

Characterization and Expression of the Gene for the Human Fc Receptor γ Subunit

DEFINITION OF A NEW GENE FAMILY*

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The high affinity IgE receptor, Fc ϵ RI, is one of the key molecules involved in allergic reactions. It is a tetrameric complex ($\alpha\beta\gamma_2$). The γ chains from Fc ϵ RI are also subunits of other Fc receptors.

We have isolated, characterized, and sequenced the gene for the human γ chain of Fc ϵ RI. It consists of five exons and spans 4 kilobases. The leader sequence is encoded by two exons, the second of which also contains the short extracellular domain, the hydrophobic transmembrane region, and the beginning of the cytoplasmic tail. Three short exons encode the remaining of the polypeptide and the 3'-untranslated flanking sequence. The transcription initiation sites have been mapped.

Comparison between the gene structures of the γ chain of the Fc receptor and of the ζ chain of the T-cell receptor indicates that these genes have evolved from a common ancestor by duplication and that they define a new gene family. In addition to being localized on the same chromosome, both genes show an analogous organization of their exons. A high level of homology is found in three of their respective exons, and the splice sites between them are identical. Furthermore, γ and ζ chains are essential for surface expression of their respective receptors. Therefore, γ chains of Fc receptors and ζ chains of T-cell receptors may also define a new family of functionally related polypeptides.

Expression studies in COS cells show that the human γ chain alone is sufficient to achieve expression of the human α chain on the cell surface, whereas both β and γ chains are required for the surface expression of the rodent α chain.

were, until recently, thought to consist of a single polypeptide. However, Fc ϵ RI is a tetrameric complex of one α , one β , and two identical disulfide-linked γ chains. Recently, we found (6) that one of the Fc γ receptors on mouse macrophages, Fc γ RIIa, is not a single-chain receptor but consists of a multisubunit complex with γ subunits identical to those from Fc ϵ RI. Furthermore, the Fc γ receptor on human natural killer cells (Fc γ RIII-2) appears to be also associated with γ subunits (7).

Here we characterize the genomic structure of the human gene for γ chains including its exon-intron borders and transcription initiation sites. We compare the genomic structures of the γ chain and of the ζ chain of the T-cell receptor and demonstrate that gene duplication occurred during evolution to generate a new gene family. Therefore, the homologies previously detected between γ and ζ chains are significant and not simply due to exon shuffling as it is observed, for example, between the low density lipoprotein receptor and complement factor C9 (8).

It had been generally assumed that the requirements for cell-surface expression are identical between species. We have recently shown (9) that surface expression of rodent Fc ϵ RI requires cotransfection of the three genes for α , β , and γ chains, whereas expression of the human α chain on the cell surface may be achieved by cotransfecting the human α chain with the rodent γ chain alone without apparent need for the β chain. Therefore, we suggested that the chimeric nature of the receptor in those experiments could be responsible for the differences observed between rodent and human α chains. Here we demonstrate that this is not the case. Rodent and human Fc ϵ RI receptors are different in their requirements for surface expression. Whereas both species need γ chains, only the rodent receptor also requires β chains.

EXPERIMENTAL PROCEDURES

Extraction of Human Basophil RNA—Basophils were isolated from venous blood following leukapheresis of 2 liters of blood (National Institutes of Health Blood Bank) by single-step isopycnic banding on Percoll (10). Human (4 ml) polymorphonucleocytes were layered onto discontinuous Percoll gradients made from solutions with densities of 1.083, 1.079, and 1.070 g/ml. Final adjustment of density was facilitated by measurement of the refractive index at 22 °C with a Bausch & Lomb refractometer. After centrifugation at 700 $\times g$ for 25 min at 22 °C, most of the basophils were found in the band at a density of 1.070–1.079 g/ml. Purity ranged from 5 to 15% with a yield of $1.5 \pm 0.4 \times 10^6$ basophils/leukapheresis pack. The cDNA library was constructed as described before (9).

