In this study the gene for the murine interleukin-11 receptor α-chain (IL-11Rα) has been characterized. The gene spans 9 kilobase pairs of DNA, and the organization of its 14 exons conforms to the pattern observed for other members of the hematopoietin receptor family. Analysis of the 5' end of the cDNA using 5' RACE showed that the first two exons, designated exons 1a and 1b, are spliced to form alternate transcripts. Transcripts initiating from exon 1b were not found in adult tissues but were present in embryonic stem cells. S1 nuclease and 5' rapid amplification of cDNA ends assays demonstrated multiple major and minor sites of transcription initiation for each exon. The putative promoter regions of both exons lacked TATA boxes, although potential recognition sites were present in the transcription initiation region of exon 1b. 

Northern analysis showed that IL-11Rα is expressed in many adult murine tissues. A second IL-11Rα-like locus containing a sequence homologous to exons 2-13 was also identified.

Interleukin (IL)-11\(^1\) was initially identified because of its ability to stimulate an IL-6-dependent plasmacytoma line (I), and subsequent work has revealed pleiotropic biological actions (2, 3). Most of these activities are shared with other cytokines including IL-6, leukemia inhibitory factor, ciliary neurotrophic growth factor, and oncostatin M (3–7). Responses to IL-11 and these other cytokines are mediated by binding of the growth factor to multisubunit receptor complexes expressed on the surface of target cells, and the overlap in biological functions may be explained in part by the sharing of receptor subunits. All the receptors involved in the formation of these complexes are members of the hematopoietin receptor family and two subunits, the leukemia inhibitory factor receptor α chain and gp130, are components of several receptors (8). IL-6, for example, binds with low affinity to its specific α chain and with high affinity to this α chain together with two gp130 subunits (9). Similarly, IL-11 binds to the interleukin-11 receptor α chain (IL-11Rα) with low affinity and to a complex of IL-11Rα and gp130 with high affinity (10).

Recently, cDNAs encoding both the murine and human α-chain of the IL-11 receptor have been cloned (10–13). The murine gene cloned by Hilton et al. (10) was identified by screening an adult mouse liver cDNA library with oligonucleotides corresponding to the WSXWS motif of the hematopoietin receptor family. When the receptor was transfected into cells it bound IL-11 with low affinity in the absence of gp130 and yielded a functional high affinity receptor in the presence of gp130 (10, 13). Neuhau et al. (11) isolated the same cDNA, which they called E12, from embryonic murine cDNA libraries using genomic probes. The genomic probes were obtained by screening a C57BL/6 genomic library with sequence flanking the integration site of an enhancer trap construct insertion in the genome of an embryonic stem (ES) cell line. These cells did not express the lacZ reporter gene present in the integrated construct in the undifferentiated state but did so in restricted regions of chimeric postimplantation embryos (11, 14). Approximately 40 kilobase pairs (kb) of genomic DNA downstream of the enhancer trap insertion was mapped using cDNA probes. Exons 2–13 were identified, but exon 1 could not be located in this region.

In this report we describe how, in the course of mapping the genomic locus of the IL-11Rα, we found an additional IL-11Rα-like locus present in the genome of some mouse strains. We describe the genomic organization of the functional IL-11Rα locus, which encodes two exons upstream of the exon containing the ATG start site. Evidence is presented that the two exons are utilized in alternatively spliced transcripts and the transcriptional start sites for each are identified. The structure of the second locus, which corresponds to the locus mapped by Neuhaus et al. (11), was also determined. In addition we present data describing the expression pattern of the IL-11Rα gene in adult murine tissues.

EXPERIMENTAL PROCEDURES

Isolation and Subcloning of the IL-11Rα Gene—A murine 129Sv liver genomic library in lambda Fix II vector (Stratagene) was screened with a IL-11Rα cDNA probe to obtain overlapping clones of the IL-11Rα gene. The probe was labeled with \((\alpha^32P)dATP\) using a random primer labeling kit (Bresacat) to a specific activity of \(>5 \times 10^6 \text{cpm/ug}\). Plaques were transferred to nitrocellulose filters and hybridized for 16 h at 65 °C in 2 × SSC (1 × SSC is 0.15 m NaCl, 0.015 m trisodium citrate), 10 × Denhardt’s solution (0.2% Ficol, 0.2% polyvinylpyrrolidone, 0.2% bovine serum albumin, 2 m sodium pyrophosphate), 1 m ATP, and 500 \(\mu\)g/ml Escherichia coli tRNA (Boehringer Mannheim) and washed at 65 °C in 0.2 × SSC, 0.1% SDS. Positive plaques were purified, and DNA was isolated using standard procedures. Phage DNA was digested with restriction enzymes and mapped by Southern blot analysis using

