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Immunology

Immunoglobulin J chain gene from the mouse

(B-lymphocyte differentiation/DNA sequence/lymphocyte-specific promoter elements/S1 mapping)

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ABSTRACT **During a primary immune response, murine B lymphocytes are induced to express the gene for the immunoglobulin J chain. As a first step in determining the mechanism of induction, genomic DNA clones encoding the murine J chain were obtained from cell lines representative of B lymphocytes before and after J chain expression. Analysis of the coding regions showed that the J chain gene has a different structure from the other immunoglobulin genes. It consists of four exons organized in a simple 7.3-kilobase transcription unit that does not require DNA rearrangement or alternative processing for expression. These structural properties indicate that transcription of the J chain gene is initiated by changes in chromatin conformation, probably involving a J chain-specific DNA-binding factor. Analysis of the 5′ flanking sequences of the J chain gene, on the other hand, showed that the promoter region contains two conserved elements that have been implicated in the lymphocyte-specific expression of the light chain genes. The sharing of these elements suggests that, once the J chain gene is activated, its transcription is regulated by mechanisms similar to those controlling the light chain genes.**

Synthesis of the immunoglobulin J chain is critical for a primary immune response (1). In this response, B lymphocytes are triggered by the appropriate antigen and lymphokine signals to differentiate into blast cells that secrete pentamer IgM antibody. The J chain is required for the assembly of the pentameric product: it serves both to couple two of the monomer IgM subunits and to ensure that the five subunits are joined in a closed ring structure.

Analyses of the primary immune response in the mouse (2, 3) have shown that J chain expression is a direct consequence of B cell-triggering. Little or no J chain RNA or protein is present in unstimulated populations of mouse splenocytes. Several days after mitogen stimulation, however, synthesis of J chain RNA can be detected and, 24 hr later, large amounts of J chain message and its protein product are found within the responding cells. Similar data have been obtained from the analyses of lymphoid cell lines (2, 4–6). B-lymphoma counterparts of unstimulated lymphocytes do not contain J chain-specific RNA transcripts, whereas plasmacytomas secreting immunoglobulin exhibit high levels both in the nucleus and cytoplasm. Taken together, these studies indicate that synthesis of the murine J chain is initiated in the stimulated B cell by transcription of a previously silent gene.

As a first step in determining the activation mechanism, we have examined the structure of the expressed and nonexpressed murine J chain gene. Genomic clones were isolated from lymphoma and plasmacytoma libraries, and the organization of the coding regions and the 5′ flanking sequences were compared. The results show that transcription of the J chain gene is activated by changes in its chromatin conformation rather than by changes in its covalent structure.

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MATERIALS AND METHODS

Isolation of J Chain Recombinant Clones. Mouse B-lymphoma genomic libraries were constructed by standard procedures (7). Briefly, DNA from the B-lymphoma cell line WEHI-231 (μ^+, k^+, J^-) (8) was digested partially with *Eco*RI to an average size of 15 kilobases (kb) and size-fractionated on sucrose gradients. Fractions enriched for DNA fragments 10–20 kb in length were pooled, and the DNA was ligated to the *Eco*RI arms of the phage vector Charon 4A and packaged *in vitro* by procedures described by Blattner *et al.* (9).

A mouse myeloma genomic library was obtained from S. L. Morrison and C. A. Milcarek (Department of Microbiology, Columbia College of Physicians and Surgeons, New York, NY). The library was constructed with DNA from the myeloma cell line MPC 11 ($\gamma 2b^+$, κ^+, J^+) (8) that was digested partially with *Eco*RI to an average size of 16 kb. The DNA fragments were ligated into Charon 4A arms and packaged as described above.

J chain recombinant clones were identified by screening the libraries by the *in situ* hybridization method of Benton and Davis (10) as modified by Maniatis *et al.* (7). The hybridization conditions for nitrocellulose filters were adapted from those described by Wahl *et al.* (11), and ^{32}P-labeled J chain cDNAs Jc3 (5) and Jc21 (12) served as probes.