Screening and Isolation of Genomic and cDNA Clones—The 5' and 3' ends of the open reading frame of the rat Fc ϵ RI γ subunit cDNA (bp¹ 1–156 and 157–253 of a *Hinf*I digest, respectively) (11) were

The binding of immunoglobulins to Fc receptors mediates important functions of the immune defense system such as phagocytosis and antibody-dependent cytotoxicity. One of these Fc receptors, Fc ϵ RI, triggers cellular degranulation and the release of potent mediators of the allergic reaction (1, 2). The same receptor also induces the secretion of important lymphokines (3–5). With the exception of Fc ϵ RI, Fc receptors

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The nucleotide sequence(s) reported in this paper has been submitted to the GenBank™/EMBL Data Bank with accession number(s) J05285.

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¹ The abbreviations used are: bp, base pair(s); kb, kilobase(s); TCR, T-cell receptor.

radiolabeled by nick translation (nick translation kit, Amersham Corp.) and used to screen independently 10^6 clones of a human leukocyte genomic library made in EMBL3 (Clontech). Hybridization was carried out on duplicate Millipore nitrocellulose filters at 35 °C overnight in $4 \times$ SSC with 40% formamide. Membranes were then washed twice for 20 min at room temperature in $2 \times$ SSC, 0.1% sodium dodecyl sulfate and twice at 35 °C in $1 \times$ SSC, 0.1% sodium dodecyl sulfate. Autoradiography was performed for 6–16 h at –70 °C using Kodak XAR-2 film, and plaques hybridizing with both probes were identified. Similar screenings were done until plaque purification was complete.

Essentially the same procedure was employed for the screening of the cDNA library using the following probes: the 353-bp *Bst*II fragment (bp 1–353) of the murine FcRI γ subunit (9), the first 30 and last 29 base pairs of the open reading frame of the rat γ chain (bp 23–52 and 255–283, respectively) (11), and the 5.1-kb *Sall* fragment of the human gene containing its 5' end.

Sequencing—Two restriction fragments of the genomic clone were found to hybridize with the 3' and 5' ends of the rat γ subunit cDNA: a 5.1-kb *Sall* fragment containing exon 1 and part of exon 2 and a 2.1-kb *Hind*III fragment spanning from before the second exon until after the end of the gene. These two fragments overlapped by 300 bp. After subcloning into the pBS⁺ phagemid vector (Stragagene), the DNA to be sequenced was purified from bacterial lysates via double cesium chloride density gradient centrifugation or polyethylene glycol precipitation. The genomic 2.1-kb *Hind*III fragment was subject to nested deletions employing the erase-a-base system (Promega Biotec) as recommended by the supplier. Single-stranded DNA was recovered from several colonies from each time point using the helper phage M13KO7 (Promega Biotec) in the presence of kanamycin (5 μ g/ml). Sequencing was performed by the dideoxy chain termination method using fluorescent M13 primer and Sequenase or Taq polymerase (Model 370 DNA sequencing system Taq DNA polymerase, Applied Biosystems, Inc.) and analyzed on a Model 370 automated sequence analyzer (Applied Biosystems, Inc.) as recommended in the manufacturer's protocol. Gaps were filled by classical radioactive dideoxy sequencing of double-stranded DNA (Sequenase kit, United States Biochemical Corp.) using 21-base pair unlabeled oligonucleotide primers synthesized on a Model 380B synthesizer (Applied Biosystems, Inc.). In addition, all exons were sequenced by radioactive sequencing on both strands to confirm the correctness of the sequence. No discrepancies between the results obtained with these two methods were detected. DNA sequences were analyzed using the program MacVector (International Biotechnologies).

Other Methods—The determination of the 5' end of the gene was accomplished according to standard procedures (12). A 550-bp probe complementary to the sequence upstream of bp +46 in Fig. 2 was prepared by extension of a 5' end-labeled 21-mer synthetic oligonucleotide. The labeled probe was hybridized overnight at 30 °C with 2 μ g of polyadenylated RNA from basophil-enriched leukocytes or with 40 μ g of tRNA and digested with 1000 units of S1 nuclease at 30 °C for 1 h.

