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Transcriptionally active DNA region that rearranges frequently in murine lymphoid tumors

(lymphoid tumor-associated translocation/aberrant immunoglobulin C_α gene/switch recombination site/sequence of recombination region/altered transcription)

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ABSTRACT **A DNA region not associated with conventional immunoglobulin gene rearrangement is rearranged in many lymphoid tumors. This region, designated here as lymphoid rearranging (LyR) DNA, was cloned from plasmacytoma J558 in which it had recombined 5′ to a constant (C) region of the α heavy (H) chain gene, C_α, within a switch (S) region, S_α, involved in the switching of C_H genes. Sequence determination established that LyR DNA had recombined within a S_α recombination unit. LyR DNA does not originate from the H chain locus, and discordance between LyR DNA and C_H copy number in certain lines suggests that LyR DNA probably derives from another chromosome. LyR DNA rearrangement is a characteristic of tumors of mature B cells; it was detected in 24 of 28 plasmacytomas and B-cell lymphomas, usually as LyR-S_α, but not in 11 Abelson retrovirus-induced lymphomas of B-cell precursors nor detectably in normal B cells. In contrast, rearrangement was observed in only 3 of 18 T-cell lymphomas, and none of seven nonlymphoid lines. Most tumor lines (49 of 52), whether lymphoid or not, contained a low level of polyadenylylated LyR transcript(s), but several new RNA species with differences in their 5′ regions appeared in B-cell lines in which LyR DNA was rearranged, suggesting that rearrangement may activate a new promoter or mode of splicing. The results suggest that the LyR-S_α rearrangement represents a translocation to chromosome 12 that alters expression of LyR-encoded genes; hence, it may have participated in lymphoid tumor oncogenesis.**

DNA rearrangement in B lymphocytes is required for immunoglobulin gene expression (reviewed in ref. 1). For the heavy (H) chain locus, a variable (V) region gene forms by fusion of V_H, diversity (D), and joining (J_H) elements, and it subsequently can be "switched" in mature B cells from the μ H chain constant (C) region gene, $C\mu$, to a more distant C region gene by recombination between switch (S) regions 5′ to the two C_H genes. Plasmacytomas, tumors of immunoglobulin-secreting cells, frequently also manifest a cytogenetically detectable translocation of the end of chromosome 15 to the region on chromosome 12 where the H chain locus lies (2). Such translocations might result in aberrant shifts of H chain genes, such as those of the α chain C region gene, C_α (3, 4). Evidence that aberrantly rearranged C_α genes in several different lines had recombined with the same unknown DNA region (K. Calame, S. Kim, and L. Hood, personal communication; ref. 5) prompted us to examine this phenomenon. We have cloned one such rearranged C_α gene, determined the sequence of the recombination region, and used probes from the incoming DNA, designated here as lymphoid rearranging (LyR) DNA, to test for rearrangement and transcription in diverse tumor lines and in normal cells. LyR DNA was rearranged in most plasmacytomas, as a recent independent study also found (6); moreover, we found that LyR DNA rearranged in B-cell lymphomas and in certain T-cell lymphomas but not in lymphomas of B-cell precursors (pre-B cells). Intriguingly, rearrangement correlates with altered transcription of LyR sequences. Our data suggest that LyR DNA probably does not derive from chromosome 12. Thus, LyR DNA rearrangement may represent an interchromosomal translocation associated with lymphoid tumors.

MATERIALS AND METHODS

Tumors and cell lines from the Salk Institute (designated S and J) and M. Potter at Litton Bionetics (Kensington, MD) are described in their catalogues; others are cited in refs. 7–10. DNA isolation and Southern blotting have been described (3). Polyadenylylated RNA was isolated (11), fractionated on methyl mercury gels (12), blotted, and hybridized as described (11). Probes were nick-translated (13) cloned DNA fragments isolated on 5% polyacrylamide gels. For cloning, *Eco*RI-digested J558 DNA was sedimented on a glycerol gradient, and fragments ≈15 kilobases (kb) long were packaged (14) into the phage λ Charon 4A. Recombinant phage were screened (15) with a 5′ C_α cDNA probe (3).

