polanovsky 1998), while the region upstream of exon 1U contains a TATA box, but has no autoregulation-related *cis*-acting elements.

Ubiquitous functioning of Oct-1 and, at the same time, its involvement in tissue-specific transcription may be realized in several ways. First, Oct-1 is able to form complexes with other nuclear proteins. Interactions of the Oct-1 protein with other transcription factors and tissue-specific co-regulators provide for fine regulation of gene expression. Cooperative interaction with Oct-1 has been shown for several transcription factors: Sp1 (Janson and Petterson 1990; Strom et al. 1996), Ap-1 (Kaushansky et al. 1994; Delhase et al. 1996), NF-1 (O'Connor and Bernard 1995), steroid hormone receptor (Bruggemeier et al. 1991), Pit-1 (Delhase et al. 1996), and the homeobox protein Pbx (Subramaniam et al. 1998). Second, pleiotropic functioning of Oct-1 and fine regulation of expression may proceed by interaction of Oct-1 with various DNA sites: the canonical oct site ATGCAAAT, non-canonical oct sites with single nucleotide substitutions, TAAT core sites, and TAATGARAT sites (Verrijzer et al. 1992; Stepchenko 1992b, 1994; Stepchenko et al. 1997a, 1997b). The affinity of Oct-1 for these sites is highly variable, and interaction with the co-activator OCA-B (Gstaiger et al. 1995; Luo and Roeder 1995; Strubin et al. 1995) and with VP-16 (O'Hare and Goding 1988) strictly depends on the site to which Oct-1 is bound.

As shown in this work, one further mechanism may be involved in transcriptional regulation by Oct-1: tissue-specific alternative splicing of *Oct-1* pre-mRNA. The *OTF-1* locus consists of more than 21 exons (Sturm et al. 1993; Riss and Laskov 1999). Oct-1 is represented in various cell lines by a set of alternatively spliced isoforms with different C-terminal amino acid sequences (Stepchenko 1992a; Das and Herr 1993; Suzuki et al. 1993; Riss and Laskov 1999). It was shown earlier that the expression ratio of certain spliced forms of *Oct-1* depends on the type of tissue considered (for example, the ratios in testes differ from those other tissues) (Jaffe et al. 1995; Riss and Laskov 1999). Some exons of the *OTF-1* locus are spliced identically in all tissues. As shown here, splicing of 1L-containing mRNAs is tissue-specific.

Mature *Oct-1* mRNA with correctly spliced exons 1L and 2 has thus far been found only in lymphoid cells. In the non-lymphoid cells tested, no correctly spliced mRNA was detected with oligo probes 1L or 5′-1L and ex2. Translation of these mRNAs in non-lymphoid cells is probably initiated from the first AUG codon in exon 2, as has been shown earlier (Das and Herr 1993). Based on comparisons of the translational efficiency of the first AUG codons of exons 1L, 1U, and 2, it appears that the context of the AUG codon in exon 1L is optimal for translation initiation. The sequence surrounding the AUG in exon 1L is cagccAUGcu; exon 1U has the sequence ucaaaAUGgc, and the first AUG in exon 2 occurs in the sequence caagaAUGaa. The consensus for translation initiation (Kozak 1991) is cc(A/G)cCAUGGc.

Tissue-specific alternative splicing of *Oct-1* mRNA in lymphocytes results in the formation of several isoforms of *Oct-1*, all containing the exon 1L (Pankratova et al., unpublished data). The two already sequenced forms, *oct-1L* and *oct-1R*, differ from each other in their expression patterns. Expression of *Oct-1L* mRNA is high in the B-cell line NS/0, spleen, lymph nodes, and thymocytes, while in the T-cell line EL-4 it is low but detectable; *Oct-1R* mRNA is expressed only in the B-cell line NS/0, spleen, and lymph nodes (Fig. 3). Both *Oct-1L* and *Oct-1R* mRNA contain at the 5′ end the short tissue-specific exon 1L. Table 1 shows that tissue-specific Oct-1 isoforms differ from the ubiquitously expressed isoforms in their N-terminal sequences. As shown by our preliminary experiments using RT-PCR, the lymphoid cells contain some more *Oct-1* mRNA isoforms bearing exon 1L at the 5′ end and varying in size (Pankratova et al., in preparation). This allows us to suggest that the differences in the N-terminal region of the Oct-1 proteins are essential for the function of these proteins in lymphocytes.