DNA Sequence Analysis. Nucleotide sequences of subcloned restriction fragments were determined as described by Maxam and Gilbert (13). Nucleotide sequences near the 5′ end of mouse J chain mRNA were determined by primer extension in the presence of dideoxynucleotides (14). The primer used in these experiments was the anticoding strand of a *Hin*fI–*Bam*HI restriction fragment isolated from the J chain cDNA Jc21 (12). The fragment was hybridized to 10 μg of poly(A)$^+$ RNA from the IgM-secreting hybrid cell line M × W 231.1b (8) in the presence of 50% formamide at 48°C for 16 hr and then was extended by treatment with 12 units of avian myeloblastosis virus reverse transcriptase (J. W. Beard, St. Petersburg, FL) at 42°C for 1 hour.

S1 Nuclease Analysis. The transcription start site in the J chain gene was identified by use of the technique of Berk and Sharp (15) as modified by Weaver and Weissman (16). A 300-base-pair (bp) fragment spanning the transcriptional start site and containing 150 bp of pBR322 sequence was labeled with [γ-^{32}P]ATP and the anticoding strand was isolated by polyacrylamide gel electrophoresis. One hundred fifty nanograms of the single-stranded probe (specific activity, 1500 cpm/ng) was hybridized to 2 μg of poly(A)$^+$ RNA from the hybrid cell line M × W 231.1b (8) at 48°C for 16 hr under aqueous conditions (17). Hybrids were trimmed with 100 units of S1 nuclease (P-L Biochemicals) per ml at 37°C for 30 min. Digestion products were identified by electrophoresis on an 8% sequencing gel next to G+A-cleavage products of the anticoding strand (13).

Abbreviations: kb, kilobase(s); bp, base pair(s).

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RESULTS

Characterization of J Chain Genomic Clones. Recombinant phages containing J chain information were isolated from *Eco*RI partial libraries of MPC 11, an IgG2b-secreting myeloma that expresses J chain, and WEHI 231, a B lymphoma that expresses membrane IgM but not J chain. These lines were chosen as sources of J chain DNA because the cells have been fused to produce hybrids that secrete pentamer IgM by complementation (8). Thus, genomic clones derived from the two parental lines could be used both to detect differences between the expressed and nonexpressed J chain gene and to assess any changes induced in the J chain gene as a result of fusion of the two genomes.

A single J chain-positive recombinant phage, MyL-1, was recovered from the myeloma library; it contained 13.9 kb of mouse DNA distributed in four *Eco*RI fragments respectively 5.2, 0.4, 1.9, and 6.4 kb long (Fig. 1, clone b). A total of 14 J chain-positive phages was isolated from the various lymphoma libraries. Of the three clones selected for more detailed study, one, LyM-1, extended 6.7 kb 5′ of the myeloma clone (Fig. 1, clone a); a second, LyM-2, was identical to the 13.9-kb myeloma clone (Fig. 1, clone c); and a third, LyM-3, extended 1.7 kb 3′ to the myeloma clone (Fig. 1, clone d). The coding information was located within these clones by a combination of restriction enzyme analysis and hybridization to ordered fragments of a J chain cDNA, Jc21 (12). Four exons were identified within the 13.9-kb clone, separated by successive introns of 1.5, 3.7, and 0.9 kb (Fig. 2). The J chain gene spanned, therefore, slightly more than 7 kb of the 22.3 kb of mouse DNA that was cloned.

Analyses of Exon 1 Structure. Exon 1 was found to have a structure typical of a eukaryote leader exon (18) (Fig. 3). It contains 98 bp that encode a 34-bp untranslated region and the first 21 amino acids of a 22-residue leader peptide. The 5′ boundary of the untranslated region was defined by S1 nuclease mapping of the transcriptional start site (Fig. 4). Two sites were identified by this method, a major one 34 bp upstream of the AUG codon and a minor one 28 bp upstream (marked by asterisks in Fig. 3). The translational start site and the leader structure were located from DNA sequence data. The amino acid sequence derived for the leader was characteristic of a signal peptide with several basic amino acids at the amino terminus, followed by a stretch of highly hydrophobic residues.