RESULTS AND DISCUSSION

DNA Recombined with a Plasmacytoma S Region. We cloned from plasmacytoma J558 a 14.3-kb *Eco*RI fragment bearing an aberrantly rearranged C_α gene, also cloned by Harris *et al.* (6). Its restriction map diverged from that of a germ-line C_α clone 1.85 ± 0.05 kb 5′ to the C_α gene (Fig. 1). Thus, the incoming LyR DNA recombined with the S_α region. To analyze the recombining regions, we determined the sequence of a 417-base pair (bp) *Xho-Pst* fragment spanning the J558 LyR-S_α recombination point (Fig. 2). Whereas the 3′ 73 residues were from S_α, the 5′ 344 did not come from S_α (18) or S_μ (19). We also derived a 110-bp germ-line LyR DNA sequence from this region by using a clone from T lymphoma ST4 (to be described elsewhere). Comparison of the sequences in Fig. 2 reveals that an adenine residue at the J558 recombination point replaced the guanine residue in the ST4 (germ-line LyR DNA) and germ-line S_α sequences. Presumably recombination generated this change.

LyR DNA and S_α Fused Within a S_α Repeat Unit. The LyR-S_α DNA fusion looks partly like C_H region switch recombination. LyR DNA entered the S_α region within a run of three of the G-A-G-C-T sequences (underlined in Fig. 2) found in most S_H repeat units (19); and, as indicated by the dotted line in Fig.

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Abbreviations: LyR DNA, lymphoid rearranging DNA; C, constant; H, heavy; S, switch; V, variable; J, joining; pre-B-cell, B-cell precursor; kb, kilobases; bp, base pair(s).

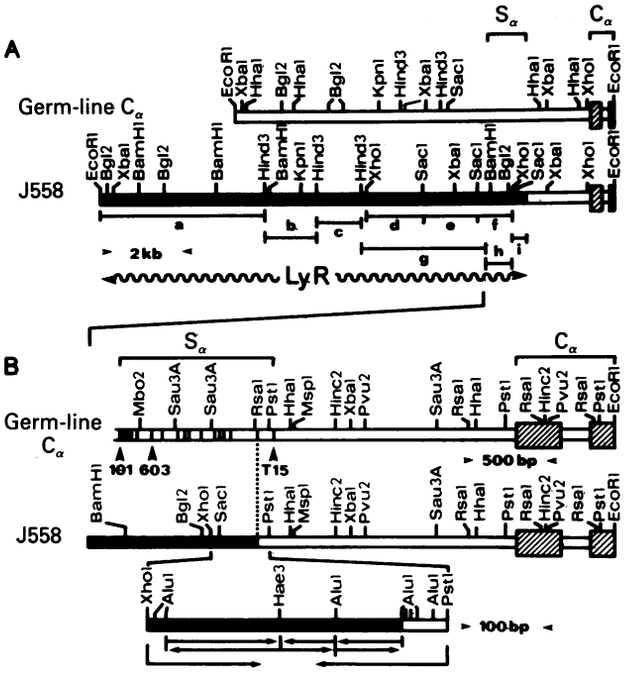

FIG. 1. Restriction maps of rearranged J558 LyR-S_α and germ-line S_α DNAs. Open bars, DNA 5′ to C_α in germ line; filled bars, incoming LyR DNA in J558. (*A*) *Eco*RI fragments. Subclones in pBR322 and fragments used as probes are lettered. (*B*) Expanded maps near the recombination point. Vertical lines represent repeated units in the S_α region implicated as switch recombination sites (16); those used in plasmacytomas MC101, McPC 603, and TEPC 15 are indicated by arrowheads. The sequence determination strategy is indicated at the bottom. Fragments were inserted into M13 vectors (16) mp8 and mp9, and the sequence was determined by the dideoxynucleotide method (17).

1*B* and the "16" in Fig. 2, the recombination point lies within the 16th of 17 ≈32-bp units of partial repeat sequences implicated in S_α region switch recombination (18). Moreover, the T-A-G-G-C-T-G (underlined in Fig. 2) 9 bp 5′ to the recombination point in germ-line S_α region approximates the consensus $\frac{C}{T}$-A-G-G-T-T-G found within 20 bp 5′ of nearly all switch sites (20). In contrast, the LyR DNA sequence lacks S region features: no repeat unit is evident, G-A-G-C-T and G-G-G-G-T are not frequent, and no $\frac{C}{T}$-A-G-G-T-T-G occurs within 140 bp 5′ to the recombination point nor 65 bp 3′ to it (Fig. 2). Moreover, probes extending 3.7 kb 5′ to the recombination point did not hybridize to cloned germ-line S_μ (21), S_α (Fig. 1), $S_{\gamma 1}$, or $S_{\gamma 3}$ (22) regions (not shown). Thus, the LyR region so far analyzed is not homologous with known S regions.