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oligonucleotide probes that were end-labeled with $^{32}$P[PATP using T4 polynucleotide kinase. Ordered HindIII and EcoRI fragments or the entire insert from the λ clones was subcloned into pUC18 or Bluescript SKII (Stratagene).

Genomic Southern Blot Analysis—DNA was prepared from murine tissues or cells using standard procedures or was purchased from the Jackson Laboratory. Samples were digested with restriction enzymes according to the manufacturer’s instructions (Boehringer Mannheim), electrophoresed through agarose gels, transferred to nylon membrane (GeneScreen Plus, DuPont NEN) by alkaline blotting, and hybridized with radiolabeled probes in dextran sulfate hybridization mixture (1 M NaCl, 10% dextran sulfate, 1% SDS, 100 μg/ml sheared salmon sperm DNA at 65°C). Membranes were washed in 0.2 X SSC, 0.1% SDS at 65°C prior to autoradiography. Estimation of copy number was performed using quantitative analysis on a PhosphorImager system (Molecular Dynamics).

Nucleotide Sequence Analysis of the IL-11Rα Gene—Plasmid DNA, purified on a cesium chloride gradient, was used as the template, and synthetic oligonucleotides were used as primers. DNA sequences were determined by using the Prism Ready Reaction Dye Deoxy Terminator Cycle Sequencing kit (Applied Biosystems) along with the 373A DNA sequencer (Applied Biosystems).

Reverse Transcriptase PCR Analysis of IL-11Rα Loci Expression—Poly(A)+ RNA was prepared from murine tissues by proteinase K/SDS extraction and oligo(dT) selection. Total RNA was prepared from bone marrow using Trizol reagent (Life Technologies, Inc.), and all samples were treated with RNase-free DNaseI (Boehringer Mannheim) prior to cDNA synthesis. Oligo(dT)-primed cDNAs were prepared in a 20-μl volume from 50 ng of total RNA or 5 ng of poly(A)+ RNA using AMV reverse transcriptase (RT; Boehringer Mannheim) under conditions recommended by the manufacturer. 1 μl of cDNA was used for PCR amplification in 20-μl reaction mixtures containing 1 × PCR buffer (Boehringer Mannheim), 0.2 μM each dNTP, 0.5 unit Taq polymerase (Boehringer Mannheim) with 100 ng of primer. The primers used to amplify the IL-11Rα cDNA fragment used for restriction fragment length polymorphism studies were: 5′-CTGCAAGGCTTCTTGGCA-GCCGG-3′ and 5′-CGTGCACCTCCTCTCCCCTCGTCT-3′. PCR conditions were 25 cycles, 95°C for 30 s, 60°C for 30 s, and 72°C for 60 s for 30 cycles. Prior to digestion with diagnostic restriction enzymes, the reaction mixture was phenol-chloroform extracted. Digested and undigested samples were electrophoresed through 6% high resolution agarose (Progen) gels, transferred to nylon membrane, and probed with oligonucleotide probes in 6 × SSC hybridization solution. For sequencing of PCR products the primers 5′-GGAAGCTTTCCACCTGATCAGTG-3′ and 5′-GCCAGGACATGAGACACAGCT-5′ were used. PCR reactions as described above, and relevant fragments were excised from agarose gels, purified, and subcloned into pCR II (Clontech).

5′ RACE and S1 Nuclease Mapping—5′ RACE-PCR was performed using a kit (Clontech) with 1 μg of poly(A)+ RNA from C3H/HeJ kidney or 129Sv ES cells. The IL-11Rα cDNA probe was made by generating a 1.6-kb fragment (nt 126-1690) of the IL-11Rα genomic locus. Purified phage clones were mapped by restriction enzyme digests and hybridization to oligonucleotide probes corresponding to various regions of the IL-11Rα cDNA. This revealed that two classes of phage clones were present, corresponding to two different but related loci (loci 1 and 2, Fig. 1). For each of the two loci, three overlapping phage clones encompassing the entire locus were characterized in detail.

