Proc. Natl. Acad. Sci. USA
Vol. 91, pp. 12530–12534, December 1994
Medical Sciences

Identification of the *TCL1* gene involved in T-cell malignancies

(chromosome 14q32.1/B-cell differentiation/lymphoid malignancies)

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Contributed by Max D. Cooper, September 21, 1994

ABSTRACT **The *TCL1* locus on chromosome 14q32.1 is frequently involved in chromosomal translocations and inversions with one of the T-cell receptor loci in human T-cell leukemias and lymphomas. The chromosome 14 region translocated or rearranged involves ≈350 kb of DNA at chromosome band 14q32.1. Within this region we have identified a gene coding for a 1.3-kb transcript, expressed only in restricted subsets of cells within the lymphoid lineage and expressed at high levels in leukemic cells carrying a t(14;14)(q11;q32) chromosome translocation or a inv(14)(q11;q32) chromosome inversion. The cognate cDNA sequence reveals an open reading frame of 342 nt encoding a protein of 14 kDa. The *TCL1* gene sequence, which, to our knowledge, shows no sequence homology with other human genes, is preferentially expressed early in T- and B-lymphocyte differentiation.**

Nonrandom chromosomal translocations are characteristic of most human hematopoetic malignancies (1). In B and T cells, chromosomal translocations and inversions often occur as a consequence of mistakes during the normal process of recombination of the genes for immunoglobulins or T-cell receptors (TCRs). These rearrangements juxtapose enhancer elements of the immunoglobulin or TCR genes to oncogenes whose expression is then deregulated (2). In the majority of the cases, the rearrangements observed in lymphoid malignancies occur between two different chromosomes. Rearrangements of the *TCL1* locus at chromosome 14q32.1 are unique, in that the other locus involved in these rearrangements, namely, the TCR α/δ locus, is also on chromosome 14 at subband q11 (3, 4). For this reason, the rearrangements observed cytogenetically are either chromosomal inversions, inv(14)(q11;q32), involving only one of the chromosomes 14 or translocations involving both chromosomes 14, such as the t(14;14)(q11;q32) or, more rarely, the t(7;14)(q35;q32) involving the TCRβ locus at 7q35 (4). These abnormalities are associated with postthymic types of T-cell leukemias, such as T-prolymphocytic leukemia (T-PLL) (5) and acute or chronic T-cell leukemias developing in patients with ataxia telangectasia (6, 7). Several of the breakpoints at 14q32.1 involved in these translocations have been cloned and characterized, but the putative *TCL1* oncogene had not been identified (6, 8–10).

We have recently cloned the entire *TCL1* locus, a chromosomal region of ≈350 kb, as determined by placement of translocation breakpoints on the long-range genomic map (11). The involvement of such a large region suggests that activation of the putative *TCL1* gene can occur from a distance of many kilobases, as previously observed for the *BCL1/CCND1* gene in mantle-cell lymphoma (12–15) and the *MYC* oncogene in Burkitt lymphoma (16, 17) and in acute T-cell leukemia (18). It also became evident from the mapping studies that the breakpoints of the different rearrangements segregate in two clusters; inversions on the centromeric side and simple balanced translocations on the telomeric side (see Fig. 1). We thus postulated that if the target gene activated by these different types of chromosomal rearrangements is the same, the gene must reside between the two clusters of breakpoints in a region of ≈160 kb. We have used two approaches to search for the elusive *TCL1* gene: exon trapping and Northern blot hybridization with unique probes derived from genomic clones adjacent to CG-rich regions. In this report we describe the isolation and characterization of the *TCL1* gene‖ and its preferential expression early in both the T- and B-lymphocyte differentiation pathways.

METHODS

Isolation of Unique Probes. DNA of P1 clones 7-4 and 20-21 were doubly digested, the former with *Cla* I and *Eco*RI and the latter with *Sal* I and *Eco*RI or with *Eag* I and *Hin*dIII, and subcloned in pBSII (Stratagene). DNA of the positive subclones was prepared by standard minipreparation method (19). Repeat-free DNA fragments were identified by Southern blot hybridization with human cot-1 DNA (20).

