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Analysis of cDNA clones specific for human T cells and the α and β chains of the T-cell receptor heterodimer from a human T-cell line

(somatic rearrangement/immunoglobulin/major histocompatibility complex/antigen recognition/leukemia)

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ABSTRACT **We report the isolation and characterization of 19 classes of nonrearranging T cell-specific cDNA clones and two cDNA clones encoding the α and β chains of the T-cell antigen receptor from a human T-cell line, Jurkat. Results indicate that the human α-chain gene, like its β-chain counterpart, undergoes somatic rearrangement in T cells. In addition, it shows sequence homology to its β-chain counterpart and immunoglobulin, indicating that the human α chain is also a member of the immunoglobulin supergene family. Sequence comparison suggests that the α chain also may be composed of variable (*V*), diversity (*D*), joining (*J*), and constant (*C*) region gene segments. The protein deduced from the cDNA sequence has a molecular weight of 29,995 and possesses six potential N-glycosylation sites. The availability of α- and β-chain genes of the T-cell receptor from the same T-cell line provides tools to study their possible roles in recognition of antigens and major histocompatibility complex products by the human T-cell receptor.**

Antigen recognition by T lymphocytes is mediated by the T-cell antigen receptor composed of an α- and β-chain heterodimer situated on the surface of these immunocompetent cells (1–3). About a year ago, we (4) and Hedrick *et al.* (5) cloned cDNAs that specified, respectively, the β chain of the human and mouse T-cell receptor (6). Subsequent studies have indicated that the genes encoding these structures undergo somatic rearrangement in T lymphocytes (7) and are homologous to the Ig genes (8). In addition, their genomic structures are similar, but not identical in organization, to Ig genes (9–13). These results indicate that genes encoding the T-cell receptor, at least the β-chain gene, are different from Ig genes, though they most likely share a common ancestor (8). The finding that the human β-chain variable (V) and constant (C) region genes (*V* and *C*) are located on chromosome 7 (14), where there are no Ig genes, confirmed that these genes are independent of Ig genes. These observations, coupled with the fact that α and β chains are approximately the same size, suggest that the α chain is probably also Ig-related and may contain similar V and C domains (8).

In this manuscript, we report the analysis of a number of human T-cell-specific cDNA clones and describe the characterization and sequence of a human T-cell clone with homology to the α chain of the human T-cell antigen receptor. The results reveal that, like the β-chain genes of the T-cell receptor (4, 5), the α-chain genes are homologous to Ig genes and undergo somatic rearrangement in T cells. While these studies were in progress, isolation of the murine α-chain cDNA (15, 16) and partial protein sequence of the human α chain (17, 18) were reported. The elucidation of the α and β chains of the T-cell receptor should provide the molecular tools necessary for the study of the recognition of antigens and major histocompatibility complex products by human T cells.

MATERIALS AND METHODS

Cells. Jurkat cell line was first isolated by Schneider *et al.* (19). All other cell lines used in these experiments have been described in our previous reports (4, 20).

Construction of cDNA Libraries. Double-stranded (ds) cDNA was generated from poly(A)$^+$ RNA of a human leukemic T-cell line, Jurkat, by using the approach described previously (4). For the subtracted library, ds cDNA was tailed by using dCTP and terminal deoxynucleotidyltransferase and inserted into the *Pst* I site of plasmid pBR322. Also *Eco*RI linkers were ligated to the ds DNA and then joined to the λgt10 phage arms. The resulting λgt10–cDNA hybrids were then packaged *in vitro* and plated onto *E. coli* strain C600 as described (21).

Cloning of T Cell-Specific cDNAs. cDNA copied from poly(A)$^+$ RNA from Jurkat was hydrolyzed in 0.1 M NaOH to remove poly(A)$^+$ RNA templates and hybridized to excess poly(A)$^+$ RNA from a B-cell line, RPMI 1788. Hybridization was carried out in 50% formamide containing 5× NaCl/Cit (1× NaCl/Cit = 0.15 M NaCl/0.015 M Na citrate, pH 7) at 42°C to C_rt of >2000; ds cDNA was then separated from the unhybridized single-stranded (ss) T-cell "enriched" cDNA with hydroxylapatite columns as described by Britten *et al.* (22). These ss cDNAs were used to construct a T-cell "enriched" cDNA library as described above.