An unexpected finding of the exon 1 analyses was a discrepancy in the 5′ leader sequence. The base pairs in Fig. 5 that are both underlined and overlined show that the sequence of a 20-bp segment in the MyL-1 clone (nucleotides 28–47) was completely different from that obtained for the comparable region in the Jc21 cDNA clone; yet the genomic and cDNA sequences corresponded exactly for the remaining 3′ 49 nucleotides of the leader. Closer examination of the discrepancy revealed that the sequences were inverted complements of each other. To determine which of the two was actually transcribed, the 5′ sequence of J chain mRNA was determined by primer extension. The template consisted of mRNA isolated from the J chain-expressing line, M × W 231.1b, and the primer was derived from the cDNA clone and contained the terminal 37 bp of the leader and 80 bp of exon 2. When the sequence of the primer extension product was examined, it was found to be identical to that present in the MyL-1 myeloma clone, thus confirming that the cloned gene was truly representative of the expressed J chain gene. Moreover, the identical sequence was also present in the LyM-2 clone from the non-J-chain-expressing lymphoma, so that the inversion in sequence could not be related to the initiation of J chain gene transcription.

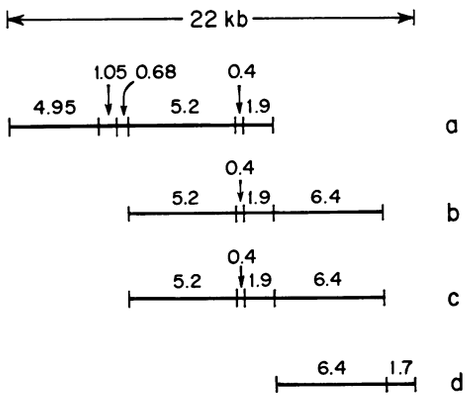

FIG. 1. *Eco*RI restriction maps of J chain genomic clones isolated from lymphoma and plasmacytoma libraries. Numbers indicate the size of fragments in kilobases. Clones: a, LyM-1; b, MyL-1; c, LyM-2; d, LyM-3.

In view of these findings, the inversion probably represented an artifact of cDNA cloning. Because the segment that was inverted is flanked by two, short, inverted repeat sequences, it is possible that a stem–loop structure formed at the end of the first cDNA strand and served as a primer to initiate synthesis of the second strand. During subsequent limited digestion with S1 nuclease, the loop may have been nicked once at the stem junction, creating a 20-bp 5′ overhang. The overhang region would be filled in under the conditions of repair synthesis used for linker ligation and, thus, an inverted form of the loop sequence would be incorporated into the cDNA clone. This explanation is consistent with the finding that the inverted segment in the cDNA is flanked at the 5′ end by a perfect *Eco*RI site contributed by the cloning linker (Fig. 5). The explanation is also consistent with the structural properties of the 5′ region of the J chain gene. Computer analyses showed that the 5′ sequence has a high potential for forming secondary structures such as stem-loops. Moreover, the structure of the 5′ sequence does not allow strand separation, even after prolonged electrophoresis. In order to isolate the single strand used in the S1 nuclease mapping experiments described above, it was necessary to start with a hybrid fragment in which the J chain leader sequence was coupled to a readily dissociable pBR322 sequence.

Analysis of the Structure of Exons 2, 3, and 4. The boundaries and contents of the exons coding for the mature J chain were determined from the nucleotide sequence of the MyL-1 clone. As the data in Fig. 3 show, exon 2 consists of 121 bp that encode amino acids −1 through 40; exon 3 includes 81 bp that specify amino acids 41 through 67; and exon 4 has 920 bp that encode the entire carboxyl-terminal half of the J chain, residues 68 through 137, as well as a large 3′ untranslated region. When the exon sequences were compared with the sequence previously determined for murine J chain cDNA (12), three nucleotide differences were observed. One was a neutral substitution in the codon specifying leucine 116; the remaining two were substitutions in the first base pair of codons 67 and 117 that changes the amino acid assignment from leucine to valine and from glycine to alanine, respectively. It is likely that these discrepancies reflected errors in the cDNA analyses because the assignments from the exon sequences agreed with protein sequence data (19). Three errors were also found in the cDNA sequence of the 3′ untranslated region. The corrections have been incorporated in the data given in Fig. 3.