Exon Trapping. The pE53 vector was kindly provided by M. Ohta (Jefferson Cancer Institute); it is a reproduction of the pMHC2 vector (21). It contains a portion of p53 exon 10, intron 10, and a portion of exon 11; a unique *Bgl* II site is present in intron 10 for cloning. DNA of P1 clones 7-4 and 20-21 (each at 1 μg) was partially digested with *Sau*3A. The digested DNA of between 0.5 and 5 kb was isolated and cloned into the *Bgl* II site of pE53. Cloned DNA, 5–10 μg, was transfected into semiconfluent COS-7 cells by using Lipofectase (BRL). After 30 h, total RNA was isolated as described by Buckler *et al.* (22). Amplification of total RNA by reverse transcription–PCR (RT–PCR) was carried out with primers and procedures described by Hamaguchi *et al.* (21).

Isolation of *TCL1* cDNA. A cDNA library was constructed with a commercial kit for λ Zap cDNA synthesis (Stratagene). The ligation was packaged with Gigapak II Gold packaging extract (Stratagene). cDNA libraries constructed from the cell lines ALL1 and 697 were kindly donated by T. Nakamura and A. ar-Rushdi, respectively (Jefferson Cancer Institute). The libraries were plated and screened with standard protocols (20).

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Abbreviations: TCR, T-cell receptor; T-PLL, T-prolymphocytic leukemia; PBL, peripheral blood leukemia; PHA, phytohemagglutinin; ORF, open reading frame; RT–PCR, reverse transcription–PCR.

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‖The sequence reported in this paper has been deposited in the GenBank data base (accession no. X82240).

Prokaryotic Expression. p697 cDNA was digested with *Nco* I and *Eco*RI, and the 5′ protruding ends were filled-in with the Klenow fragment of DNA polymerase I (19). The purified DNA fragment was ligated to pQE30 (Qiagen, Chatsworth, CA) previously digested with *Bam*HI and blunted with the Klenow polymerase. Positives clones were selected and the presence of a continuous open reading frame (ORF) between the vector ATG and the cDNA ATG was confirmed by sequence analysis. Induction of expression of the cloned sequences and purification of the recombinant peptide were carried out according to Qiagen.

***In Vitro* Translation.** A plasmid, pALL1, containing full-length *TCL1* cDNA was linearized by digestion with *Cla* I and transcribed and translated *in vitro* using the TNT Coupled Reticulocyte Lysate system (Promega).

RT-PCR. First-strand DNA synthesis was performed using 1 μg of total RNA with either Moloney murine leukemia virus (BRL) or avian myeloblastosis virus or Superscript (BRL) reverse transcriptase and respective reaction buffers with either oligo(dT) or random primers; 10% of the reaction mixture was subsequently used for each single PCR amplification. Amplification of DNA from isolated populations of bone marrow B cells, T-cell lines, peripheral blood lymphocytes (PBLs), phytohemagglutinin (PHA)-stimulated PBLs, and thymus cells was carried out with *TCL1* primers p9A (TGCTGCCAGATGACTGATGT) and RevIII (CAAATGGAATCCTCCTTGGC), under the following conditions: denaturing 1 min at 94°C, annealing 1 min at 58°C, and elongation 1 min at 72°C for a total 30 cycles. Amplification of DNA from patients with T-PLL was carried out with *TCL1* primers Daudi uni1 (AGGCCTATGACCCCCACC) and Daudi rev2 (CATTCCTCCCAGACCCCA), under the same conditions as above, except for the annealing temperature, which was 60°C. The PCR internal standard used primers specific for the β-actin gene were used: A1 (TCATCACCATTGGCAATGAG) and A2 (CAGTGTGTTGGCGTACAGGT). These primers were used under the same conditions as the *TCL1* primers.