Blot-Hybridization Analysis. Blot-hybridization analysis of T-cell and non-T-cell RNA was carried out by the procedure of Thomas (23). RNA was extracted from different cells in the presence of guanidine thiocyanate. Poly(A)$^+$ was isolated by using an oligo(dT)-cellulose column and then treated with glyoxal. Poly(A)$^+$ RNA (2 μg) was electrophoresed through 1% agarose in 10 mM sodium phosphate buffer (pH 7.0). Transfer of the RNA to nitrocellulose membrane was carried out as described (23).

Southern Blot Analysis. Southern blot analysis with T cell-specific cDNAs or the T-cell antigen receptor α-chain cDNA was performed as described (24). In short, DNA was extracted from T cells or non-T-cells and digested overnight with 10 units of restriction enzyme per μg of DNA. DNA (10 μg) was electrophoresed through 0.8% agarose and transferred to nitrocellulose filters as described by Southern (24). Hybridization to [^{32}P]dCTP-labeled nick-translated DNA fragments was as described (7).

DNA Sequencing. For DNA sequencing, the λgt10.Y14 recombinant was digested with *Eco*RI, and the cDNA insert

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Abbreviations: V, variable; C, constant; D, diversity; J, joining; kb, kilobase(s); ds, double-stranded; ss, single-stranded; ALL, acute lymphoblastic leukemia.

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was purified twice by electrophoresis through 1% low-melting-point agarose and then further digested with *Taq* I, *Hpa* II, or *Sau*3A1. *Taq* I fragments were ligated into the *Acc* I site of phage M13 mp9 or the *Eco*RI–*Acc* I site of M13 mp10, *Hpa* II fragments were ligated into the *Acc* I site of M13 mp9, and *Sau*3A1 fragments were ligated into the *Bam*HI site of M13 mp9. DNA sequencing was performed by using the dideoxy chain-terminating inhibitor method of Sanger *et al.* (25, 26).

RESULTS

Nonrearranging T Cell-Specific cDNA Clones from the Human Leukemic T-Cell Line Jurkat. T cell-specific cDNAs were obtained by the subtraction method combined with differential hybridization as described (4). These T cell-specific clones were then grouped into 19 different groups on the basis of their cross-hybridization to each other and the sizes of messages to which they correspond in T cells or thymocytes. In addition, these clones were analyzed to examine whether they undergo somatic rearrangement in DNA from T cells (leukemic cells) when compared to the corresponding germ-line DNA (normal bone marrow cells from the same patient). With restriction enzymes *Bam*HI, *Eco*RI, and *Hin*dIII, Southern blot analysis did not show any gene rearrangement for these T cell-specific clones. Some of the messages from which these clones were derived also could be found in thymocytes, while others were found only in Jurkat. Some examples of these studies are illustrated in Fig. 1. Fig. 1 *Upper* shows the result of blot-hybridization analysis with pY4, pY17, and pY25 as probes. Whereas mRNA homologous to pY17 could be found only in Jurkat cells, messages corresponding to pY4 and pY25 could be found in both Jurkat cells and thymocytes. An example of Southern blot analysis of these T cell-specific clones is shown in Fig. 1 *Lower*. This figure indicates that, with restriction enzymes *Bam*HI, *Hin*dIII, and *Eco*RI, no rearrangement could be detected for pY25. Table 1 summarizes the results of these analyses.