Primer extension using an end-labeled oligonucleotide complementary to bp 26–46 in Fig. 2 was accomplished by hybridizing 2 μ g of poly(A) RNA or 20 μ g of tRNA overnight at 55 °C followed by extension with reverse transcriptase at 45 °C for 90 min.

IgE rosetting assays were performed as described before (11), and the Southern blots as specified elsewhere (13).

RESULTS AND DISCUSSION

Genomic Cloning—A 33-kb genomic clone was isolated from a human leukocyte genomic library by screening with rat γ subunit cDNA probes. Two restriction fragments were generated from this clone. One of these hybridized with a probe corresponding to the 5' end of the rat γ chain, and the other hybridized with a 3' end-containing probe. Both fragments were entirely sequenced (Fig. 1). The organization of the human γ subunit gene was determined from consensus sequences for exon-intron boundaries (14). The transcription initiation sites were mapped using primer extension assays (Fig. 2) and confirmed by S1 nuclease protection assay (data not shown). These experiments showed the major start site to be 25 bp upstream of the start codon. Indeed, this site corresponds to the beginning of one of the cDNA clones that we isolated (see below). Other potential initiation sites are

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-500 tgatcaacat ggagaacccc catctctact aaaaatacaa aattagctgg
-450 gcgtggtggt gcatgcctgt aatgccagct actcggggagg ctgagagaaat
-400 cgcttgaacc tgggaggcgg aggttgccggt gagcccgagat ggcgcatttg
-350 cactccagcc tgggcaacaa agcaagagctc cgtctcaaaa aaaaaaaaaa
-300 aaaaaaaaaa ctgaaccagg tggagtgga aatggcagat gtgacagcc
-250 tttctcagc gtgagagctc cctcattctt ttgggttaga gttggtcatt
-200 gaagggctga cgcttaagag cccagatctc ccaactccct tagttggcct
-150 tccgggagac gacgggtctc ttgtgcagga aggggaagg gccaagcat
-100 gggggaagcc gtggcaggaa gagggggact ctgtggtcag ggaactgctc
-50 gctgagcaca gctgcacagt gctgtCAGAA CGGCCGATCT CCAGCCCAAG
+1 ATGATTCCAG CAGTGGTCTT GCTCTTACTC CTTTGGTTG AACAGCAGG
51 taagagggtt tgtgagggat agcgtgantg gctccagggt ggaagtccag
101 agcttgggtc tgaggggcaa gtcaaacaca ggtgaaggaa gggtgacagt
151 gggtaggtgg gcataggagg accctgaggg tagtccctct cagcccgac
201 ccagggcaat agactcatag ttccctcctt tcttnttggc ttcttacttc
251 attccagatc tttctccgta ttattattat tattttggag atggagctct
301 gctctgtcac ccagggtgga gtgacgtggc gcaactctta ctgactgcaa
351 cctctgcctc ctgggttcaa gcgattctcc tgectcaggc tcccagtagt
401 ctgggactac aggtgcccgc caccacgccc ggttaagta agtattttg
451 gtagaacccg gtttctgcga ttgtgacagg tagtgccttg aactctgac
501 tcaagtgtac caccacccct gacctcccaa agtgctggga ttactggtgt
551 gagccactgc acccagctat tattattatt aaaaaagac agggctctac
601 ttggttggcc acatcgtctc tgaactccgt gcctcaagca attctccac
651 ctgcgctccc caaagtgtca ctgtgcctgg ctgacttttc tcttttcagg
701 gttgatccaa agtggcaggg gaagggtctg gttgtaggc atgaagagct
751 ggtctgtgta aacgcctcat ttctcatgat gagcatttcc catggggtgc
801 ctttgggtct gtctgctggg agctgatctc tagctggttt aatatacaaa
851 gcacccttgg tncataaatt cagactgactc gaagagctga ccagagagaa
901 tcaactgaac ccaggagggt gaggttcagc tgagccaaga tcgccacct
951 gacattctagc ctgggggaca gtagtagact ccgtctcaaa aaaaaaaaaa
1001 agattttaca tataatctct tatctatcta tctatataca cacacacaca
1051 catcacaca cacacacaca cacacacaca cacatatata tatatataga
1101 gagagagaga gagagagaga gagagagaga tacccttag gaaggtagga