Isolation of $CD34^+CD19^+$ Cells by Immunofluorescence Cell Sorting. Bone marrow cells were obtained from 18- to 22-week aborted fetuses in accordance with policies established by an institutional review board. Mononuclear bone marrow cells were then isolated by centrifugation of cell suspensions over a Ficoll/Hypaque gradient (23). The monoclonal antibodies used for cell surface analysis included anti-human Leu-12, which recognizes the pan-B cell antigen CD19, anti-human HPCA-2, which detects the early stem cell marker CD34 (Becton Dickinson), and goat anti-human IgM (Southern Biotechnology Associates). For two-color surface analysis for cell sorting, viable FBM cells were incubated with fluorescein isothiocyanate-conjugated anti-CD34 antibodies or goat anti-human IgM for 15 min on ice, washed with PBS containing 2% (vol/vol) HIFCS, and counterstained with phycoerythrin-conjugated monoclonal antibody specific for CD19. Subpopulations of lymphocytes were sorted according to immunofluorescence and light scatter characteristics with a FACStar instrument (Becton Dickinson). The lymphocyte subpopulations collected were $CD34^+CD19^-$, $CD34^+CD19^+$, $CD19^{lo}\mu^-$, $CD19^{hi}\mu^-$, $CD19^+\mu^{lo}$, and $CD19^+\mu^{hi}$. Cells were collected and counted, and total RNA was extracted using Tri-Reagent (Molecular Research Center).

Cell Lines and Lymphocytes. The majority of the cell lines were obtained from American Type Culture Collection. SupT11 is a cell line derived from patient NL (24). Peripheral lymphocytes were isolated from whole blood by centrifugation on a Ficoll/Hypaque gradient, followed by a 1-h adherence to Petri dishes to remove the monocytes. Stimulation with PHA was carried at a final concentration of 0.1% for 3 days. Patients 62 and 312 presented with T-PLL involving an inversion of chromosome 14, inv(14)(q11;q32.1).

RESULTS

Cloning of the *TCL1* Gene. The search for the *TCL1* gene was focused on the region included between the two sets of breakpoints of ≈160 kb and encompassed by the P1 clones 7-4 and 20-21 (11), as illustrated in Fig. 1. To identify transcribed sequences, the area surrounding restriction sites of rare cutter enzymes in these two P1 clones was subcloned and unique probes were isolated. The recognition sites of rare cutting enzymes (such as *Mlu* I, *Nru* I, and *Not* I), rich in CG