LyR DNA Rearrangement Is Lymphoid Tumor-Associated. To determine the cell types showing LyR DNA rearrangement,

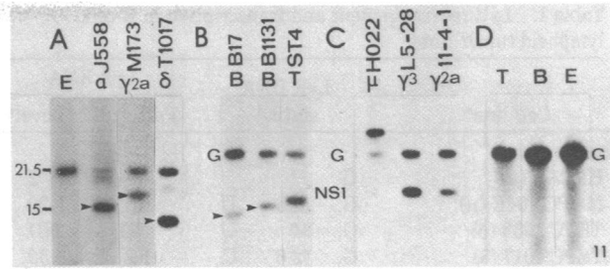

FIG. 3. Rearrangement of the LyR DNA region in lymphoid cells. (*A*) Plasmacytomas expressing α, γ2a, and δ heavy chains and embryo (lane E) DNA. (*B*) B- and T-cell lymphomas. (*C*) Hybridomas. (*D*) Peripheral T cells (BALB/c lymph node; lane T), BALB/c nude spleen cells (lane B), and embryo (lane E) DNA. *Eco*RI digests (15 μg) fractionated on 0.7% agarose gels were hybridized to probes b and c in Fig. 1. Arrowheads indicate fragments also detected by the 5′ C_α probe. Sizes of fragments are in kb. G, germ-line LyR DNA; NS1, rearranged LyR DNA from NS1 parent.

we analyzed 57 lymphoid and 6 nonlymphoid tumor lines. Fig. 3 shows representative Southern (23) blots, Table 1 gives data for lymphoid B-cell lines, and Table 2 gives data for T-cell and nonlymphoid lines. Twenty-one of 23 plasmacytomas had the germ-line *Eco*RI fragment of ≈21.5 kb and a new fragment, typically 14 to 17 kb long; these included lines secreting μ, δ, γ3, γ1, γ2a, γ2b, and α chains. Of five B-cell lymphomas, which express surface immunoglobulin, three had rearranged LyR DNA. In contrast, all 11 Abelson murine leukemia virus-induced pre-B-cell lymphomas had only germ-line LyR DNA. This striking difference from other tumors of B lineage might relate to acute retroviral induction, although rearranged LyR DNA was found in W267, one of two plasmacytomas induced by Abelson murine leukemia virus (plus oil). Alternatively, the pre-B-cell lines might not rearrange because of dormant switch machinery, although one of these lines (18-81) switches C_H gene expression (24). Surprisingly, LyR DNA was rearranged in 3 of 18 T lymphomas: STRij-4 and STRij-1, which were induced by a slow retrovirus (7), and TIKAUT, a spontaneous AKR lymphoma (10). LyR DNA was not rearranged in the nonlymphoid lines—three myeloid, one macrophage, and two sarcoma lines, and NIH3T3 fibroblasts.

To assess normal T and B cells, we examined peripheral T cells and spleens of nude mice (Fig. 3*D*). No rearrangement was detected; control experiments with low levels of five plasmacytoma DNAs added to embryo DNA suggested that 10–20% rearrangement would have been detectable within such polyclonal populations. To test monoclonal B cells, we analyzed one μ-chain- and three γ-chain-producing hybridomas (three lines shown in Fig. 3*C*). In three lines, the only rearranged fragment

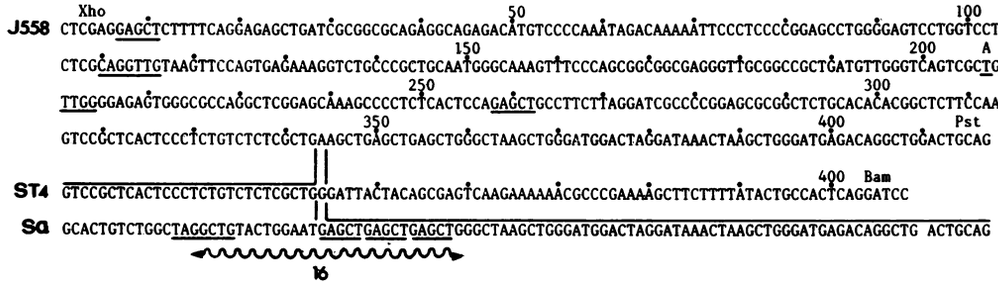

FIG. 2. Relationship of J558 LyR-S_α DNA sequence to germ-line LyR (ST4) and germ-line S_α (Sa) sequences. Overlining indicates LyR DNA and S_α germ-line sequences which have recombined in J558. The guanine at position 410 was not present in the published S_α sequence (18). The "16" denotes an S_α repeat (see text). The ST4 sequence was determined from the *Bam*HI site. Sequences implicated in switch recombination are underlined.