Expression of Clone pY14. In addition to the nonrearranging T cell-specific cDNAs described above, T-cell receptor β- and α-chain cDNAs also were isolated from a T-cell (Jurkat) cDNA library. With the use of DNA sequence information (20), 20 β-chain cDNAs were identified among the T cell-specific clones. With oligonucleotide probes corresponding to the mouse α chain (15, 16), the positive human clone, pY14, was also confirmed. The expression of clone pY14 is illustrated in Fig. 2. RNA was prepared from cells of T-cell lineage as well as non-T-cell lineages. Blot-hybridization analysis indicated that the human thymocytes from two individuals, blast cells from a patient with T-cell leukemia, and two of the three leukemic T-cell lines (Jurkat and HPB-ALL; ALL is acute lymphoblastic leukemia) expressed a message of $\approx$1.6 kilobases (kb), corresponding to the pY14 sequence. In addition, a shorter message of about 1.3 kb was observed in HBP-ALL cells. This short message also could be detected in lower amounts in B-cell line RPMI 1788. However, pY14 failed to hybridize with RNA from a leukemic T-cell line (CEM), a erythroleukemia line (data not shown), and a bladder tumor line (MGHU-1) (data not shown). To examine whether the expression of these messages, especially the 1.3-kb message in B-cell lines, may be due to the expression of sequences homologous to the V and/or C region of the cDNA pY14, RNA was examined with a 5′-end (*Eco*RI–*Sau*3A fragment, nucleotides 1–529 in Fig. 4) and a 3′-end (*Hpa* II–*Hpa* II fragment, nucleotides 591–980) probe of the cDNA. Fig. 2*b* shows that all T cells, except for a leukemic T-cell line, CEM, contain messages homologous to the 3′ end of pY14 (C region; see below). In addition, a shorter message of about 1.3 kb of B-cell lines was found to hybridize with the 3′-end probe. However, when the 5′-end probe was used (V region, see below), hybridization was observed only toT-cell line Jurkat and thymocytes (Fig. 2*c*). Hybridization of two thymocytes samples was considerably weaker for the 5′-end probe than for the complete cDNA probe or the 3′-end probe. No hybridization was observed to other T- or B-cell RNAs.

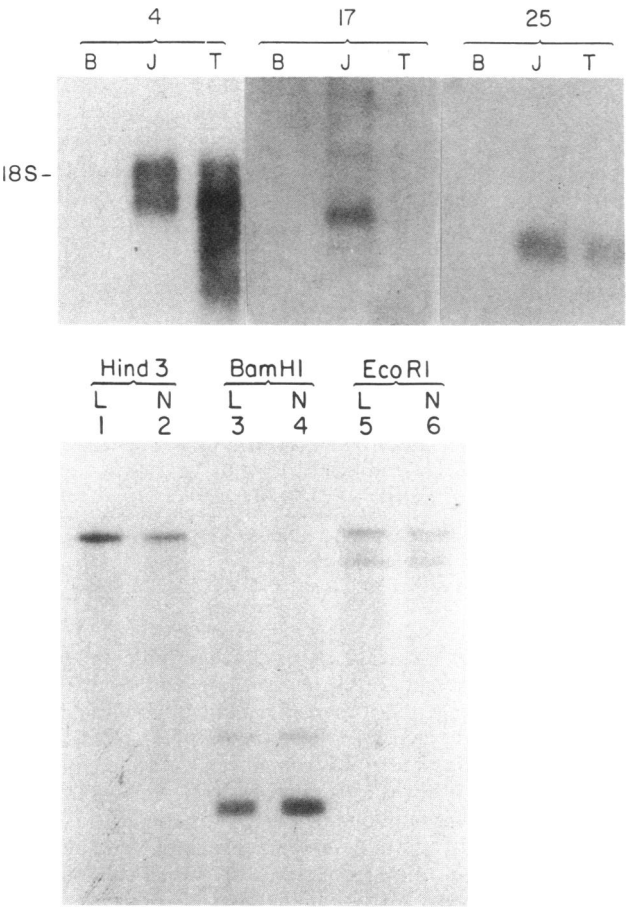

FIG. 1. Blot-hybridization and Southern gel analysis of nonrearranging cDNA clones pY4, pY17, and pY25. (*Upper*) Poly(A)$^+$ RNA from B-cell line RPMI 1788, T-cell line Jurkat, and thymocytes was analyzed by blot hybridization gel analysis using cDNA inserts from clones pY4, pY17, and pY25. Lanes: B, B cells; J, Jurkat cells; T, thymocytes. (*Lower*) DNA was extracted from T-cell leukemia blast cells and fibroblast cultures from the same patient. DNA was digested with *Bam*HI, *Hin*dIII, or *Eco*RI and analyzed with a cDNA insert from clone pY25. Lanes: L, leukemic blasts; N, normal fibroblasts.