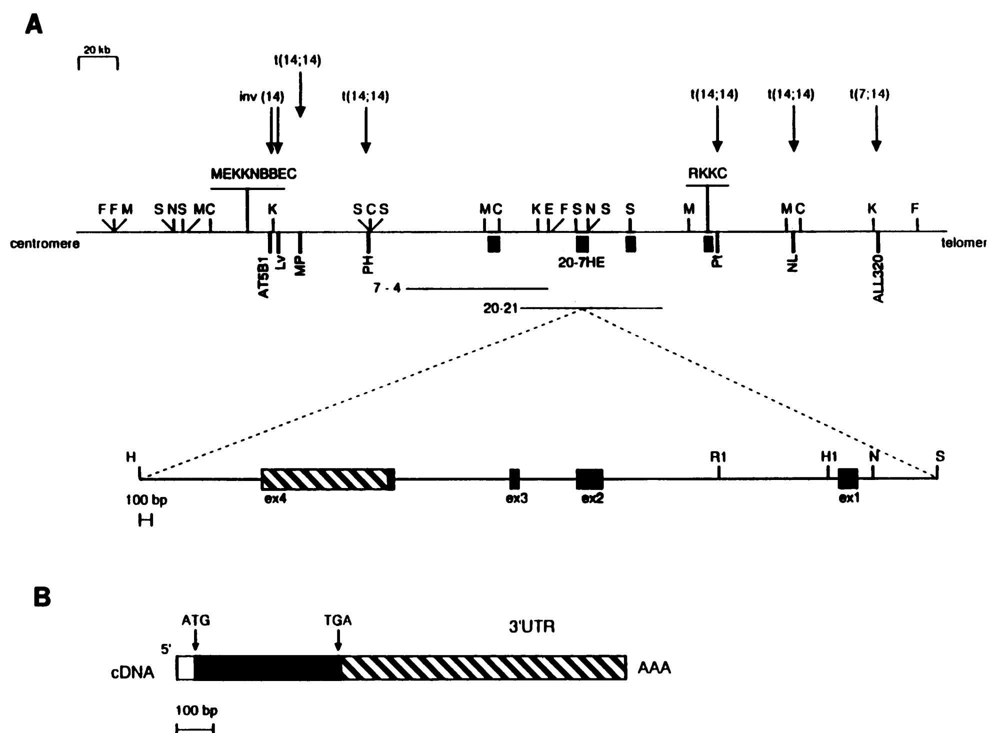

FIG. 1. Genomic and cDNA organization of the *TCL1* gene. (*A*) Genomic organization of the *TCL1* locus on chromosome 14q32.1. Vertical bars refers to cloned breakpoints in the literature [see Virgilio *et al.* (11) for references]. Restriction sites are given for *Bss*HII (B), *Cla* I (C), *Eag* I (E), *Sfi* I (F), *Ksp* I (K), *Mlu* I (M), *Not* I (N), *Nru* I (R), *Eco*RI (R1), *Sal* I (S), *Hin*dIII (H), and *Bam*HI (H1). P1 clones 7-4 and 20-21, covering the 140-kb region between the two clusters of cloned breakpoints, are shown by horizontal bars. Solid boxes represent probes used for RNA screening. A *Sal* I–*Hin*dIII genomic fragment with the organization of the four exons of the *TCL1* gene is enlarged. (*B*) *TCL1* cDNA structure. An open box represents 5′ untranslated region; a solid box represents encoding sequence, and a hatched box represents the 3′ untranslated region.

content, may indicate the existence of a CpG island; such CpG islands are often found in the proximity of transcribed genes (25). Four probes were generated in this way, 7-4CE, 20-7SE, 20-7HE, and 9-1KK (see Fig. 1), and hybridized to Northern blots containing RNAs from lymphoid and myelogenous cell lines. Only the probe 20-7HE, derived from sequences adjacent to a *Not* I site (Fig. 1), detected a transcript in the RNA from hematopoetic cell lines. This transcript ≈1.3 kb was clearly visible in the pre-B acute lymphoblastic leukemia cell line ALL380 and in the endemic Burkitt lymphoma cell line Daudi (Fig. 2). Three cDNA libraries, constructed from RNA from a endemic Burkitt lymphoma cell line (Daudi) and two pre-B-cell lines (697 and ALL1), all of which expressed high levels of the 1.3-kb transcript, were screened with the 20-7HE probe, and positive clones were obtained from each library. These clones were designated pAlDaudi, pAI1.5, and p697.

In a parallel effort to identify transcripts, the P1 clones 20-21 and 7-4 were partially digested with *Sau*3A and cloned into an exon-trapping vector containing exon 10, intron 10, and exon 11 of the p53 gene. Several putative exons were isolated, but the majority were due to aberrant splicing at cryptic splicing sites. Some trapped DNA fragments contained *Alu* repeat sequences and one had high homology to transposon-like sequences. However, the sequence of one of the trapped fragments matched the sequence of the cDNA isolated from the 697 and ALL1 libraries and was later found to correspond to exon 3 of the gene.

Sequence Analysis of cDNA Clones. All three cDNA clones were entirely sequenced and the complete sequence of pAI1.5 is shown in Fig. 3. Upon sequence comparison, pAI1.5 and p697 cDNAs were found to be identical, except for a base-pair substitution at position 404 where a cytidine in pAI1.5 is a thymidine in p697 cDNA. pAlDaudi is incomplete at the 5′ end, missing the first 88 nt, and additionally showed two small internal deletions: the pentamer ATGGT at position 394 and the octamer CTGCCCTT at position 707 (Fig. 3). All three clones of cDNA had 3′ untranslated regions of slightly different length; pAI1.5 contains the longest one with the presence of a consensus polyadenylylation signal at position 1293.

Sequence analysis of the isolated cDNAs showed the presence of two long ORFs. Frame 1 contains an ORF of 342 nt with a starting ATG codon at position 46, located within a perfect Kozak consensus sequence, and with a stop codon at position 388 (Fig. 3). This ORF potentially encodes for a protein of 114 amino acids with a predicted molecular mass of 13.5 kDa. Frame 2 contains an ORF with a starting ATG codon at position 383 and a stop codon at position 773, to give a putative protein of 14.5 kDa. However, the presence of a point mutation in this second ORF, a deletion in two of the three independently isolated cDNA clones, and the position of this ORF on only the last exon led us to believe that the second ORF is not translated.