1901 tgatttgatt ttttaattg cacaacactt cccctctcag agaccagag
1951 agtgagtaat agggcagagt aacaggagnt ggaatccata tagctgtggt
2001 catccccca gccttngtgg caggngnaaa ggtatctgta aggtctggnn
2051 nnaacacaga cacttttttt tttttttttt tttttttaca tttttaagtt
2101 tcttgtggtg gnnnagaaga caacaaggct ganctaggag atgaccaatg
2151 atagagtaat tgcttctctc cctctcccca gctcacatcc ttccgtgcca
2201 gccctcagcc acaggtcaca gaacttagta gagactagta tttgggttct
2251 tcaactgaat ttgccactac ctctccctcc cactaccatc ctggctgag
2301 gttttgggtt cagtcagagt gactcagatg ggtcccttga ggtggataaa
2351 gtgctcaatg gtgctgaag aaccacagt ctcaaaaaga aaaggtggg
2401 ggctgagggg gaaggcctcn attattagtc cgtgtgagtc ccatttcaat
2451 agaaccccca agcttctcat ctagcctcag ccacttaggtg tgggaggagg
2501 gaagggtgaag ggcagtgga gggcagtaga aacagaaatt tcttcccta
2551 gacggctccc ctccaggcnc tgcctacac cccagagccc ctctcccttc
2601 ctccctctag taccagatcc tccctgatac ccccgacccc atgggcatcc
2651 tctatcccc cagCGGCCCT GGGAGAGCCT CAGCTCTGCT ATATCTGGA
2701 TGCCATCTCTG TTTCTGTATG GAATGTCTCT CAGCCTCTCT TACTGTCCAG
2751 TGAGgtagc gctgggagg gtgggtaag ggtcgaagg ggaagtgga
2801 ggaaggagc agcaaggatt cgaagagaag gaataaaagg ggaatccca
2851 caaagtttgg aggggaaggg gatgggacct taacttacc ttactgata
2901 accttctccc cattccagAT CCAAGTGGCA AAGCAGCTA TAACAGCTA
2951 TGAGgtatgg accctctac acctggtgtg gacaactttt cagacctca
3001 gccctctcgg ggctctagcc ttgggtttcc ggccctctgg gagggctgcc
3051 tctcaggtgc tgatctgcac acactcttgc ccactccctc ccacttacc
3101 tagccaagcc acaagtaaaa tatcagcagg tgacagggaa gaatcaagca
3151 tagagtata aagaatatgt gagagacttg ggttagatgt ctcgggtgta
3201 tatgtgtgct tgtagccatg ttgggcaaca ggtatcatgt cccagagtgt
3251 ccatgtgagt gccctctagc ccaaggtggc tggctgccc cccccatgc
3301 tcccttgggt ggggagagat ctgagggggc ctggagaaag ttgggtctt
3351 taatcttttg ctctcttttg ctctgcagAA ATCAGATGGT GTTTACACGG
3401 taagtgtgcc tacctcccc acccaggaag tcagcagaag aggtgggat
3451 tttgagcgt ctttgaagg ccggtggggg gaggggggct tgtggaggt
3501 ggggagggcc tctgatggac tcagctcct gatcgccctt tgactccat
3551 ctccagggcc TGAGCAGCAG GAACAGGAG ACTTACGAGA CTCTGAAGCA
3601 TGAGAAACCA CCACAGTAGC TTAGAGTAG ATGCGGTCTT ATTCTCTTT
3651 GGCTTCTGGT TCTCCAGCC CTCATGGTTG GCATCACATA TGCCGCTAG
3701 CCATTAACAC CAGCTGGGCC TACCCCTATA ATGATCTGT GTCTAAAT
3751 AATATACAGC AGTGGTTTCT CTTCCCTGTT AAAGACTAAT GTCAGATGC
3801 TGTTTACGGA TATTATATT CTAGTCTCAC TCTCTGTCC CAGCCTTCTT
3851 CTCTTCCGCA TTCCCACTC CAGCTAAAAT TTGGGAAGGG AGAACCCCA
3901 ATAAACTCTC CATTGACTGC ACTCTTATCA ttcatctatt cattatcat
3951 agatttattc agtctctgct aagcactaga tacagctttt cagttccaga
4001 actcacagtc taatggactt cagagctatt ttgctcgact gagggataaa