When the exon structure of the mouse J chain gene was compared with that of the human gene (20), a striking similarity was apparent (Table 1). In each case, the information for the mature J chain is encoded in three exons; the counterpart exons are essentially equivalent in length, exhibit

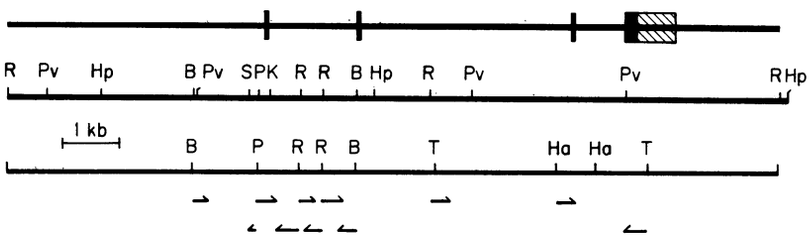

FIG. 2. The murine J chain gene and its flanking sequences. (*Top*) Exon organization of the gene. (*Middle*) Restriction map (B, *Bam*HI; Hp, *Hpa* II/*Msp* I; K, *Kpn* I; P, *Pst* I; Pv, *Pvu* II; R, *Eco*RI; S, *Sst* I). (*Bottom*) Sequencing strategy for MyL-1 clone (B, *Bam*HI; Ha, *Hae* III; P, *Pst* I; R, *Eco*RI; T, *Taq* I).

more than 80% identity in nucleotide sequence, and have identical exon–intron boundaries. This high degree of homology at the DNA level strengthens the evidence from protein studies that J chain is one of the most conserved elements in the immunoglobulin system (10, 20, 21). On the other hand, a comparison of the surrounding introns and 3′ untranslated sequences showed that these regions differ considerably in length and nucleotide content. The extent of divergence observed is consistent with the hypothesis that large stretches of noncoding sequences within a gene can function as buffers to maintain critical coding sequences (22).

Analysis of the 5′ Flanking Region. The coding regions of the murine J chain gene, including both exons and introns, appeared to be unique sequences as judged by their patterns of hybridization to total mouse DNA. In contrast, the 5′ flanking region was found to contain sequences that are repeated often in the mouse genome. Fragments from a 3-kb region spanning the *Pvu* II–*Bam*HI sites (Fig. 2) gave a heavy

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                                                                --GTAGAGAGCTCTATTTAAACATCTCAACAGGGCCCTGACTCT
GCACTTGTCAGCTTGGGGTTCATACATTGCTGAAGCACAGATGAGCCATCAAATCCCAGCTTTCTATTAGAGGGAAACACGTAAGTATGAACCATGAGCGTCT
                          pd                                                                    dc
TTCCAGAGTAGCATGCAGTTGAAACCTGAAGCTGTGATGACTGCAGCTCACCTGTCCTGGGGTTATTTTTAAGAAAGCAGAAGCAGCATGATTTGCACACCTC
                                                                                  Exon 1
                      **    *                                    Met Lys Thr His Leu Leu Leu Trp Gly Val Leu
TTATAGACACACAGTTGGCCGTGGCTTTTGGCTTCAGTCTTTCAACAGTGAAGACAAG ATG AAG ACC CAC CTG CTT CTC TGG GGA GTC CTC