To confirm the presence of an ORF and its ability to encode a protein, the entire cDNA was subcloned into the prokaryotic expression vector pQE30. Fig. 4 shows the specific induction of a 14-kDa protein and the protein after purification. These results were also confirmed by *in vitro* translation (data not shown). To study the genomic structure of the gene,

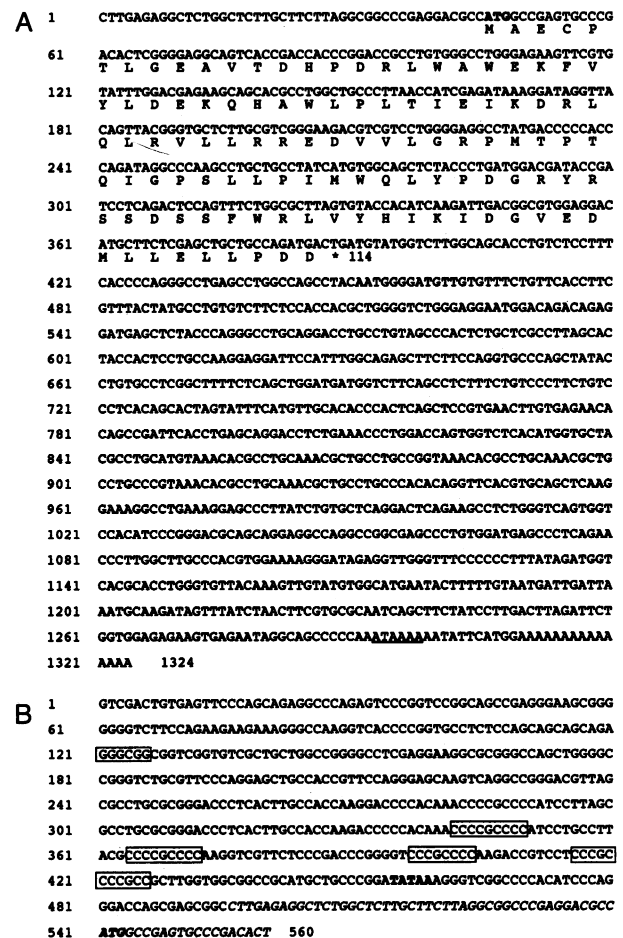

FIG. 3. cDNA sequence and 5′ genomic sequence of *TCL1*. (*A*) cDNA sequence of *TCL1*. The initiation codon ATG is shown in boldface type, and the polyadenylylation signal is underlined. (*B*) Genomic sequence 5′ to the cDNA. SP1 binding sites are boxed, the TATA box and the start codon are in boldface type, and the cDNA sequences are in italic type.

a *Sal* I–*Hin*dIII fragment, containing the entire cDNA, was subcloned and sequenced. The map and the structure of the gene are shown in Fig. 1: the gene is composed of four small exons with a 3′ untranslated region of ≈800 nt. The sequence immediately 5′ to the cDNA showed the presence of five binding sites for the SP1 transcription factor and a TATA box at position −41 (Fig. 3*B*); these data confirm that we have isolated the complete cDNA.

Expression of the *TCL1* Gene in T-Cell Leukemia. To determine whether the isolated gene is deregulated in cells with the t(14;14)(q11;q32) translocation, we carried out a Northern blot analysis comparing the amount of *TCL1* transcript present in resting PBLs, PHA-activated PBLs, SupT11 cells [a cell line established from a patient with acute T-lymphocytic leukemia with a t(14;14) chromosomal translocation (10, 25)], and a variety of human cell lines derived from T-cell leukemias (Table 1).

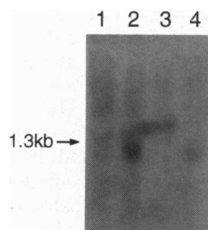

FIG. 2. Northern blot hybridization with probe 20-7HE. Each lane contains 11 μg of total RNA from the following cell lines. Lanes: 1, HeLa; 2, Daudi; 3, K562; 4, All380.