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FIG. 1. Sequence of gene for human Fc receptor γ chain. The numbers on the left refer to the nucleotide number beginning at the start codon as position +1; nucleotides preceding it are represented by negative numbers. The start and stop codons, the polyadenylation signal, and the CAAT and the GC boxes are in **boldface**. Exons are indicated by underlined upper-case letters and introns by lower-case letters. The major transcription initiation site is shown as the start of the first exon. The portion of the first intron which is not shown has now been sequenced. The complete sequence of the gene has been submitted to GenBank. Bases which could not be assigned with certainty are denoted by *n*.

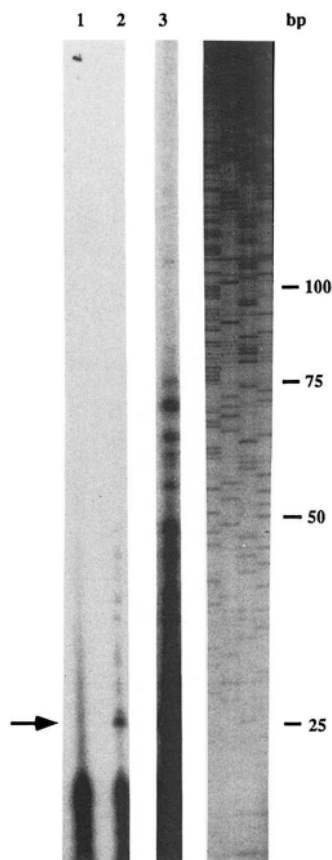


FIG. 2. **Determination of transcription initiation sites.** An end-labeled oligonucleotide complementary to bp 35–56 in Fig. 1 was hybridized to tRNA as a negative control (lane 1) or to poly(A) RNA from basophil-enriched leukocytes (lane 2) and extended with reverse transcriptase, and the product was separated on an 8% polyacrylamide gel. Lane 3 represents an overexposure of lane 2 to show the minor start sites. A sequencing reaction of a known stretch of DNA was run as a size standard in parallel on the right. The numbers on the far right refer to the distance to the start codon. The arrow points to the major transcription initiation site.

also seen further upstream up to bp –109. As is usual with multiple start sites, no TATA box is observed in the region which should contain the promoter (15, 16). However, a GC-rich region, which includes a GC box in reverse orientation, is found upstream of the transcriptional start sites at positions –149 to –135 before the start codon. Further upstream, a CAAT box is located in reverse orientation at bp –199. 5' of the potential promoter region, an Alu sequence is found, ending with a 23-bp poly(A) at position –290.

The complete gene spans 4 kb, contains five exons, and has been entirely sequenced (Fig. 1). The first exon contains the entire 5'-untranslated region and most of the leader peptide. It is followed by a large intron of 2.6 kb, which represents 67% of the total gene and contains Alu sequences. The second exon encodes the last 5 base pairs of the leader peptide, the short extracellular domain, the transmembrane region, and the first 9 base pairs of the intracellular portion. It is followed by two short exons of 36 and 21 base pairs. Introns 2 to 4 span 163, 424, and 157 bp, respectively. The remainder of the intracellular tail is found in the fifth exon, which is 368 bp long and includes the entire 3'-untranslated sequence.

A unique polyadenylation signal (AATAAA) is found 25 bp upstream of the end of the last exon. The latter is immediately followed by a T-rich sequence probably involved in the termination of the mature mRNA (17). The calculated total length of the mRNA (591 bp) is in agreement with results

obtained by Northern blots (750 bp) (18) if one accounts for the poly(A) tail.