To confirm the presence of two loci in genomic DNA, Southern blots of 129Sv genomic DNA were probed with a radiolabeled 1.1-kb BamHI genomic fragment from probe clone 11.4 as a probe. When DNA was digested with BamHI, this probe hybridized to the expected 1.1-kb band, and also detected additional bands at 850 and 250 bp, which corresponded to locus 2 (which has a BamHI site in exon 10 (Fig. 2B)).

The overall structure of both IL-11Rα-like loci was determined by completely sequencing each. The two published sequences of the IL-11Rα cDNA differed upstream of the ATG (10, 11). Locus 1 both 5′-untranslated region, 1′S, and 3′ untranslated region were presented. One, designated exon 1b was 1.2 kb upstream of exon 2, whereas the other, designated exon 1a, was a further 1.9 kb upstream of exon 2 (Fig. 1). Locus 1 clones contained all the sequence of the IL-11Rα cDNA in 14 exons spanning approximately 9 kb. The structure of locus 2 was identical to locus 1 except that exons 1a and 1b were not present. The sequence of the two loci diverged 800 bp upstream of exon 2 and comparison of 2 kb of this upstream sequence with the EMBL and GenBank data bases did not reveal homology to other data base entries. Despite sequencing for 4 kb downstream of exon 13, the divergence point between the two loci was not identified. Within this region the two loci were highly homologous (approximately 95% nucleotide identity) except for a 636-bp insertion in the second exon (shown as a broken line in Fig. 1). Southern hybridization of genomic probes containing exons 1a or 1b to murine 129Sv genomic DNA to showed that these exons were present only in a single copy (not shown).

Sequence of the Genomic IL-11Rα Gene—The sequence of the exons of the IL-11Rα gene agreed with the cDNA sequences present in the GenBank data base except for nucleotide 20 of exon 1a (G→C), the absence of nucleotide 17 of exon 1b and a single nucleotide difference, resulting in an amino acid substitution at codon 337 (Val→Ala), which was in agreement with one published sequence (11) but not the other (10).

The intron-exon structure of the IL-11Rα gene was similar to that of other members of the hematopoietin receptor family (Fig. 3). The 5′-untranslated region was generated by exons 1a and 1b (which are utilized in alternative transcripts, see below).
The immunoglobulin-like domain was encoded by exons 3 and 4 and the two halves of the hematopoietin receptor domain by exons 5–9. In contrast with other members of the hematopoietin receptor family, a 34-bp exon (exon 6) was present between the exons containing conserved cysteine residues in the first half of the hematopoietin domain (Fig. 3). The transmembrane domain was encoded by exon 11 with exons 12 and 13 coding for the cytoplasmic portion of the receptor. Intron-exon junctions around and between the hematopoietin receptor subdomains (flanking introns 4, 7, and 9) occurred after the first nucleotide of a codon (phase type 1), a feature that is conserved in the hematopoietin receptor family (16, 17). All splicing junctions followed the GT-AG rule, and the extended sequence around the splice donor and acceptor sites was consistent with the consensus sequences established for mammalian genes (Table I) (18, 19).

and exon 2 contained the ATG-start codon and signal sequence. The immunoglobulin-like domain was encoded by exons 3 and 4 and the two halves of the hematopoietin receptor domain by exons 5–9. In contrast with other members of the hematopoietin receptor family, a 34-bp exon (exon 6) was present between the exons containing conserved cysteine residues in the first half of the hematopoietin domain (Fig. 3). The transmembrane domain was encoded by exon 11 with exons 12 and 13 coding for the cytoplasmic portion of the receptor. Intron-exon junctions around and between the hematopoietin receptor subdomains (flanking introns 4, 7, and 9) occurred after the first nucleotide of a codon (phase type 1), a feature that is conserved in the hematopoietin receptor family (16, 17). All splicing junctions followed the GT-AG rule, and the extended sequence around the splice donor and acceptor sites was consistent with the consensus sequences established for mammalian genes (Table I) (18, 19).