Alignment of related genes allows comparative structural analysis of the alternatively spliced exons. The

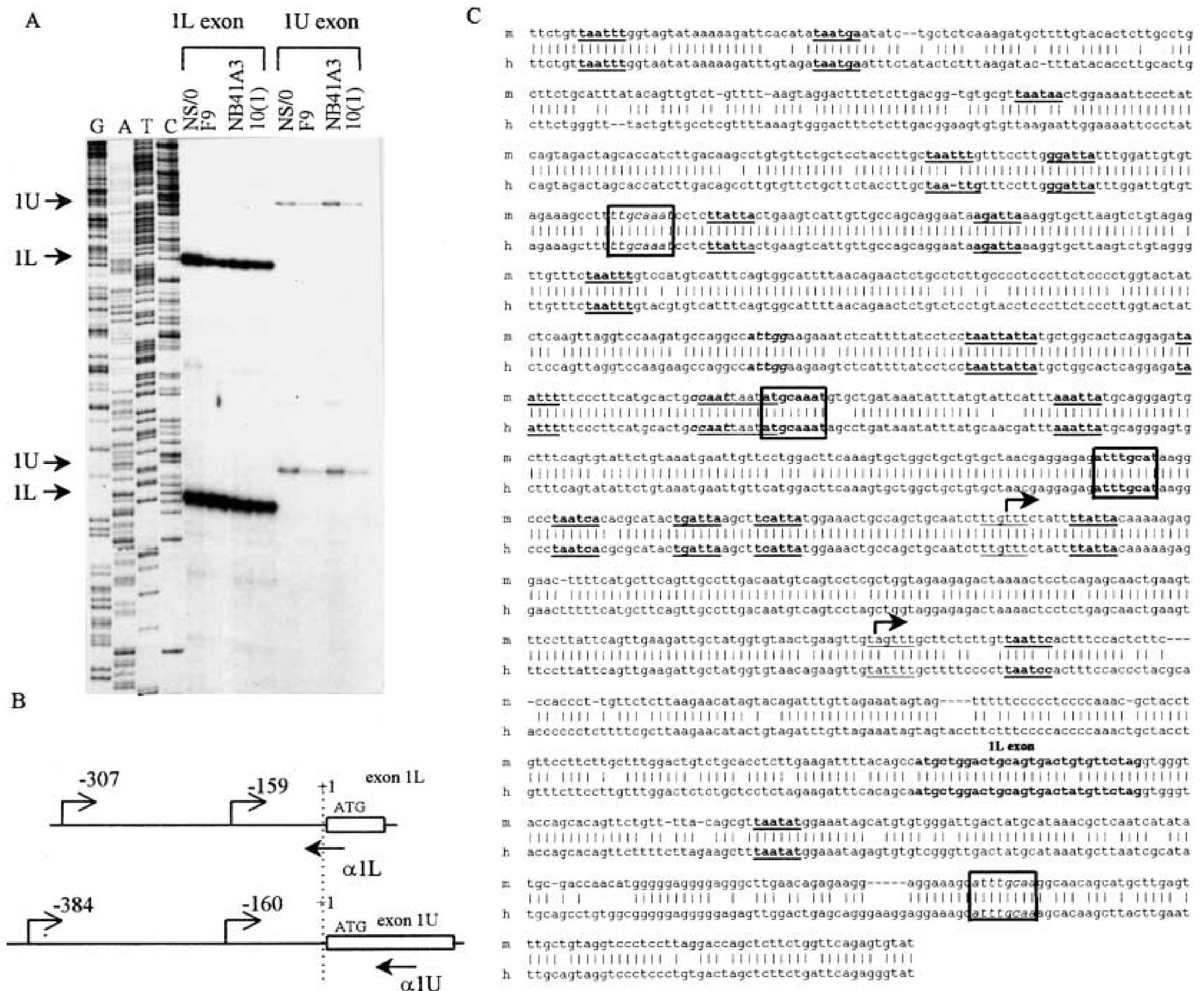

Fig. 4 A Transcription of the *oct-1* gene. **A** Transcription start sites upstream of exons 1U and 1L of the murine *oct-1* gene revealed by primer extension analysis. The marker lanes (G,A,T,C) show the sequence of the upstream region of exon 1L; the primer for the sequencing reaction was oligo α1L. **B** Design of the experiment. The *arrows* show the positions of the primers. **C** Alignment of murine (Pankratova and Polanovsky 1998) and human (GenBank Accesion No. AL136984) genomic DNA sequences containing exon 1L (shown in *bold*). The *boxed* sequences represent oct sites (*bold*) and oct-related sites (*italics*); TAAT core sites are shown in *bold and underlined*; transcription start sites are indicated by the *arrows*