Somatic Rearrangement of pY14 in T Cells. In order to determine the germ-line organization of the genes corresponding to pY14 and whether they undergo rearrangement in T cells, DNA from 15 T cells and four non-T-cells was digested with restriction enzymes *Eco*RI, *Bam*HI, *Hin*dIII, *Bgl* II, *Pvu* II, and *Xho* I. The digested DNA was examined by Southern gel analysis using the complete insert of pY14 as a probe (Fig. 3). Although no difference in banding patterns was found in all of the non-T-cell samples examined, different but varied banding patterns were observed in DNA from several T-cell lines and leukemic T cells from patients. For example, with the restriction enzyme *Bam*HI, six bands can be seen in germ-line DNA, whereas only five germ-line fragments in a DNA sample from the T-cell line Jurkat and three bands in a sample from a patient with T-cell leukemia could be observed. No apparent gene rearrangement was found for the T-cell line CEM. Similarly, seven germ-line bands were observed with *Eco*RI, while only five bands were detected in Jurkat DNA. Another example of rearrangement

Table 1. T-cell clones from Jurkat cDNA library

Class	Size of mRNA, kb	No. of clones*	Expression of cells† B	J	T	Rearrangement	Clone designation
A	3.0	3	−	+	−	−	
B	UD	3				−	
C	1.7	1	−	+	+	−	
D	2.0/1.4	1	−	+	+	−	pY4
E	1.3	1	−	+	−	−	pY17
F	1.0	1	−	+	+	−	pY25
G	2.2/2.0/1.0	1				−	
H	UD	1				−	
I	UD	1				?	
J	UD	1				−	
K	UD	1				−	
L–S	ND	1 each				−	
β chain	1.3/1.0	20	−	+	+	+	
α chain	1.6/1.3	1	±	+	+	+	pY14

UD, undetectable; ND, not done; ?, not clear.
*Total clones = 44.
†B, B-cell line RPMI 1788; J, Jurkat; T, Thymus.

was seen in DNA from leukemic cells digested with *Hin*dIII. To estimate how many of these germ-line bands may be *V* or *C* region fragments and if rearrangement can be found using the *C* region probe, we hybridized the *Bam*HI-, *Hin*dIII-, *Bgl* II-, and *Pvu* II-digested DNA from normal and leukemic cells with a *C* region probe (the 3′ end of pY14). Results in Fig. 3 *Right* indicate that only one or two bands could be assigned to the *C* region. In addition, no rearrangement could be found with this probe in DNA from a patient with T-cell leukemia digested with these restriction enzymes.

Nucleotide and Deduced Protein Sequences of pY14. A sequence of 1101 nucleotides of pY14 is shown in Fig. 4. It has a long open reading frame with the first methionine codon ATG at nucleotide 190 and a TGA termination triplet at position 1021. A protein composed of amino acids of this open reading frame has a molecular weight of 29,995. There