The nucleotide sequence of the exons for locus 2 was very similar to locus 1. The amino acid substitution at codon 317 was also present in this locus. Fourteen other nucleotide changes were identified, three of which resulted in changes in the predicted amino acid sequence; codon 283 (Ala → Thr), codon 319 (Pro → Leu), and codon 401 (Asp → Glu). The other changes were conservative. The intronic sequences were also well conserved (approximately 96% identity). The intron-exon borders were identical in the two loci.

Locus 2 Is Not Present in All Mouse Strains—Genomic DNA samples from fourteen mouse strains were digested with SacI, BamHI, and SphI and probed with cDNA probes. As illustrated in Fig. 4, four of the fourteen strains lacked locus 2. The absence of the locus 2 in these strains was confirmed with Southern analysis using additional restriction enzyme digests and cDNA probes, thereby establishing that the apparent absence of bands corresponding to the second locus was not due to a restriction fragment length polymorphism. In two strains, NZB/BINJ and AKR/J, densitometric analysis demonstrated that the intensity of the bands corresponding to the locus 2 was increased more than 6-fold relative to that of the IL-11Rα locus. This observation suggests that more than one copy of locus 2
per haploid mouse genome is present in these strains.

Tissues from different mouse strains were screened for mRNA transcripts originating from locus 1 or 2 using an RT-PCR restriction fragment length polymorphism strategy. Seven bone marrow and kidney RNA samples were analyzed: in four locus 2 was present, and in three it was absent. These samples were reverse transcribed, and PCR was performed using primers within IL-11Rα exons 10 and 12 (see "Experimental Procedures"). In exon 11, locus 1 contained a SacI site that was absent in locus 2. In addition, a BamH I site was present in exon 11 only in locus 2. A portion of each RT-PCR product was digested with BamH I or SacI, and the undigested and digested samples were electrophoresed through 6% high resolution agarose gels, transferred to a nylon membrane, and probed with radiolabeled oligonucleotides. In each case the restriction fragment length polymorphism pattern in the amplified cDNA was consistent with transcripts arising from locus 1 (Fig. 5). To confirm this result, cDNA prepared from poly(A)+ RNA from C3H/HeJ kidney and 129Sv embryonic stem cells was amplified with primers lying within exons 10 and 12, and the 274-bp product was purified and subcloned into pCR II (Clontech). Thirty subclones, fifteen from each cDNA source, were sequenced. All were of locus 1 type (data not shown).

Identification of the Transcriptional Start Sites of the IL-11Rα Gene—To examine the 5’ end of the IL-11Rα mRNA, two independent approaches were used. None of the IL-11Rα cDNA clones we had obtained (10)2 contained exon 1b. Therefore 5’ RACE was performed to identifying initiation sites and to establish the splicing pattern of the two exons encoding the 5’-untranslated region. Using the anchor oligonucleotide and an oligonucleotide 527–503 nt upstream from the initiator ATG, a single PCR product of about 640 bp was detected on agarose gels by ethidium bromide staining and by hybridization with an internal oligonucleotide. 73 subclones of this 5’ RACE product were sequenced: 12 from adult kidney RNA, 21 from adult liver RNA, and 40 from ES cell RNA. All the transcripts from kidney and liver RNA contained exon 1a spliced directly to exon 2. In contrast, about 10% of positive subclones of 5’ RACE products from ES cell RNA contained exon 1b. All the exon 1b-type transcripts initiated in genomic DNA upstream of the published exon 1b cDNA and did not contain exon 1a. Transcripts containing both exons were not found despite screening several hundred transformants containing 5’ RACE products with exon 1a- and 1b-specific oligonucleotides. The multiple initiation sites identified upstream of both exons using the 5’ RACE strategy are indicated in Fig. 6. To determine which of these were major initiation sites, S1 nuclease was performed using probes specific for the two alternative first exons. The probes contained the first 82 bp of cDNA for exon 2 fused to a 503- or 298-bp genomic DNA fragment containing exon 1a (probe p1a) or exon 1b (probe p1b), respectively. Using p1a, three sites of transcription initiation were detected in RNA from kidney. The longest protected band, of 170 bp (Fig. 7), corresponds to the nucleotide shown as +1 in Fig. 6. This 5’ site lies 20 nt up-