Table 1. LyR rearrangement and transcription in B-cell lymphoid tumor lines

Cell line*	LyR DNA status†			LyR RNA Pattern‡	LyR RNA Level§
Plasmacytoma					
HPC-76 (μ)	G			—	<2
MOPC 104E (μ)	G,	14.5	U	R	20
TEPC 1033 (δ)	G,	≈34	U	ND	ND
TEPC 1017 (δ)	G,	12.6	C_α	R1	*50*
Y 5606 (γ_3)	G,	14.0	C_α	R1	*30*
P3 (γ_1)	G,	14.0	U	R2	*7*
MPC 11 (γ_{2b})	G,	16.5	U	R	ND
MOPC 173 (γ_{2a})	G,	15.9	C_α	R1	*25*
HOPC 1 (γ_{2a})	G,	14.3	C_α	R	10
SAMM 368 (γ_{2b}, α)	G,	13.0	C_α	R	10
TEPC 609 (γ_{2b}, α)	G,	16.8	C_α	R	20
ABPC 4¶ (α)	G			G	5
J 558.2BU.1 (α)	G‖,	14.9	C_α	R2	9
S 107 (α)	G,	16.2	C_α	R	4
MOPC 315 (α)	G,	14.9	C_α	ND	ND
McPC 603 (α)	G,	13.6	C_α	ND	ND
S 117 (α)	G,	15.5	C_α	ND	ND
S 194 (α)	G,	14.0	C_α	ND	ND
EPC 109 (α)	G,	14.5	C_α	R1	20
BFPC 61 (α)	G,	14.3	C_α	R	ND
WEHI-267¶ (α)	G,	15.6	C_α	R1	20
A** (α)	G,	≈15	C_α	R	ND
MOPC 41A (κ)	G,	18.5	C_α	R1	2
B lymphoma					
WEHI-279 (μ, NZC)	G‖,	14.3	U	G	1
WEHI-231 (μ, NZB F1)	G			G	≈8
BALTNLM 17	G,	12.6	C_α	R	10
BALTELM 1131	G,	13.1	C_α	R1	4
2PK-3 (γ_{2a})	G			G	4
Pre-B lymphoma‖					
18-48	G			ND	ND
18-81	G			G	7
AVRij-1	G			G	4
RAW 8	G			G	4
ABLS-8	G			G	3
ABLS-19	G			G	2
ABLS-5	G			G	<0.5
ABLS-1	G			ND	ND
ABPL-1	G			ND	ND
ABPL-2	G			ND	ND
NR-18	G			ND	ND
L1210 (DBA/2)	ND			G	3

ND, not determined; —, not detected.
* Strain of origin is BALB/c unless indicated otherwise.
† G denotes the germ-line *Eco*RI fragment of ≈21.5 kb, and the size of any rearranged fragment is given in kb. C_α denotes a LyR rearrangement to the region 5′ to gene C_α (see text) and U to unknown region(s) other than Cα.
‡ The R transcript pattern has the 2.0- and 1.85-kb species, and the G pattern has the 2.3- to 2.4-kb pattern. Lines examined with probe f are denoted as R1 or R2, depending on the extra species detected (see Fig. 4*A*).
§ An estimate for the molecules per cell of LyR transcripts (see text). Italicized numbers are based on several determinations, but most are order-of-magnitude estimates.
¶ Lines derived by infection *in vivo* or *in vitro* with Abelson murine leukemia virus.
‖ Only low amounts of germ-line (21.5) fragments. J558 also contained a 20-kb fragment hybridizing to LyR probes (see Fig. 3*A*) but not to C_α.
** Plasmacytoma of unknown origin.