Ala Ile Phe Val Lys Val Val Leu Val Thr G
GCC ATT TTT GTT AAG GTT GTC CTT GTA ACA G GTAGGTGGTACCTATACAATAACACCAGATAAAAGGGAAAATGTGTGTTCAGGTCTAAAGA
CTAAATCTACTCTTCTACTGGCTACGTGGACACTCAGC------ 20 bp -------ACTGAACAGCTAGTCACCTTCTAACCTCATTAGGCAGTGATAAAA
AAAAAAAAAAAAAAAAAGAATGATCATTGATCTCTTTGTTTTTTTTTTTTTTCTTCTGTTTGGCTACTCCAACCTACAACATAATAAAATAAATACTTTGGGG
GTATCTATAAGTGTGGCTACACTTATAAACCCATGTATAACTTTAAAACCAATAGCCTCTCCTTGAGACTCTTTAATTACTATTCTAGAGAAGTGAGGTAATA
ACTTTGCTAATTATGATATAGATTGTATTTTGATTTTGATTTTTATCTCCCCAGAGAAATGGA-GTCAGAGAGTGAAAACTGACTCTCA------ 20 bp -
-------TAGGAAATATTAATACAGGCCTTGTTTCTCTTTCTTGTTGAATCTGTGTATTGATTGTGATTATTGTTATGAAAAAATATCGATAGTTTACGAAAG
TTTTGGTGGAGAGTATTAAATCTTACAAAATAAGATAGTCTTGGGAGAAAAGATACTTCTAATACGATTTGAGGGAAATCTTTTTTTTCAGGAAGCAATGGTA
GTTGCGGAAGGACTCTGTTTGCAGTTGGGTTTATAAAGACTGGCTTTCAAGATTTCTTTGATTGGGGAATAGTCTAAATTTCTGCTTTATTTTTCATTTAGGT
GTTTTCGTCGAATTTTACCATGTGCCCTCCCTAAAATAATTAGAAGCATTAGATATAAAT------ 20 bp -------TAGCTGCTCTTGAATTTTTCCAA
CGAAGAAAAAGAAAATTCTCTTAAAATTCTTTGCTCTTTTCGATTAGAAAAGAAAACAAATAGAAAGACTAGGACTTATGAACAATAAAAATTAAAGTTTTTG
ATCCA-GCATGGTGGTGCACACTTGTAACCTCAGCACTCAGGAGATGGAAGTAGGGCGTGCAGAATTTAGAATCAACCATAGCTGCAAAGTGAGTTTCAGGCT
ATCCTGACTACATGAGACTTGTCTGCTATCTTCAGGTAAGAAAGGCAAATTATCTCATCTTAGCACATAATGCACTTAAAAAAAAAAAAAGACAGACAATACC
TCTTTATGTAATGCAGGGTGTCATGAAAGTTCCTAGGTAGTCC-AGGCAGACCTT-AATTTCCCATCCTCCCTCCTCAATTTCCCAAGCGCTCGGATAGCAGG

                                                                                  ly Asp Asp Glu Ala Thr Il
CCTGCACAGTGACACCAAAGACAACATAGAGTTCTGTTTTCCTTTTTCATGATATAGTTTTACCTTTGAAACCCAAG GT GAC GAC GAA GCG ACC AT
                                  Exon 2
e Leu Ala Asp Asn Lys Cys Met Cys Thr Arg Val Thr Ser Lys Ile Ile Pro Ser Thr Glu Asp Pro Asn Glu Asp I
T CTT GCT GAC AAC AAA TGC ATG TGT ACC CGA GTT ACC TCT AAA ATC ATC CCT TCC ACC GAG GAT CCT AAT GAG GAC A

le Val Glu Arg Asn Ile Arg Ile Va                                                                 l Val Pro Le
TT GTG GAG AGA AAT ATC CGA ATT GT GTTGTGCATTCACCTT---- ~ 3.7 kb ------CTGTCTCTCTCTCTTTTCAG T GTC CCT TT
                                                                  Exon 3
u Asn Asn Arg Glu Asn Ile Ser Asp Pro Thr Ser Pro Leu Arg Arg Asn Phe Val Tyr His Leu Ser Asp Va
G AAC AAC AGG GAG AAT ATC TCT GAT CCC ACC TCC CCA CTG AGA AGG AAC TTT GTA TAC CAT TTG TCA GAC GT GTAA--
                                                  Exon 4
                  1 Cys Lys Lys Cys Asp Pro Val Glu Val Glu Leu Glu Asp Gln Val Val Thr Ala Thr Gln Ser
 ~ 0.9kb -TTCTCAG C TGT AAG AAA TGC GAT CCT GTG GAA GTG GAG CTG GAA GAT CAG GTT GTT ACT GCC ACC CAG AGC