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2 L. Robb, D. J. Hilton, and C. G. Begley, unpublished data.
The 5′-flanking regions of exons 1a and 1b were sequenced (Fig. 6). Neither contained TATAAA or CCAAT sequences. As indicated in Fig. 6, consensus binding sites for transcription factors such as Sp1, AP1, AP2, and c/EBP were present in the 5′-flanking regions (20). GATA (21), NF-κB (20), and Ets (22) recognition sequences were present upstream of the exon 1a major site of transcription initiation. A purine-rich stretch (nt 260 to 277) was present upstream of the exon 1b major site of transcription initiation. This motif has also been found upstream of the cap site of other promoters of hematopoietin receptor genes that lack TATA boxes (16). Comparison of 390
bp upstream exon 1b with the sequence for the human IL-11Rα locus (23) showed 66% identity. Within this region, the purine-rich stretch, Ap2 and Sp1 motifs not in the murine locus were conserved in the human gene (Fig. 8).

Expression of the IL-11Rα Gene in Adult Tissues—Poly(A)⁺ RNA was prepared from tissues of adult BALB/c mice and E10.5 embryo and examined for expression of the IL-11Rα by Northern blot analysis with a radiolabeled probe from the region of the IL-11Rα cDNA encoding the extracellular domain (probe a, Fig. 1). A 1.8- and a 1-kb transcript were observed in all the tissues studied with the relative intensity of the two varying between tissues (Fig. 9). A similar pattern was observed when other cDNA probes from the extracellular domain were used. Message was most abundant in kidney, liver, and embryo. When the blot was stripped and reprobed with a SacI-EcoRI (nt 1202–1303) fragment from the region of the cDNA encoding the cytoplasmic portion of the receptor, only the longer transcript was detected. This suggests that the smaller transcript could encode a soluble form of the receptor. However, despite differential screening of kidney and liver cDNA libraries using both probes, we were unable to isolate alternative cDNA clones that could represent this transcript.

**Fig. 6.** 5' flanking sequence of exons 1a and 1b of the IL-11Rα gene. The 5' upstream sequences of alternative first exons 1a and 1b are shown. Intron-exon boundaries are displayed. The major start sites for each transcript, as determined by S1 nuclease analysis, is indicated as +1 and a large arrow. Other large arrows indicate additional start sites identified by S1 nuclease analysis. Transcription initiation sites identified by screening cDNA clones generated using 5' RACE are indicated by small arrows with the number of clones identified with this transcription initiation site shown. The potential recognition sequences for transcription factors are indicated. A purine-rich stretch upstream of the major site of transcription initiation upstream of exon 1b is shown in lowercase letters.

**Fig. 7.** S1 nuclease. Poly(A)⁺ RNA from kidney (K) (6 μg/lane) or ES cells (ES) (4 μg/lane) was hybridized with HindIII-cut, end-labeled probe 1α or probe 1b at 33°C for 2 h. S1 nuclease digestion was carried out at 30°C for 2 h. Yeast tRNA was used in parallel experiments as a control (C). The S1-digested products were run on a 6% polyacrylamide gel with end-labeled HindIII digested φX174 DNA as size markers. The sizes of the probes, protected fragments and of the size markers are shown in base pairs. Undigested probe (P) is indicated.
and Ap2 consensus sites are shown. A purine-rich stretch is indicated in legend to Fig. 6 and of the human gene as in Ref. 23. Exon 1b have been aligned. Exon 1b sequence is identical, and both contain a complete open reading frame, so it is possible that the second locus could encode a functional protein, despite the absence of the 5' exons. To test this, we used an RT-PCR-RFLP analysis to detect transcripts from this second locus in RNA prepared from the bone marrow and kidney of mouse strains that had both loci and, as a control, strains that lacked the second locus. In these tissues, within the limits of sensitivity of this detection strategy, transcripts from the second locus were not found. Nor were they detected by sequencing thirty cDNA subclones from C3H/HeJ kidney or 129SvES cells. Further analysis will be required to ascertain if locus 2 is transcribed or whether it is a pseudogene.

DISCUSSION

Southern analysis of murine genomic DNA and mapping of genomic phage clones using murine IL-11Rα cDNA probes detected the presence of two IL-11Rα-like loci. Both loci were characterized, and whereas one encoded the entire IL-11Rα protein, despite the absence of the 5' untranslated exons were the first exons of two alternatively spliced transcripts. Transcripts initiating from exon 1b were not found in adult liver or kidney but comprised around 10% of the IL-11Rα transcripts in ES cells. We did not find any cDNA containing exon 1b during hybridization screening of adult liver and kidney libraries. However Neuhaus et al., who obtained IL-11Rα cDNA clones from E11.5 and E12.5 embryo cDNA libraries, reported a cDNA containing only exon 1b (11). These results suggest that the exon 1b IL-11Rα splice variant may be confined to embryonic tissues and that alternative splicing of the first exon could provide a developmental control mechanism for IL-11Rα expression.