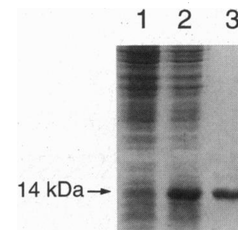

FIG. 4. Prokaryotic expression of the *TCL1* gene product. SDS/PAGE of bacterial lysates with pQEtcl-1. Lanes: 1, uninduced; 2, induced; 3, purified.

We detected high levels of expression in SupT11 cells (Fig. 5*A*). No expression was detectable in several other tumor-derived T-cell lines lacking the *TCL1* translocation, such as MOLT-4, HUT 78, Jurkat, and SupT1 cells (Fig. 5*B* and Table 1). These results were also confirmed by the sensitive assay of RT–PCR as shown in Fig. 5*C*. Of interest is the fact that SupT1 cells carry an inverted chromosome 14, inv14 (q11;q32), in which the TCRα locus is not juxtaposed to the *TCL1* but is positioned in front of the immunoglobulin heavy chain locus at 14q32.3 (26, 27). Thus an inversion of chromosome 14 that does not involve the *TCL1* locus is unable to deregulate the *TCL1* gene. Furthermore, we performed a semiquantitative RT–PCR analysis on cells from two patients with T-PLL carrying an inversion of chromosome 14, inv(14)(q11;q32). Both showed high expression levels of the *TCL1* gene, comparable to those observed in the SupT11 cell line (Fig. 6).

Expression of the *TCL1* Gene in Tumors and Normal Human Tissues. A large number of RNAs from tumor cell lines, both of lymphoid and nonlymphoid origin, were screened to study the pattern of expression of the *TCL1* gene. The results summarized in Table 1 reveal that the *TCL1* gene is expressed at high levels in pre-B cells and in endemic Burkitt lymphoma cells, which express cell surface IgM and do not secrete immunoglobulin (28), but is not expressed in sporadic Burkitt

Table 1. Expression of TCL1 mRNA in cell lines

Cell line	Tumor	Translocation	RNA
RS(4;11)	ALL	t(4;11)	–
MV(4;11)	ALL	t(4;11)	–
B1	ALL	t(4;11)	–
ALL380	ALL	t(8;14), t(14;18)	+
ALL-1	ALL	t(9;22)	+
BV173	ALL	t(9;22)	+
RPMI 8866	B-lymphoblastoid	NA	–
GM1500	B-lymphoblastoid	Normal	–
RPMI 8226	Myeloma	Multiple rearrangements	–
U226	Myeloma	Multiple rearrangements	–
P3HR-1	Endemic Burkitt	t(8;14)	+
AKUA	Endemic Burkitt	t(8;14)	+
Daudi	Endemic Burkitt	t(8;14)	+
SKDHL	Sporadic Burkitt	t(8;14)	–
BL 2	Sporadic Burkitt	t(8;22)	–
RS 11846	High-grade B-cell lymphoma	t(14;18), t(8;22)	+
K562	CML	t(9;22)	–
PEER	T-ALL	Multiple rearrangements	–
Jurkat	T-ALL	Multiple rearrangements	–
MOLT-4	T-ALL	t(7;7), 6q-	–
CEM	T-ALL	Multiple rearrangements	–
Sup T1	T-ALL	inv(14)(q11;q32.3)	–
SupT11	T-ALL	t(14;14)(q11;q32.1)	+
HUT 78	T-Sezary Syndrome	NA	–
HL60	AML	Multiple rearrangements	–
KG-1a	AML	Multiple rearrangements	–
U937	Histiocytic lymphoma	Multiple rearrangements	–
I32	Retinoblastoma	Multiple rearrangements	–
MGC	Gastric carcinoma	Multiple rearrangements	–
KATO	Gastric carcinoma	Multiple rearrangements	–
SW 48	Colorectal carcinoma	Multiple rearrangements	–
LNCap	Prostate carcinoma	Multiple rearrangements	–
PC3	Prostate carcinoma	Multiple rearrangements	–
T98G	Glioblastoma	Multiple rearrangements	–

Cell lines with multiple rearrangements do not have translocations or rearrangements at 14q32.1. NA, not done; ALL, acute lymphocytic leukemia; CML, chronic myeloid leukemia; T-ALL, acute T-lymphocytic leukemia; AML, acute myeloid leukemia.