Asn Ile Cys Asn Glu Asp Asp Gly Val Pro Glu Thr Cys Tyr Met Tyr Asp Arg Asn Lys Cys Tyr Thr Thr Met Val
AAC ATC TGC AAT GAA GAC GAT GGT GTT CCT GAG ACC TGC TAC ATG TAT GAC AGA AAC AAG TGC TAT ACC ACT ATG GTC

Pro Leu Arg Tyr His Gly Glu Thr Lys Met Val Gln Ala Ala Leu Thr Pro Asp Ser Cys Tyr Pro Asp
CCA CTT AGG TAT CAT GGT GAG ACC AAA ATG GTG CAA GCA GCC TTG ACC CCC GAT TCT TGC TAC CCT GAC TAGCTTGAACA
CCATGCAGCTCGTTGTCCTTAGAGGCTCTCCATTTGCACCCAGGAAGTTATACTCGTCGCTAATGAATTTGAAAC-AGGGTTTTTTTTTCCCCCTGTGGTATA
AAACTAATGTTCCCTTTCAAATCATTAGAATATCAGAATTGCTGTCGTTGTTGTGTAACTCTC
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FIG. 3. Selected DNA sequences from the murine J chain gene. Amino acid sequences encoded in the four exons are shown above their corresponding codons. A potential TATA box is underlined (third row) and the positions of the major and minor transcriptional initiation sites are marked by asterisks. The conserved regulatory elements, the decanucleotide sequence (dc), and the pentadecanucleotide sequence (pd) are both underlined and overlined. Distances in base pairs between DNA sequences have been estimated from restriction map information.

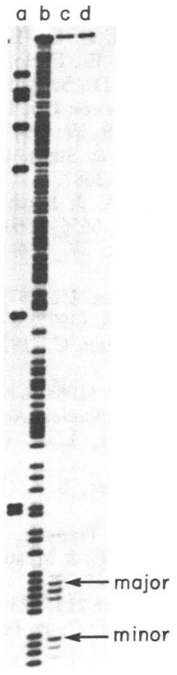

FIG. 4. S1 mapping of the transcriptional start site of the murine J chain gene. Poly(A)$^+$ RNA from the J chain-expressing cell line M × W 231.1b and the J chain-nonexpressing cell line WEHI 231 was hybridized to a 5′ end-labeled single-stranded probe spanning the region of the transcriptional start site, digested with S1 nuclease, and electrophoresed on an 8% urea/polyacrylamide gel. Lanes: a, end-labeled ϕX174 *Hae* III fragments; b, G+A ladder of the probe; c, S1 nuclease-resistant fragments from M × W 231.1b RNA; d, S1 nuclease-resistant fragments from WEHI 231 RNA. Major and minor start sites were assigned by primer extension mapping of this region. The position of the major transcriptional start site agreed with the major termination product.

smear of hybridization with DNA from all inbred mouse strains tested. The identity of the repetitive element(s) has yet to be determined.

The 300 bp immediately adjacent to the transcriptional start sites was free, however, of such repetitive sequences. This region was found to be organized similarly to the regions upstream of light chain variable gene segments (23, 24) (Fig. 3). The common elements include a short "TATA" sequence beginning at position −24 from the transcriptional start site

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GENOMIC J CHAIN SEQUENCE

5'                MetLysThrHisLeuLeuLeuTrpGly   3'
   GAGTGAAGACAAGATGAAGACCCACCTGCTTCTCTGGGGA

   CTCACTTCTGTTCTACTTCTGGGTGGACGAAGAGACCCCT


Jc21 cDNA SEQUENCE

5'   EcoRI  GlyGlySerSerSerCysLeuLeuTrpGly   3'
   AAGAATTCCAGGTGGGTCTTCATCTTGTCTTCTCTGGGGA

   TTCTTAAGGTCCACCCAGAAGTAGAACAGAAGAGACCCCT
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FIG. 5. Discrepancy in the 5′ leader sequence of J chain genomic and cDNA clones. The segments of inverted sequence are both underlined and overlined and the flanking inverted repeats in the genomic DNA are underlined. See text for detailed explanation.