Oct-1 and lymphocyte-specific Oct-2 proteins are the most closely related among the POU family genes. It is interesting to note that exon 1L of *oct-1* and the first exon of *oct-2* (Sturm et al. 1993) have 57% homology and each encodes 10 amino acid residues. It was previously shown that B-cell-specific transcription of Ig genes is induced by interaction of either Oct-1 or Oct-2 with the co-activator protein OCA-B (O'Hare and Goding 1988; Gstaiger et al. 1995; Strubin et al. 1995). As shown by Shah et al. (1997), Oct-1 is the most potent activator of an Ig promoters in conjunction with cognate Ig gene enhancers in B cells. This result provides molecular evidence that Oct-1 may be the critical regulator of Ig gene transcription during the development of B cells.

Oct-1 is known to be involved in lymphocyte-specific regulation of some other genes (Ullman et al. 1991; Kaushansky et al. 1994; Pfeuffer et al. 1994; Luo and Roeder 1995; Shah et al. 1997; Wu et al. 1997). These data allow us to suppose that tissue-specific alternative splicing of *Oct-1* mRNA and generation of exon-1L-containing isoforms in lymphocytes may be related to lymphocyte differentiation and lymphocyte-specific expression of immunoglobulin and lymphokine genes.

Acknowledgements This work was supported by the Russian Foundation for Basic Research (Grant No. 99-04-49180), the State Program Frontiers in Genetics, and the Russian National Program on the Human Genome, and by the grant of a fellowship for young scientists to Dr. E. V. Pankratova from the Presidium of the Russian Academy of Sciences.

References

Bruggemeier U, Kalf M, Franke S, Scheidereit C, Beato M (1991) Ubiquitous transcription factor OTF-1 mediates induction of the MMTV promoter through synergistic interaction with hormone receptors. Cell 64:565–572

Chomczynski P, Sacchi N (1987) Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. Anal Biochem 162:156–159

Das G, Herr W (1993) Enhanced activation of the human histone H2B promoter by an Oct-1 variant generated by alternative splicing. J Biol Chem 268:25026–25032

Delhase C, Castrillo J, de la Hoya M, Rajas F, Hooghe-Peters EL (1996) AP-1 and Oct-1 transcription factors down-regulate the expression of the human *PIT1/GHF1* gene. J Biol Chem 271:32349–32358

Fletcher C, Heintz N, Roeder RG (1987) Purification and characterization of OTF-1, a transcription factor regulating cell cycle expression of a human histone H2B gene. Cell 51:773–781

Gstaiger M, Knoepfel L, Georgiev O, Schaffner W, Hovens GM (1995) A B-cell coactivator of octamer-binding transcription factors. Nature 373:360–362

Imai S-I, Nishibayashi S, Takao K, Tomifuji M, Fujino T, Hasegawa M, Takano T (1997) Dissociation of Oct-1 from the nuclear peripheral structure induces the cellular aging-associated collagenase gene expression. Mol Biol Cell 8:2407–2419

Jaffe J, Hochberg M, Riss J, Hasin T, Reich L, Laskov R (1995) Cloning, sequencing and expression of two isoforms of the murine Oct-1 transcription factor. Biochim Biophys Acta 1261:201–209

Janson L, Petterson U (1990) Cooperative interactions between transcription factors Sp1 and OTF-1. Proc Natl Acad Sci USA 87:4732–4736

Kaushansky K, Shoemaker SG, O'Rork CA, McCarty JM (1994) Coordinate regulation of multiple human lymphokine genes by Oct-1 and potentially novel 45 and 43 kDa polypeptides. J Immunol 152:1812–1820

Kim MK, Lesoon-Wood LA, Weintraub BD, Chung JH (1996) A soluble transcription factor, Oct-1, is also found in the insoluble nuclear matrix and possesses silencing activity in its alanine-rich domain. Mol Cell Biol 16:4366–4377

Kozak M (1991) An analysis of vertebrate mRNA sequences: intimations of translational control. J Cell Biol 115:887–903

Luo Y, Roeder RG (1995) Cloning, functional characterization, and mechanism of action of the B-cell-specific transcriptional coactivator OCA-B. Mol Cell Biol 15:4115–4124

O'Connor M, Bernard HU (1995) Oct-1 activates the epithelial-specific enhancer of human papillomavirus type 16 via a synergistic interaction with NFI at a conserved composite regulatory element. Virology 207:77–78