Table 2. LyR rearrangement and transcription in lymphoid T-cell and nonlymphoid lines*

Cell line	DNA status			LyR RNA Pattern	LyR RNA Level
Lymphoid T-cell					
STRij-4	G, 14.1		U	G*	9
STRij-1	13.1		U	G*	6
EL-4 (C57BL)	G			G	5
S49	G			G	4
TIKAUT (AKR)	≈33		U	G*	13
BW5147 (AKR)	G			G	1
WEHI-7	G			G	<1
WEHI-22	G			G	13
WEHI-112 (NZB)	G			ND	ND
P 1798	G			G	8
BL/VL3 (C57BL/Ka)	G			ND	ND
BALENTL 5	G			G	1
BALENTL 9	G			—	<1
BALENLM 14	G			G	2
1.4.2 (C57BL/Ka)†	G			ND	ND
1.2.1 (C57BL/Ka)†	G			ND	ND
1.4.4 (C57BL/Ka)†	G			ND	ND
999 (C57BL/Ka)†	G			ND	ND
WEHI-222 (A.TL)	ND			G	4
WEHI-242 (A.TL)	ND			G	7
Myeloid					
WEHI-3B	G			G	≈25
WEHI-265†	G			G	≈45
WEHI-274†	G			G	≈25
Macrophage					
J774	G			ND	ND
Mast cell tumor					
HC (LAF1)	ND			G	7
P815 X-2 (DBA/2)	ND			G	5
Erythroleukemia					
F4N (DBA/2)	ND			G	9
Sarcoma					
EMT6	G			G	1
WEHI-164	G			—	<0.5
Fibroblast					
NIH/3T3 (NIH SWISS)	G			ND	ND

ND, not determined; G, germ line; U, rearrangement to unknown region.
* Transcript slightly larger than typical germ-line one.
† Lines derived from tumors induced by infection with Abelson murine leukemia virus. Thymomas arose after intrathymic injection (9).

was the 14-kb fragment from the NS1 tumor parent. Although the fourth line (HO22; ref. 25) had a new (≈33 kb) fragment, the 14-kb NS1 fragment was seen only on long exposure, so a secondary NS1 rearrangement may have given the 33-kb fragment. No LyR DNA rearrangement due to the normal B cell was found in eight IgA-expressing hybridomas (6). Thus, LyR DNA rearrangement appears to be confined largely, if not exclusively, to lymphoid tumors, primarily of mature cells of B lineage.

Most LyR DNA Rearrangements in BALB/c Mice Are to the 5′-Flanking Region of C_α. Most rearranged LyR DNA fragments also hybridized with a 5′ C_α cDNA probe, as indicated in Table 1 and by arrows in Fig. 3*A* and *B*. These apparent LyR-S_α DNA fusions were found in 17 of the 21 plasmacytomas, including lines expressing μ, δ, γ3, and γ2a and α chains, and in two of the three B-cell lymphomas but not in the three T-cell lymphomas. In contrast to these BALB/c tumors, none of 11 NZB lines with rearranged Lyr DNA (6) had recombined 5′ to C_α. This genetic difference in targets for LyR DNA rearrangement might reflect differences in the S_α region, LyR DNA, or the rearrangement machinery.

Most Cell Lines Contain Polyadenylylated LyR RNA and New Species Appear in Lines with Rearranged LyR DNA. Polyadenylylated RNA was electrophoresed, and gel blots (11) were hybridized with LyR probes. Most lymphoid and nonlymphoid tumor lines (49 of 52) had transcripts detectable with probes d or e in Fig. 4*A*. Lines with only germ-line LyR DNA displayed partially resolved 2.3- and 2.4-kb RNA species and sometimes traces of a 1.85-kb RNA, probably due to cross-hybridization with residual 18S rRNA; this "germline transcript pattern," designated G in Tables 1 and 2, was found in seven nonlymphoid lines, in 10 T-cell lymphomas without rearranged LyR DNA (two shown in Fig. 4*B*), and in all seven pre-B-cell lines examined (one shown in Fig. 4*B*). In striking contrast, lymphoid B-cell lines with a rearranged LyR allele (R in Fig. 4*A*) had a prominent new 2.0-kb RNA species and a 1.85-kb component too intense to be due to rRNA (Fig. 4*B*). Although the relative amounts of the 2.3-, 2.0-, and 1.85-kb species varied in different lines, these "rearranged transcript patterns," designated R, were seen in all 17 plasmacytomas and B-cell lymphomas with rearranged LyR DNA except B-cell lymphoma WEHI-279 (Table 1). These included lines expressing diverse H chains and with LyR DNA rearranged elsewhere than in the S_α region, such as P3 (Fig. 4*D*) and MOPC104E. This excellent correlation argues that the R transcripts derive from the rearranged LyR allele. If LyR transcription were altered in B-cell lines independently of rearrangement, R rather than G transcripts would have been expected in B-cell lymphoma 2PK3 and plasmacytoma ABPC 4, which have only germ-line LyR DNA.