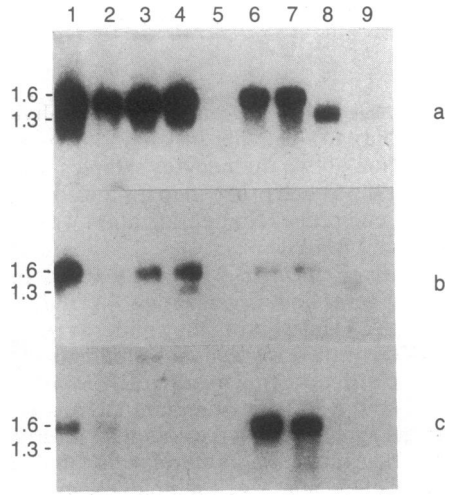

FIG. 2. Expression of pY14 in T cells and non-T-cells. Poly(A)$^+$ RNA from T cells and non-T-cells was examined by blot-hybridization analysis. The probes used were total pY14 insert (*a*), *Hpa* II–*Hpa* II fragment of pY14 (nucleotides 591 to 980 in Fig. 4), corresponding to the C region of the α chain (*b*), and the *Eco*RI–*Sau*3A fragment of pY14 (nucleotides 1–529 in Fig. 4), corresponding to the V region (*c*). Lanes: 1 and 2, human thymocytes; 3, T-cell leukemic cell; 4, HPB-ALL; 5, CEM; 6 and 7, Jurkat; 8, B-cell line RPMI 1788; 9, B-cell line RPMI 3638. Size markers are indicated in kb.

are two stretches of uncharged amino acids, from amino acid 1 to 20 and from 253 to 272. It is possible that the first stretch of nonpolar amino acids corresponds to a signal peptide, while the second stretch resembles a transmembrane anchor, suggesting that this is a transmembrane protein. The protein sequence has regions similar to the signal, V, D, J, and C regions of Ig and T-cell receptor β-chain proteins (Fig. 5). Six potential glycosylation sites were identified, with one in the V region (amino acid 43), one in the J region (amino acid 118), and four in the C region (amino acids 169, 203, 214, and 250). Comparison of the DNA and protein sequences of pY14 with those of the murine α-chain cDNA and the partial protein sequence of the human α chain indicates that very high homology can be found between pY14 and these sequences, making it likely that pY14 encodes the human α chain. This deduced protein sequence shows extensive similarity to the β chain from Jurkat and the murine λ light chain throughout most of its sequence (Fig. 5). The highest homology can be found near the cysteine residues at amino acids 42, 110, and 159 of pY14 and within the putative J region. Like the β-chain protein, the human α chain contains an additional peptide that extends beyond the COOH terminus of the murine λ light chain. The overall homology of the α-chain protein to that of the β chain is about 30%, while the similarity to the murine λ chain is about 26%.

DISCUSSION

We describe here the isolation and analysis of 19 T cell-specific cDNAs from a human T-cell line, Jurkat. Messages homologous to some of these clones were found to be transcribed in thymocytes as well as in Jurkat. Genomic DNA corresponding to these clones does not appear to undergo somatic rearrangement in T cells, and the functions of proteins encoded by these clones are unknown, although they may be involved in thymic differentiation or specialized T-cell functions. It would be of particular interest to determine if they correspond to some of the known differentiation antigens identified by T cell-specific monoclonal antibodies (28).

In addition to these apparently nonrearranging clones, two cDNA clones, which correspond to the α and β chains of the T-cell receptor heterodimer of the T-cell line Jurkat, were sequenced and demonstrated to undergo somatic rearrangements in T cells.