The five exons should generate transcripts encoding a polypeptide of 86 residues, identical in length to the previously sequenced mouse (9) and rat (11) γ chains (Fig. 3). A leader peptide of 18 amino acids is followed by a short extracellular segment of 5 residues, a transmembrane domain of 21 residues, and an intracellular tail of 42 amino acids. Among mouse, rat, and human γ chains, 86% of the bases are identical in the open reading frame compared to only 60% in the overall sequence. The polypeptide contains 86% identical amino acid residues among the three species. The high level of conservation in the γ chain polypeptide contrasts with a low level in the α chain polypeptide, where only 36% identical amino acids are found in the corresponding species (9). It is reasonable to postulate that the structure of the γ chain has been maintained because of its functional importance.

Comparison of Fc Receptor γ Chain and TCR ζ Chain Genes: A New Family of Genes—The genes for the γ chain of Fc ϵ RI and of other Fc receptors (see below) and for the ζ chain of the TCR (16) show analogous organizations of their respective exons (Fig. 4). Exon 1 of both genes encodes most of the leader peptide. Exon 2 corresponds to the last 2 amino acids of the leader peptide, the short extracellular region, the transmembrane domain, and the first 3 residues of the intracellular segment. The remainder of the cytoplasmic tail is encoded by short exons of 21–81 bp. When compared to the γ subunit gene, there is an insertion of three additional exons in the ζ subunit gene, resulting in a cytoplasmic tail that is 70 amino acids longer. The last exon of the γ chain (exon 5) encodes the final 20 amino acids and that of the ζ chain (exon 8) encodes the final 21 amino acids; and in both cases, the last exon also contains the entire 3'-untranslated sequence.

The second exon of the γ chain is homologous to the second exon of the ζ chain: 58% identical amino acids are found between human γ and ζ chains and 55% between mouse γ and ζ chains (9). Similarly, the last two exons of γ and ζ chains show a significant level of homology which was previously undetected: 33 and 44% identities between mouse γ and ζ chains and between human γ and ζ chains, respectively. It should be noted that the ζ chain, unlike the γ chain, has been proposed to contain a consensus sequence for an ATP-binding site (19) within the C-terminal part homologous to the γ chain, although binding of ATP has not yet been shown directly. The localization of the γ and ζ subunit genes on mouse chromosome 1 (20, 21), their similar genomic and structural organization, and the sequence homologies imply that gene duplication has generated these two genes. A later insertion or deletion of three exons could explain the difference of length between γ and ζ chains.

In addition to sharing a common genomic structure, both γ and ζ chains form disulfide-linked homodimers. Since the ζ chain contains only 1 cysteine residue located at the external border of the transmembrane domain, this residue must be involved in the dimerization of ζ chains. Therefore, the corresponding cysteine in the γ chain is likely to participate in a disulfide bridge between γ chains. Whether the second cysteine, present in the γ chain at the internal border of the transmembrane helix, is also involved in an additional disulfide bridge remains to be determined. Furthermore, both polypeptides associate noncovalently with other subunits to yield multimeric complexes. The type of interaction of the γ chain with α and β chains in Fc ϵ RI is reminiscent of the association of the ζ chain with $\alpha\beta$ chains and the CD3 complex in the case of the TCR. Both γ and ζ chains dissociate easily during solubilization, but their association with the other