Unlike the B-cell tumors, all three T-cell lymphomas with rearranged LyR DNA gave a 2.3- to 2.5-kb RNA, shown for ST1 in Fig. 4*C*; this is slightly larger than the typical G transcript and comprises two species.

Estimates based upon the hybridization signal from a known amount of LyR DNA fragments (Tables 1 and 2) indicate that pre-B-cell lymphomas and T-cell lymphomas typically contain ≈2–10 molecules per cell of the 2.3-kb RNA, and plasmacytomas contain from ≈2 to ≈50 molecules per cell of the 2.0- and 1.85-kb species.

Transcripts of LyR DNA Differ in Their 5′-Terminal Regions. We determined the orientation of LyR transcripts by using probes from single-stranded M13 phage. The top strand probe (Fig. 4*C*) labeled the G and R transcripts, in all eight lines tested (two not shown), whereas the bottom strand (not shown) hybridized only to a minor 1.5-kb RNA unique to plasmacytoma EPC 109. Because all LyR transcripts derive from the top strand, in lines with LyR-S_α DNA fusion they come from the DNA strand opposite to α chain mRNA.

Differences between the 5′ regions of G and R transcripts revealed with probes near the J558 recombination point suggest that rearrangement activated a new promoter or mode of splicing. The 2.3-kb germ-line RNA was labeled by probe i (data not shown), the region of known sequence, but not by probe f (Fig. 4*A*); thus, it must be spliced from region i to e (Fig. 4*A*). In contrast, transcripts of rearranged LyR DNA were not labeled by probe i but were by probe f, which gave pattern R1 or R2 in Fig. 4*A*. The more common R1 pattern has the 1.85- and 2.0-kb species and one or two others of 1.2–1.5 kb (Fig. 4*D*); the R2 pattern, with several species of 1.85–2.8 kb, was found with P3 (Fig. 4*D*) and J558, perhaps indicating that different rearrangements yield distinct transcripts. The 5′ ends of the major transcripts of rearranged DNA probably lie within LyR region f because the RNAs were not labeled by a *Pst* fragment spanning the 5′ C_α region up to the J558 recombination point; the major transcripts of LyR DNA also lack C_α coding sequences (data not shown).

LyR DNA Sequences Appear to Arise Outside the H Chain Locus, Probably from a Separate Chromosome. The size of the germ-line LyR *Eco*RI fragment (21.5 kb) and the LyR restriction map (Fig. 1) exclude its arising from the J_H–C_H locus (26) or the known *D* locus (27). Much of the V_H locus and the entire V_H–J_H region can be excluded because pre-B-cell lymphomas with V_H–*D*–J_H joins on both alleles have deleted those regions (S. Cory, unpublished data) but retain germ-line LyR DNA (Table 1). The V_H locus also appears unlikely because all six V_H probes that we have tested revealed restriction site polymorphism, but none was detected with LyR DNA probes in BALB/c, NZB, A/J, AKR, DBA, C3H, SJL, CBA, or C57Bl mice. Evidence that Lyr DNA is not closely linked to the H chain locus is that plasmacytomas M104E and S117 appear haploid for the H chain locus (not shown) yet show both germ-line and rearranged LyR DNA (Table 1). Conversely, an ST1 subline with both germ-line and rearranged J_H alleles shows one rearranged but no germline LyR DNA fragment (with probes b and f).

These discordances in copy number could reflect chromosome loss, if LyR DNA is not from chromosome 12. To test this, we exploited the tendency of cell hybrids to discard chromosomes. We examined a line (Cl26) cloned from a TIKAUT–A/J lymphocyte fusion (by W. Thomas and J. F. A. P. Miller) because *Eco*RI digests distinguish the C_μ genes of TIKAUT (AKR strain) and A/J and the TIKAUT LyR from A/J Lyr DNA (Fig. 5). Significantly, Cl26 retained some A/J S_μ (arrowed) and C_μ regions (not shown) but no detectable A/J LyR DNA. Thus A/J C_μ and LyR DNA behaved as unlinked markers. The simplest interpretation is that the Cl26 population had lost all copies