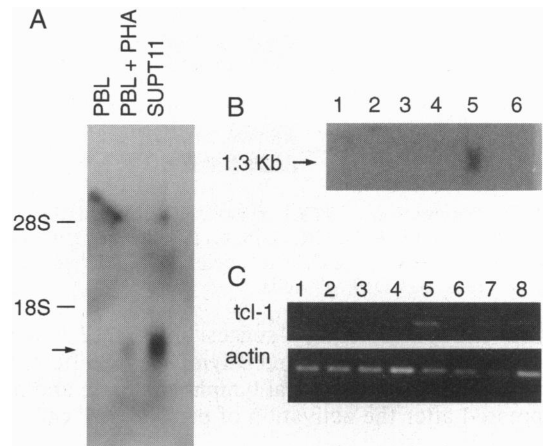

FIG. 5. Expression of *TCL1* in various T cells. (*A*) Northern blot hybridization of stimulated and nonstimulated PBLs with a *TCL1* probe, p697; 11 μg of RNA was loaded per lane. (*B*) Northern blot of RNA from T-cell lines. Lanes: 1, CEM; 2, MOLT-4; 3, HUT 78; 4, SupT1; 5, SupT11; 6, Jurkat. (*C*) RT–PCR with *TCL1* primers, p9A and RevIII, and with actin-specific primers, Actin1 and Actin2. Lanes: 1, CEM cells; 2, HUT 78 cells; 3, MOLT-4 cells; 4, SupT1 cells; 5, SupT11 cells; 6, PBLs; 7, PHA-activated PBLs; 8, fetal thymus cells.

lymphomas, which secrete immunoglobulin. This pattern of B-lineage expression is illustrated by the presence of *TCL1* transcripts in 697, ALL-1, and BV173 cell lines, all with a pre-B-cell phenotype, and by its absence in the pro-B lines and in B-lymphoblastoid cell lines, such as GM1500 and RPMI 8866.

Expression of the *TCL1* gene was evaluated at different stages of normal B-cell differentiation. Fetal bone marrow B-cell subpopulations were isolated by flow cytometry, cDNAs were prepared, and PCR was carried out with a primer from exon 3, p9A, and a primer from the 3′ untranslated region, RevIII, to give a fragment of 270 bp (Fig. 7). No signal is present in the $CD34^+CD19^-$ stem-cell-rich fraction; weak expression appears in the $CD34^+CD19^+$ subpopulation of pro-B cells, and expression peaks in IgM-negative pre-B cells expressing high levels of CD19. *TCL1* expression persists in immature IgM^+ B cells (Fig. 7) in the fetal bone marrow. *TCL1* transcripts were also detected in fetal thymocytes (Fig. 5*C*), but not in T cells in the circulation, unless these were activated *in vitro* (Fig. 5 *A* and *C*). When the fetal thymocytes were sorted into subpopulations, *TCL1* transcripts were detected in the progenitor subpopulation of $CD4^-CD8^-CD3^-$ thymocytes, but not in the cortical population ($CD4^+CD8^+$) (data not shown).

No expression of *TCL1* was observed in myelogenous cell lines or in cell lines derived from gastric (MCG, KATO), mammary (MCF7), prostate (LNCap, PC3), and colorectal (SW48) carcinomas (Table 1). No expression of this gene was observed in polyadenylylated RNA isolated from a variety of normal human tissues including heart, brain, placenta, lung, liver, skeletal muscle, kidney, and pancreas (data not

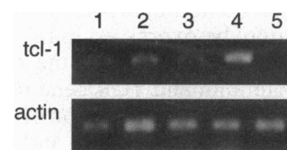

FIG. 6. Expression of *TCL1* in two patients with T-PLL. RNA (≈5 ng) isolated from patients with leukemia was used for cDNA synthesis, followed by amplification with *TCL1* primers, Daudi uni1 and Daudi rev2. Lanes: 1, Daudi; 2, SupT11; 3, patient 312; 4, patient 62; 5, Jurkat.