Table 1. Comparison of the structure of the mouse and human J chain genes

Gene segment*	Length, kb		% sequence identity†
	Mouse	Human	
Exon 2	0.019	0.122	81
Exon 3	0.081	0.081	86
Exon 4	0.211	0.208	82
Intron 2	3.7	4.5	I‡
Intron 3	0.9	0.670	I‡
3′ untranslated	0.709	0.787	I‡

*Exon 1 and intron 1 are omitted because data are not yet available for these segments of the human J chain gene.
†In the calculation of sequence identity, sequence gaps (insertions or deletions) were excluded.
‡I, insignificant.

and two tissue-specific control sequences, a decanucleotide that starts at position −73 and a pentadecanucleotide that starts at position −135 from the transcriptional start site (25, 26). The pentadeca- and the decanucleotide elements in the J chain promoter region differ by 1 and 2 bp, respectively, from the consensus sequence (25) for the light chain gene promoter elements.

DISCUSSION

Analyses of the murine J chain gene show that the information is organized in a simple transcription unit spanning 7.3 kb of the mouse genome. The primary structure of this unit is independent of the transcriptional state of the gene. No differences were detected in the sequence of the J chain DNA whether the clones examined were derived from a myeloma cell line that expresses J chain or from a B lymphoma line that does not. Similar results (27) have been obtained by restriction mapping of the J chain gene in cell lines and tissues representative of progressive stages in B-cell differentiation; all the cleavage sites identified in embryonic J chain DNA were found to be maintained throughout the life history of the B cell.

The structural properties of the J chain gene indicate that transcription is activated by changes in chromatin conformation. Such a mechanism is supported by the methylation pattern of the J chain gene (27, 28). Restriction mapping with methyl-sensitive enzymes has shown that the three *Hpa* II sites encoded in the J chain cistron are heavily methylated in J chain-negative cell lines but become completely undermethylated in J chain-positive cells, indicating that transcription is associated with a more open, extended chromatin conformation. Similar evidence has been obtained by use of a second measure of chromatin structure, DNase I sensitivity (29). The expressed J chain gene was found to be severalfold more susceptible to nuclease cleavage than the nonexpressed gene. Moreover, the expressed gene contains a site directly upstream from the coding regions that is hypersensitive to DNase I digestion and, thus, could mark the interaction of a regulatory protein (30, 31). Taken together, these findings suggest that the chromatin changes are initiated in the 5′ flanking sequence and then propagated through the entire gene structure.

The J chain gene differs both in structure and mechanism of activation from the other immunoglobulin genes. The heavy and light chain genes are complex units that encode multiple segments specifying the variable regions as well as one or a limited number of segments specifying the constant regions (32). Expression of these genes is known to require two changes in structure, a recombination of variable region gene segments (33) and a modification in chromatin induced by protein interaction (34, 35) at a downstream enhancer

sequence (24, 36, 37). In contrast, the J chain gene does not undergo DNA rearrangement nor does it appear to contain an enhancer sequence. Analyses of the downstream introns have failed as yet to identify the consensus sequence (25) or DNase I sensitivity (38) characteristic of enhancer elements (unpublished data). Thus, the distinctive properties of the J chain gene suggest that its expression in the stimulated B cell is effected by an independent mechanism involving a J chain-specific DNA-binding transcriptional factor.

On the other hand, the 5′ flanking sequence of the J chain gene contains elements that have been implicated in the control of light chain gene transcription (25). Deca- and pentadecanucleotide sequences homologous to those present in the J chain gene are found in all light chain genes examined to date, 50 to 150 bp upstream of the coding regions. Evidence has been obtained from gene-transfer experiments that these conserved sequences are recognition sites for factors that determine the correct initiation of light chain gene transcripts and contribute to the lymphocyte-specific expression of the transfected genes (25, 39). In view of these findings, it would appear that once the J chain gene is activated by a specific signaling mechanism, its transcription is regulated by mechanisms similar to, if not identical with, those controlling the light chain genes. It is interesting that the 5′ flanking regions of the J chain- and light chain genes share the same decanucleotide element, whereas the 5′ flanking regions of the heavy chain genes contain the inverted complement of this sequence at the same position (25, 26, 40). Perhaps this arrangement provides a means for programming J chain expression after light chains, and thus monomer IgM subunits, have been synthesized (41).

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