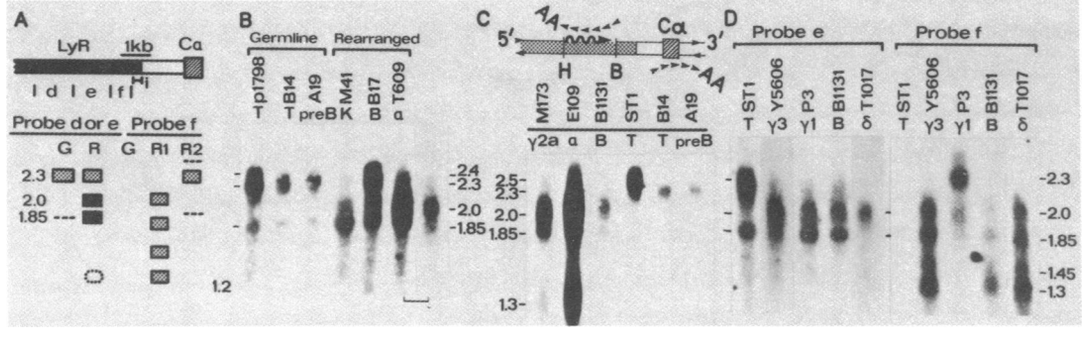

FIG. 4. Polyadenylylated LyR transcripts. (*A*) Diagram defining the "germ-line" (G) and "rearranged" (R) transcript patterns (see text). (*B*) Transcripts hybridizing to probe e in two T-cell lines and a pre-B-cell line (germ line) and in a B-cell line and two plasmacytomas (rearranged). A lighter exposure for T609 is shown on the right. B17 illustrates a line with comparable amounts of the G and R transcripts. (C) Orientation of LyR transcripts determined with a probe prepared by insertion of a *Hin*dIII–*Bam*HI fragment g in (Fig. 1) into M13. (*D*) Differences in the 5′ regions of LyR transcripts revealed by probe *f*. Each lane contained 2–5 μg of mRNA.

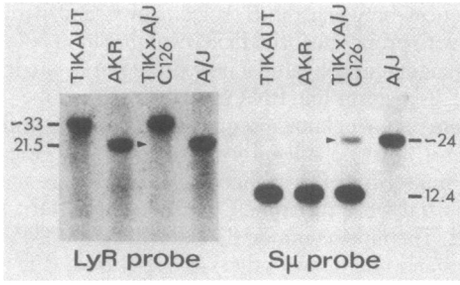

FIG. 5. LyR DNA region may not be located on chromosome 12. Duplicate *Eco*RI digests were hybridized with LyR probes b + c (Fig. 1) and an S_μ probe (5′ terminal R1-*Hha* fragment of Ch-H76μ1; figure 1 in ref. 7); a C_μ cDNA probe gave the same result as the S_μ probe did. Arrows indicate the positions of A/J LyR and C_μ fragments.

of the A/J chromosome bearing LyR DNA but not all copies of A/J chromosome 12.

CONCLUSIONS

LyR is a transcriptionally active region of mouse germ-line DNA (>21 kb long) that has rearranged in most tumors of mature lymphoid B-cells. The C_H gene switch recombination machinery may be implicated because in BALB/c mice ≈80% of these rearrangements were to the S_α region, and the J558 fusion was with an S_α region repeat unit. Because no LyR DNA rearrangement in 11 NZB lines involved the S_α region (6) or seemingly any other S_H region, the two strains in which plasmacytomas can be induced must differ in targets for LyR DNA rearrangement. The polyadenylylated RNAs in B-cell lines with rearranged LyR DNA differed from the germ-line transcript towards their 5′ ends. If, as seems likely, these potential mRNAs arise from the rearranged LyR allele, rearrangement must have activated a new promoter, or mode of splicing. The three T-lymphoma rearrangements may be a different class because none were to the S_α region, and the RNA species were unlike those in plasmacytomas.

Discordance between LyR DNA and C_H copy number in four cell lines suggests that LyR DNA does not derive from chromosome 12. Thus, LyR DNA may be the first region undergoing interchromosomal translocation to be characterized at the molecular level. Identifying its chromosome of origin would resolve whether LyR-S_α DNA fusion corresponds to the chromosome 15/12 shift in plasmacytomas (2) or to a previously undetected translocation. The strong association of LyR DNA rearrangement with lymphoid tumors suggests that it contributed to their oncogenesis.

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