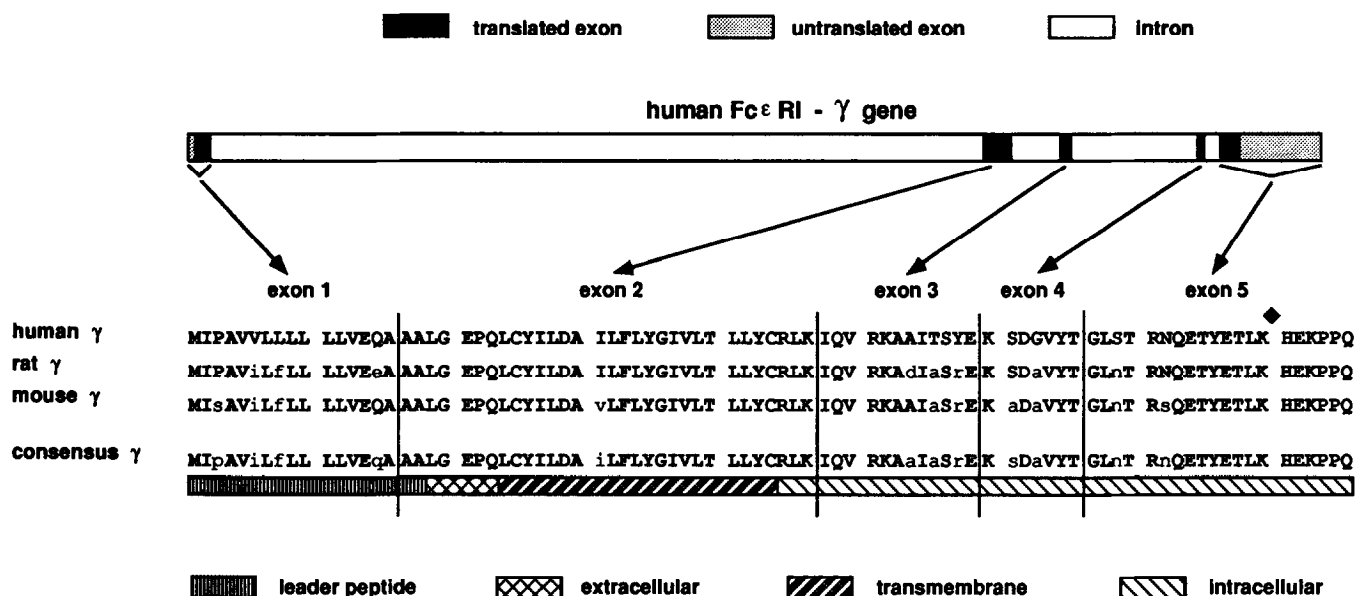


FIG. 3. Genomic organization of γ subunit of human Fc receptor (top) and comparison of γ chain polypeptide sequences between species (bottom). The relative positions of the exons and introns are depicted. The alignment of the three species was accomplished with the program MacVector. In the consensus sequence, an upper-case letter indicates a perfect match between all three species, and a lower-case letter indicates a match between two. Interruptions by vertical lines refer to the exon boundaries of the human gene. The black diamond shows the presumed post-translational cleavage site (11).

subunits can be maintained when the appropriate detergent and concentration are used (22–24).

Differential Requirements in Expression of Human and Rodent $\text{Fc}\epsilon\text{RI}$ Receptors—To facilitate expression studies, we isolated cDNA clones corresponding to the human γ chain. A basophil-enriched leukocyte cDNA library was screened with rodent γ chain probes, and four clones of 1.6 kb were isolated. Their sequence in the open reading frame was identical and corresponded exactly to the predicted sequence from the gene. Interestingly, the flanking regions contained Alu sequences with sequence variations between the clones (data not shown). These variations are not necessarily surprising since the library was prepared from the blood of several individuals. Whether they correspond to allelic differences, to polymorphisms, or possibly to the existence of more than one gene is currently under investigation.

Four independent transfections of COS-7 cells with the human α chain resulted in only 0.007% of the cells expressing IgE receptors as measured by an IgE rosetting assay (Table I). In contrast, cotransfection of human α and γ subunit cDNAs yielded $6.5 \pm 1.4\%$ rosetting cells. Cotransfection of rodent β subunit cDNA together with human α and γ subunit cDNAs did not increase the efficiency of expression: $5.6 \pm 3.1\%$ rosetting cells were observed. In contrast, rodent $\text{Fc}\epsilon\text{RI}$ can only be expressed efficiently on the cell surface by co-

transfection of all three cDNAs. Therefore, the requirements for efficient expression of the α chain on the cell surface are clearly different between rodent and human.