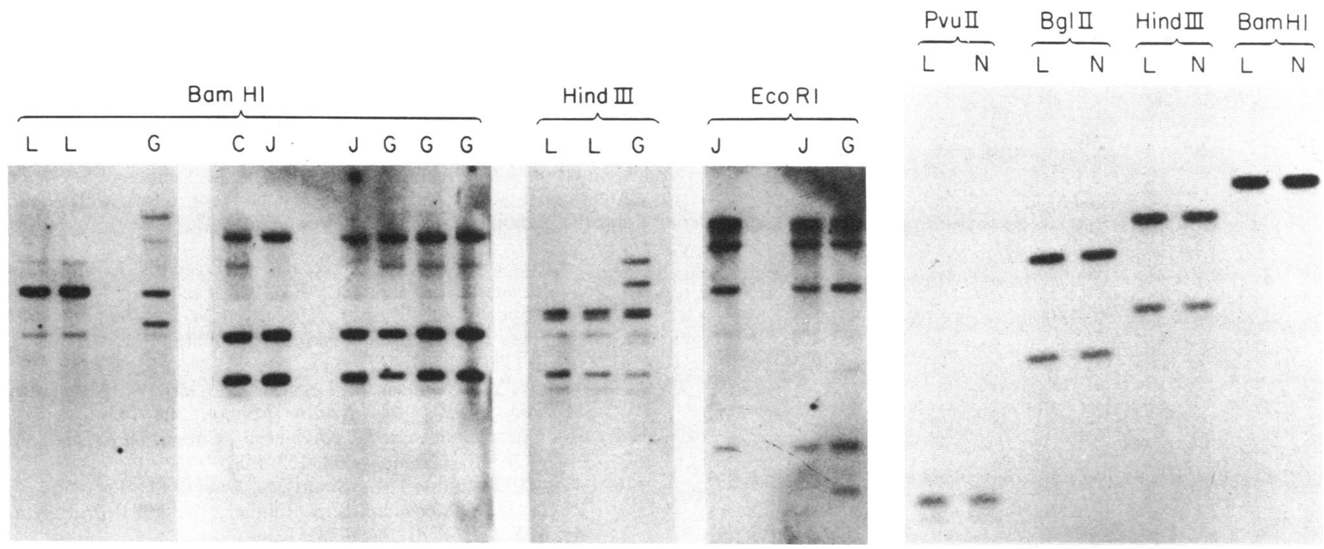

FIG. 3. Southern gel analysis of T cells and non-T-cells. DNA was extracted from T cells and non-T-cells and digested with the restriction enzymes indicated. The DNA was analyzed by Southern gel analysis using as probes the complete pY14 insert (*Left*) and the *C* region (*Hpa* II–*Hpa* II fragment, nucleotides 591–980 of Fig. 4) (*Right*). Lanes: G, germ line; L, leukemia T cells; J, T-cell line Jurkat; C, T-cell line CEM.

Like the β chain, the α-chain gene messages (1.6 kb and 1.3 kb) are found mainly in T-cell lines, leukemic T cells, and thymocytes. A lower level of the short transcript also can be found in some B cells. These apparently truncated messages in B cells are likely to be similar to those of Ig heavy chains in T cells (29) or the 1.0-kb message of β-chain genes (12, 13, 20). However, it is not known at this time whether they are similar to the message from the *D/J*-rearranged β-chain genes (12, 13, 20) or whether they represent a transcript from an unrearranged α-chain gene (20).

In common with the T-cell receptor β-chain genes and Ig genes, α-chain genes undergo somatic rearrangement in T cells. The finding that rearrangement can be detected only in certain T cells raises interesting questions as to the role of the α chain in specialized T cells and the genomic organization of these genes. One possibility is that the α-chain genes are not utilized in all T cells, a situation similar to the alternative use of λ and κ chains in Ig. It would be of interest to determine if the third rearranging T-cell genes described by Saito *et al.* (30) may be an alternate chain. Another possibility is simply that rearrangement of α-chain genes cannot be demonstrated because of the inherent genomic structures and organization of the α chain. The findings that rearrangement can be demonstrated with the use of only a few restriction enzymes and that only rearrangements of *V* genes are detected in these T cells support this possibility. It is likely that the *J* gene segments and possible *D* gene segments are located at a long distance (presumably 5′) away from the *C* genes. A third explanation may be that the β-chain genes rearrange before the α-chain genes. The finding that the cell line CEM rearranges and expresses the β- (20) but not the α-chain genes is not inconsistent with this hypothesis.

In agreement with data obtained by protein analysis, glycosylation sites can be found in the deduced α- and

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GGGGGGGGGGGGGGGGGGGGAACACATCCAGGCTCCTTAAGAGAAAGCCTTTCTTTAACCATTTTTGAAACCCTTCAAAGGCAGAGACTTGTCCAGCCTAACCTGCCTGCTGCTCCTAGC
        10        20        30        40        50        60        70        80        90       100       110       120
                                                                      |<-- L
                                                                      MetLeuLeuLeuLeuValProValLeuGluValIlePheThrLeuGlyGly  -17
TCCTGAGGCTCAGGGCCCTTGGCTTCTGTCGCTCTGCTCAGGGCCCTCCAGCGTGGCCACTGCTCAGCCATGCTCCTGCTGCTCGTCCCAGTGCTCGAGGTGATTTTTACCCTGGGAGGA
       130       140       150       160       170       180       190       200       210       220       230       240
 L -->|<-- V
ThrArgAlaGlnSerValThrGlnLeuGlySerHisValSerValSerGluGlyAlaLeuValLeuLeuArgCysAsnTyrSerSerSerValProProTyrLeuPheTrpTyrValGln  -57
ACCAGAGCCCAGTCGGTGACCCAGCTTGGCAGCCACGTCTCTGTCTCTGAAGGAGCCCTGGTTCTGCTGAGGTGCAACTACTCATCGTCTGTTCCACCATATCTCTTCTGGTATGTGCAA
       250       260       270       280       290       300       310       320       330       340       350       360