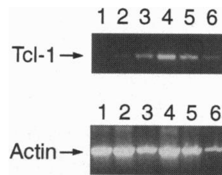

FIG. 7. Expression of *TCL1* in isolated subpopulation of bone marrow B cells by RT–PCR. Lanes: 1, $CD34^+CD19^-$ cells; 2, $CD34^+CD19^+$ cells; 3, $CD19^{lo}\mu^-$ cells; 4, $CD19^{hi}\mu^-$ cells; 5, $CD19^+\mu^{lo}$ cells; 6, $CD19^+\mu^{hi}$ cells.

shown). Thus, these results suggest that *TCL1* is constitutively expressed early in T- and B-lymphocyte differentiation within their respective central lymphoid tissues and may be reexpressed after the activation of peripheral T cells.

DISCUSSION

The *TCL1* gene is located in a chromosomal region banded by two clusters of breakpoints. In its strategic position, between the two clusters of breakpoints, the *TCL1* gene becomes juxtaposed to TCR-Cα/δ regulatory elements in both types of rearrangements involving 14q32.1. For inversions, the *TCL1* gene is telomeric to the 14q32.1 break; hence, the central part of the chromosome between q11 and q32 has flipped upside down and Cα/δ has been positioned centromeric and in proximity to the *TCL1* gene; the same holds true for translocations with inverted duplication. For simple translocations, the gene is centromeric to the breaks and does not move during the rearrangement. In this case the break on the other chromosome 14 occurs in TCR α/δ locus that moves to a region telomeric to the *TCL1* gene. In this model of activation the *TCL1* gene is activated by the control elements of the TCR gene, whether they are positioned 5′ of the *TCL1* gene, as for translocations, or 3′ to *TCL1*, as for inversions. A similar situation has been observed in Burkitt lymphomas, where the immunoglobulin enhancers can be located upstream or downstream to the *MYC* oncogene (16, 18, 29, 30). Similarly, immunoglobulin enhancers are found downstream to the *BCL2* gene in follicular lymphomas (31, 32) and upstream to the *BCL2* gene in B-cell chronic lymphocytic leukemia (33).

The study of a variety of cell lines for the expression of the *TCL1* gene indicates that it is expressed preferentially in cells of lymphoid lineage. Constitutive expression of *TCL1* begins in normal B-lineage cells as early as the $CD34^+CD19^+$ pro-B-cell stage. Its expression peaks in pre-B cells, which express high levels of CD19 but no cell surface IgM, and its expression persists in immature IgM^+ cells in the bone marrow. In contrast, mature B cells in the periphery do not express *TCL1*. These findings parallel the results obtained with the lymphoid cell lines where pro-B-cell lines with the t(4;11) chromosome translocation failed to express *TCL1*, while pre-B-cell lines expressed *TCL1* transcripts. A similar pattern of *TCL1* expression is noted for early T-lineage cells. Immature thymocytes, including the intermediate $CD4^+/CD8^+$ population, express *TCL1* transcripts, whereas mature T cells in circulation do not, unless they are activated, when *TCL1* transcripts may be expressed in relatively low levels. These data suggest that expression of the *TCL1* gene may be linked to immunoglobulin and TCR gene rearrangement and expression. The high level of expression of *TCL1* in leukemic T cells with the t(14;14) translocation and the inv(14) inversion, but not in leukemic T-cell lines with other types of chromosomal rearrangements, strongly supports the conclusion that this gene becomes deregulated as a consequence of its juxtaposition to the α/δ TCR locus.

We thank K. Gripp for providing patient samples, A. ar-Rushdi and T. Nakamura for contributing cDNA libraries, D. Rasio for technical support, and S. Smith for providing the cell line Supt11. We are also grateful to H. Alder for automated DNA sequencing. We also thank K. Huebner and P. Burrows for critically reading the manuscript. This work was partially supported by National Institutes of Health Grant CA39860 to C.M.C. M.D.C. is a Howard Hughes Medical Institute Investigator and L.G.B. is a fellow of the Cancer Research Institute.

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