The IL-11Rα gene is a member of the hematopoietin receptor superfamily. These receptors are characterized by four cysteines and a series of alternating hydrophobic and polar residues in a characteristic spacing in the extracellular domain and a five-amino acid W6XW motif lying between the cysteines and the transmembrane domain (24, 25). Like the IL-6Rα, leukemia inhibitory factor receptor α, ciliary neurotrophic factor receptor α, granulocyte colony-stimulating factor receptor, and granulocyte-macrophage colony-stimulating factor receptor α, the IL-11Rα has immunoglobulin-like domains upstream of the hematopoietin receptor domain. Genetic structures of many members of this family have been reported, and comparison of these reveals a conserved pattern of structural homology. In most instances, the cytokine receptor motif is encoded by four exons. In the IL-11Rα an 11-amino acid exons separates the...

3 Nandurkar, H. H., Robb, L., and Begley, C. G., unpublished data.
two cysteine containing exons in the first half of the hematopoietin receptor domain. (Fig. 3). This additional exon is not present in other hematopoietin receptors. The pattern of intron phasing in the hematopoietin receptor family is highly conserved and this, together with the overall structural conservation, has led to the suggestion that the hematopoietin receptor family may have arisen by gene duplication from a single ancestral gene (16, 17, 26, 27). The process of gene duplication and (re)transposition are two mechanisms by which the hematopoietin receptor family may also have arisen. The high degree of sequence identity between the exonic and intronic sequences of the IL-11Rα locus and the second locus identified in this study suggests it may have arisen by a relatively recent partial gene duplication event.

As with many of the hematopoietin receptors, the regions upstream of the two alternate first exons for the IL-11Rα mRNA lack typical TATA boxes and have multiple initiation sites. The potential promoter regions do, however, have consensus sites for the binding of several transcription factors. The potential promoter regions do, however, have consensus sites for the binding of several transcription factors (Fig. 6). A purine-rich stretch upstream of the major site of transcription initiation has been identified in several of the hematopoietin receptors including human granulocyte-macrophage colony-stimulating factor receptor α, human granulocyte colony-stimulating factor receptor, human IL-2Rγ, and the human Mpl receptor (16, 28) and is present at nt −60 upstream of the exon 1b transcription initiation site. Comparison of the human and murine IL-11Rα loci revealed a high degree of conservation of the sequences upstream of the major site of transcription initiation of exon 1b, including conservation of the purine-rich stretch and Sp1 and Ap1 sites (23). The function of these putative regulatory sequences remains to be evaluated.

Northern analysis detected IL-11Rα expression at variable levels in all the adult murine tissues examined. Expression was also observed in E10.5 embryo and in ES cells. These observations are consistent with and extend those of those of Neuhaus et al. (11), who used in situ hybridization to demonstrate expression in the E8.5 yolk sac, in mesenchymal tissues at E10.5, and, after E10.5, in many developing tissues including mesenchymal tissue, vessels, peritoneal and ependymal cells, parts of the peripheral nervous system, epidermal and dermal structures, and skeletal elements. Unlike this study, they did not, however, observe expression of IL-11Rα in ES cells. In addition to the predicted 1.8-kb transcript, we also observed a 1-kb transcript. In some tissues, such as liver, and in ES cells, this was the predominant transcript. Because this shorter transcript was not detected using a cytoplasmic probe, it may encode a soluble form of the IL-11Rα. Alternative splicing has been implicated in the generation of soluble receptor forms of many members of the hematopoietin receptor family (reviewed in Ref. 29). Cherel et al. identified a shorter mRNA transcript of the human IL-11Rα that lacked the cytoplasmic domain, and they postulated that this might encode a soluble form of the receptor (12). We have, however, been unable to isolate murine cDNA clones encoding the short transcript, and until this is achieved, together with identification of protein isoforms of the IL-11Rα, the origin and any function of the short IL-11Rα transcript remains uncertain.

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