TyrProAsnGlnGlyLeuGlnLeuLeuLeuLysTyrThrSerAlaAlaThrLeuValLysGlyIleAsnGlyPheGluAlaGluPheLysLysSerGluThrSerPheHisLeuThrLys  -97
TACCCCAACCAAGGACTCCAGCTTCTCCTGAAGTACACATCAGCGGCCACCCTGGTTAAAGGCATCAACGGTTTTGAGGCTGAATTTAAGAAGAGTGAAACCTCCTTCCACCTGACAAAA
       370       380       390       400       410       420       430       440       450       460       470       480
                                    V ---->|<--- (D) ---->|<---                 J                              -->|<--C
ProSerAlaHisMetSerAspAlaAlaGluTyrPheCysAlaValSerAspLeuGluProAsnSerSerAlaSerLysIleIlePheGlySerGlyThrArgLeuSerIleArgProAsn  -137
CCCTCAGCCCATATGAGCGACGCGGCTGAGTACTTCTGTGCTGTGAGTGATCTCGAACCGAACAGCAGTGCTTCCAAGATAATCTTTGGATCAGGGACCAGACTCAGCATCCGGCCAAAT
       490       500       510       520       530       540       550       560       570       580       590       600

IleGlnAsnProAspProAlaValTyrGlnLeuArgAspSerLysSerSerAspLysSerValCysLeuPheThrAspPheAspSerGlnThrAsnValSerGlnSerLysAspSerAsp  -177
ATCCAGAACCCTGACCCTGCCGTGTACCAGCTGAGAGACTCTAAATCCAGTGACAAGTCTGTCTGCCTATTCACCGATTTTGATTCTCAAACAAATGTGTCACAAAGTAAGGATTCTGAT
       610       620       630       640       650       660       670       680       690       700       710       720

ValTyrIleThrAspLysThrValLeuAspMetArgSerMetAspPheLysSerAsnSerAlaValAlaTrpSerAsnLysSerAspPheAlaCysAlaAsnAlaPheAsnAsnSerIle  -217
GTGTATATCACAGACAAAACTGTGCTAGACATGAGGTCTATGGACTTCAAGAGCAACAGTGCTGTGGCCTGGAGCAACAAATCTGACTTTGCATGTGCAAACGCCTTCAACAACAGCATT
       730       740       750       760       770       780       790       800       810       820       830       840
                                                                                                   C -->|<-- TM
IleProGluAspThrPhePheProSerProGluSerSerCysAspValLysLeuValGluLysSerPheGluThrAspThrAsnLeuAsnPheGlnAsnLeuSerValIleGlyPheArg  -257
ATTCCAGAAGACACCTTCTTCCCCAGCCCAGAAAGTTCCTGTGATGTCAAGCTGGTCGAGAAAAGCTTTGAAACAGATACGAACCTAAACTTTCAAAACCTGTCAGTGATTGGGTTCCGA
       850       860       870       880       890       900       910       920       930       940       950       960
                                      TM -->|<-- CY
IleLeuLeuLeuLysValAlaGlyPheAsnLeuLeuMetThrLeuArgLeuTrpSerSer***
ATCCTCCTCCTGAAAGTGGCCGGGTTTAATCTGCTCATGACGCTGCGGCTGTGGTCCAGCTGAGATCTGCAAGATTGTAAGACAGCCTGTGCTCCCTCGCTCCTTCCTCTGCATTGCCCC
       970       980       990      1000      1010      1020      1030      1040      1050      1060      1070      1080

TCTTCTCCCTCTCCAAACAGA
      1090      1100
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FIG. 4. Nucleotide and deduced amino acid sequences of T-cell clone pY14. The deduced amino acid sequence is derived from the only open reading frame in the nucleotide sequence. The cysteine residues are underlined, and the potential N-glycosylation sites are indicated by interrupted underlines. Regions in addition to V and C: L, leader sequence; D, diversity; J, joining; TM, transmembrane; and CY, cytoplasmic. These regions are assigned by comparison with their β-chain counterparts (20).