O'Hare P, Goding CR (1988) Herpes simplex virus regulatory elements and the immunoglobulin octamer domain bind a common factor and are both targets for virion transactivation. Cell 52:435–445

Pankratova EV, Polanovsky OL (1998) Oct-1 promoter region contains octamer sites and TAAT motifs recognized by Oct proteins. FEBS Lett 426:81–85

Pfeuffer I, Klein-Hessling S, Heinfling A, Chuvpilo S, Escher C, Brabletz T, Hentsch B, Schwarzenbach H, Matthias P, Serfling E (1994) Octamer factors exert a dual effect on the IL-2 and IL-4 promoters. J Immunol 153:5572–5585

Riss J, Laskov R (1999) Expression of novel alternatively spliced isoforms of the oct-1 transcription factor. Biochim Biophys Acta 1444:295–298

Ryan AK, Rosenfeld MG (1997) POU domain family values: flexibility, partnerships, and developmental codes. Genes Dev 11:1207–1225

Shah PC, Bertolino E, Singh H (1997) Using altered specificity Oct-1 and Oct-2 mutants to analyze the regulation of immunoglobulin gene transcription. EMBO J 16:7105–7117

Stepchenko AG (1992a) The nucleotide sequence of mouse OCT-1 cDNA. Nucleic Acids Res 20:1419

Stepchenko AG (1992b) Interaction of Oct-binding transcription factors with a large series of "noncanonical" oct sequences. Primary sequence of murine Oct-2B cDNA. Dokl Akad Nauk (Russia) 325:175–178

Stepchenko AG (1994) Noncanonical Oct sequences are targets for mouse Oct-2B transcription factor. FEBS Lett 337:175–178

Stepchenko AG, Luchina NN, Polanovsky OL (1997a) Conservative Val47 residue of POU homeodomain: role in DNA recognition. FEBS Lett 412:5–8

Stepchenko AG, Luchina NN, Pankratova EV (1997b) Cysteine 50 of the POU H domain determines the range of targets recognized by POU proteins. Nucleic Acids Res 25:2847–2853

Strom A-C, Forsberg M, Lillhager P, Westin G (1996) The transcription factors Sp1 and Oct-1 interact physically to regulate human U2 snRNA gene expression. Nucleic Acids Res 24:1981–1986

Strubin M, Newell JW, Matthias P (1995) OBF-1, a novel B cell-specific coactivator that stimulates immunoglobulin promoter activity through association with octamer-binding proteins. Cell 80:497–506

Sturm RA, Cassady JL, Das G, Romo A, Evans GA (1993) Chromosomal structure and expression of the human OTF1 locus encoding the Oct-1 protein. Genomics 16:333–341

Subramaniam N, Cairns W, Okret S (1998) Glucocorticoids repress transcription from a negative glucocorticoid response element recognized by two homeodomain-containing proteins, Pbx and Oct-1. J Biol Chem 273:23567–23574

Suzuki N, Peter W, Ciesiolka T, Gruss P, Scholer H (1993) Mouse Oct-1 contains a composite homeodomain of human Oct-1 and Oct-2. Nucleic Acids Res 21:245–252

Ullman KS, Flanagan WM, Edvards CA, Crabtree GR (1991) Activation of early gene expression in T lymphocytes by Oct-1 and an inducible protein, OAP40. Science 254:558–562

Veenstra GJC, van der Vliet PC, Destree OHJ (1997) POU domain transcription factors in embryonic development. Mol Biol Rep 24:139–155

Veenstra GJC, Peterson-Maduro J, Mathu MTh, van der Vliet PC, Destree OHJ (1998) Non-cell autonomous induction of apoptosis and loss of posterior structures by activation domain-specific interactions of Oct-1 in the *Xenopus* embryo. Cell Death Differ 5:774–784

Verrijzer CP, Van der Vliet PC (1993) POU domain transcription factors. Biochim Biophys Acta 1173:1–21

Verrijzer CP, Alkema MG, van Weperen WW, van Leeuwen HC, Strating MJJ, van der Vliet PC (1992) The DNA binding specificity of the bipartite POU domain and its subdomains. EMBO J 11:4993–5003

Witt O, Albig W, Doenecke D (1997) Transcriptional regulation of the human replacement histone gene H3.3B. FEBS Lett 408:255–260

Wu CD, Lai EJ, Huang N, Wen X (1997) Oct-1 and CCAAT/enhancer-binding protein (C/EBP) bind to overlapping elements within the interleukin-8 promoter. The role of Oct-1 as a transcriptional repressor. J Biol Chem 24:2396–2403