Moreover, we found that the surface expression of other Fc receptors, mouse $\text{Fc}\gamma\text{RIIa}$ (25) and human $\text{Fc}\gamma\text{RIII-2}$ (26–28), also required γ chains identical to those from $\text{Fc}\epsilon\text{RI}$ (6, 7). Taken together, these observations underline the critical role played by γ chains in allowing $\text{Fc}\epsilon\text{RI}$ and these other Fc receptors to reach the cell surface.

The ability of the γ chain to allow surface expression of α chains of $\text{Fc}\epsilon\text{RI}$ is analogous to the role of the ζ chain in the expression of the TCR-CD3 complex. In the intracellular sorting of the murine T-cell receptor, the ζ chain is necessary for the complete complex to reach the cell surface (29, 30). In its absence, the TCR pentameric complex ($\alpha\beta\gamma\delta\epsilon$) assembles in the endoplasmic reticulum and is then targeted to lysosomes. The ζ chain specifically prevents this degradation pathway and permits only the complete heptameric complex ($\alpha\beta\gamma\delta\epsilon\zeta_2$) to reach the plasma membrane. It will be interesting to assess whether differences between the murine and human systems will be observed as in the case of $\text{Fc}\epsilon\text{RI}$. Future studies will have to address whether the role of the γ chain for the Fc receptors is similar to that of the ζ chain for the TCR. Since signal transduction studies have already shed light on the possible role of the ζ chain (31), it will now be of great

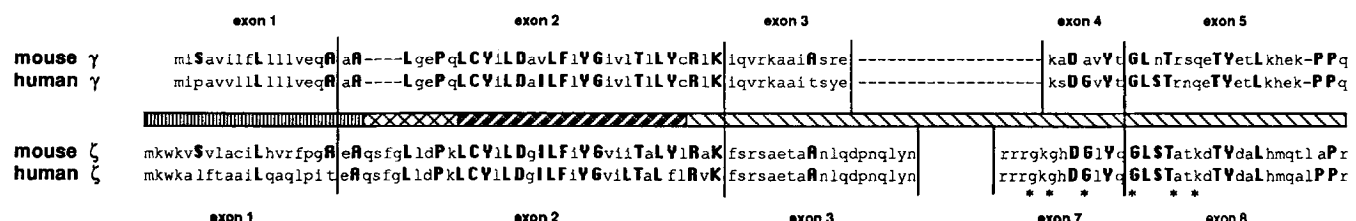


FIG. 4. Alignment of the Fc receptor γ chain and TCR ζ chain. Assuming a similar genomic organization for the different species, an alignment is shown between human and mouse γ and ζ chains as described for Fig. 3. Asterisks indicate the amino acids of the ζ chain corresponding to the consensus sequence for an ATP-binding site (19).

TABLE I
Transfection experiments in COS-7 cells

Transfected genes	Surface expression	
	Rosetting cells	n
	%	
Rodent genes ^a		
— ^b	0	10
α	0.004 $\pm$ 0.002	6
$\alpha\beta$	0.015 $\pm$ 0.007	2
$\alpha\gamma$	0.016 $\pm$ 0.005	2
$\beta\gamma$	0	1
$\alpha\beta\gamma$	3.9 $\pm$ 1.6	26
Human genes		
—	0	10
α	0.007 $\pm$ 0.003	4
$\alpha\gamma$	6.5 $\pm$ 1.4	4
Chimeric combination		
$\alpha_{\text{human}}\beta_{\text{rodent}}\gamma_{\text{human}}$	5.6 $\pm$ 3.1	4

^a Refers to rat and mouse genes; data for rodent genes are from Ref. 9.

^b —, negative control.

interest to evaluate whether similar properties can be attributed to the γ chain.

The ζ - γ chain family may contain more members and be important in signal transduction. It is likely that the η chain of the T-cell receptor will be another member. In addition to sharing structural similarities with the ζ chain, the η chain forms a heterodimer with the ζ chain and seems to be involved in signaling (32). Other potential candidates are the recently discovered γ chain that is disulfide-linked to the β subunit of the interleukin-2 receptor² and the 12-kDa molecule associated with the ζ chain in CD3 negative natural killer cells (33).

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