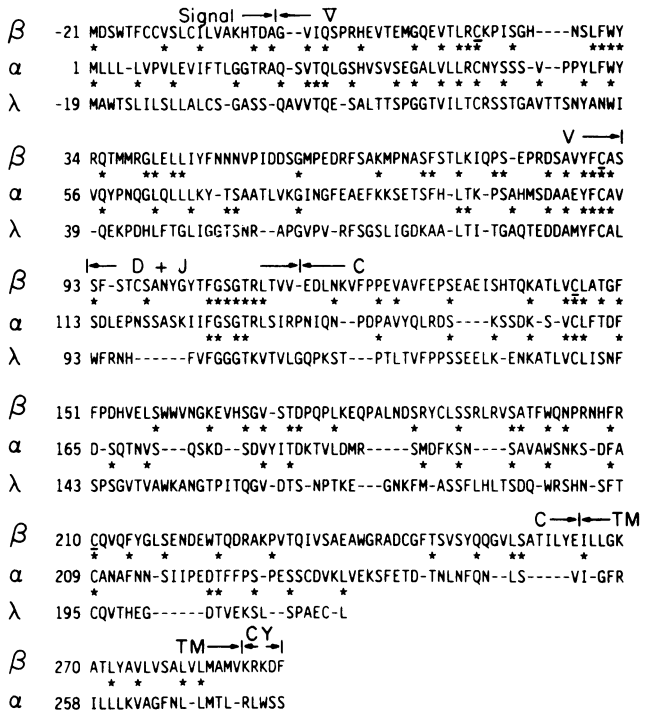

FIG. 5. Direct comparison of the deduced amino acid sequence of clone pY14 with those of the β chain of Jurkat and murine λ light chain. Identity between the sequences is indicated by an asterisk. Gaps (−) were introduced to increase matching. The single-letter code for amino acids is used. Rows: β, JUR-β1, corresponding to the β chain of Jurkat (20); α, pY14, corresponding to the α chain; λ, murine λ light chain (27).

β-chain protein sequences. Two potential N-glycosylation sites have been described for the human β chain (one in the V and one in the C region) (4), while six can be found in the α-chain protein sequences described here (one in the V, one in the D/J junction, and four in the C region). This would explain why the α chain, which is composed of a shorter amino acid backbone, possesses a greater apparent molecular weight (1, 31). The presence of four potential N-glycosylation sites in the C region of the α chain but only one in that of the β chain would ensure detection of the former as an apparently larger protein in most cases (1, 31).

The successful cloning of the β- and α-chain genes of the T-cell receptor allows one to ask and possibly answer many interesting questions pertaining to the contribution of each chain to the generation of T-cell antigen receptor diversity and antigen recognition. Preliminary observations in the present communication and those described for the murine α chain (15, 16) would suggest that there may be more germ-line α-chain *V* genes than their β-chain counterparts (9). Like in the β chain, it is also possible that D regions are present in the α chain (see Fig. 5); however, confirmation will have to await the identification of germ-line *D* gene segments. Also it would be interesting to determine if these putative α-chain *D* gene fragments, like those of the β chain, play an important role in the generation of diversity.

Recently, we have been able to reconstitute an active T-cell antigen receptor by DNA transfer (unpublished data). It is hoped that the use of α- and β-chain genes from functionally defined T-cell lines and this DNA transfer technology (unpublished data) will provide long-awaited answers to many of the questions about the interactions of T cells with other immunocompetent cells as well as with antigens and major histocompatibility complex products.

Note Added in Proof. A similar α-chain cDNA has also been isolated (32).

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