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Breakage of the T cell receptor α chain locus in non malignant clones from patients with ataxia telangiectasia

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Summary. Patients with ataxia telangiectasia (A-T) develop specific chromosome translocations, which may confer a proliferative advantage, resulting in the appearance of large clones in the peripheral blood lymphocytes. These lymphocytes are not malignant. Using in situ hybridisation techniques we have investigated a consistent 14q11 translocation breakpoint observed in a t(X;14)(q28;q11) translocation clone from each of two different patients and a t(14;14)(q11;q32) clone from a third patient. In all cases the chromosome translocation involved breakage within the α chain locus of the T cell receptor (TCRα), between the variable and constant regions, at 14q11. Chromosome rearrangement involving breakage within TCRα can therefore precede the development of malignancy. Further chromosomal rearrangement may be required in these patients, for progression to the leukaemic state.

Introduction

Specific chromosome translocations have been associated with human tumours especially leukaemias and lymphomas. Burkitt's lymphoma and chronic myeloid leukaemia are perhaps the best known examples where the c-*myc* and c-*abl* proto-oncogenes are associated with the immunoglobulin heavy chain locus (IgH) and the breakpoint cluster region *(bcr)* respectively (Croce and Nowell 1986; Shtivelman et al. 1985). There are also examples of other specific chromosome translocations in B cell lymphomas which are associated with particular histological types (Croce and Nowell 1986). T cell tumours have now also been reported with particular chromosome rearrangements; specifically involving region 14q11 (Zech et al. 1986; Hecht et al. 1984) which contains the α chain locus of the T cell receptor (TCRα) (Caccia et al. 1985). Several translocations, all involving chromosome 14, have now been described where the breakpoint at 14q11 is within TCRα. These include t(11;14)(p13;q11) (Lewis et al. 1985; Erikson et al. 1985), t(11;14)(p15;q11) (Le Beau et al. 1986), t(8;14)(q24;q11) (Shima et al. 1986; McKeithan et al. 1986; Mathieu-Mahul et al. 1986; Erikson et al. 1986), t(10;14)(q24;q11) (Kagan et al. 1987) and inv(14)(q11q32) (Baer et al. 1985, 1987; Mengle-Gaw et al. 1987). It is possible therefore that TCRα may play a role in the pathogenesis of T cell tumours.

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Ataxia telangiectasia patients show the occurrence of clonal and sporadic chromosome rearrangements specifically at chromosome sites 7p14, 7q35 and 14q11 (McCaw et al. 1975; Aurias et al. 1980; Al Saadi et al. 1980; Taylor et al. 1981; Taylor 1982; O'Connor et al. 1982; Aurias and Dutrillaux 1986) which correspond to the bands to which the T cell receptor γ chain, β chain and α chain genes map respectively (Caccia et al. 1985; Isobe et al. 1985; Mure et al. 1985). A further specific chromosome breakage point in these lymphocytes is at 14q32 (Taylor et al. 1981; Taylor and Butterworth 1986). Some A-T translocation cells have an unusual proliferative advantage with the result that the expanding clone can occupy 80%–100% of the mitogen-stimulated T cell population for a number of years in the absence of any malignancy (Taylor et al. 1981; Taylor 1982). A-T patients do however have a greatly increased predisposition to T cell chronic lymphocytic leukaemia (Spector et al. 1982) which can arise from within clones with t(14;14)(q11;q32) or inv(14)(q11q32) rearrangements (McCaw et al. 1975; Sparkes et al. 1980; Taylor and Butterworth 1986). These clones may therefore be regarded as premalignant lesions. A major advantage of studying these patients therefore is that the sequence of events, beginning with normal lymphocytes, progressing to premalignant clones, and eventually to a true malignant phenotype can potentially be followed.

We show here using in situ hybridisation techniques that the break in chromosome 14 at q11 in non malignant clone cells from ataxia telangiectasia patients occurs within TCRα. These observations show that a translocation involving breakage of TCRα in this instance is by itself insufficient for the development of malignant change.

Materials and methods

Chromosome spreads

Chromosome spreads were made from phytohaemagglutinin-stimulated lymphocytes cultured for 72 h and lipsol banded for in situ hybridisation (Barton et al. 1982). For trypsin banding, slide preparations of metaphases were incubated overnight at 60°C, immersed in Hanks Balanced Salt Solution (1:1 10× HBSS/1× HBSS) for 10 min, washed in pH 6.8 buffer, immersed in 2.8% trypsin in buffer for about 50 s and rinsed in saline. Metaphases were stained with 20% Leishmans stain in pH 6.8 buffer for 4 min.

In situ hybridisation

The variable region probe was obtained by sequential digestion with *Sau*3A and *Eco*RI of plasmid pY14 (Yanagi et al. 1985). The 529-bp fragment corresponding to TCRVα was purified by electroelution and used directly for nick translation. The DNA hybridisation probes were labelled with [^{3}H]TTP and [^{3}H]dCTP to a specific activity of at least 3×10^7 dpm/μg by nick translation. Chromosomes were treated with RNase for 1 h and denatured in 60% formamide, 0.1 m*M* EDTA, 5 m*M* Hepes pH 7.0 at 55°C for 7 min. A 20-μl sample of hybridisation buffer (50% formamide, 0.6 *M* NaCl, 5 m*M* Hepes, 1 m*M* EDTA, 10% dextran sulphate pH 7.6) containing the probe was heated to 100°C in an Eppendorf tube for 7 min, and applied to each slide, which was then sealed with a coverslip. Hybridisation took place overnight (16 h) at 43°C. Coverslips were then gently removed, slides washed in 2 × SSC (0.3*M* NaCl, 30 m*M* sodium citrate pH 7) at room temperature, incubated 1 h in 2 × SSC at 55°C and in 50% formamide, 2 × SCC for 30 min (four times) and soaked overnight in 2 × SCC. Finally, the slides were dehydrated through an alcohol series, air dried, and coated with Ilford K2 emulsion and exposed for 14 and 28 days. Following developing the slides were rinsed in tap water for 20 min, stained with 10% Giemsa in Sorensons buffer for 40 min, rinsed in buffer and air dried. The level of staining was checked before the slide was mounted.

Results

Trypsin banding of the translocation cells

We have studied here three A-T patients two of whom, AT8BI and AT1CT, had a large t(X;14)(q28;q11) clone and the third patient, AT2BI, had a large t(14;14)(q11;q32) clone (Taylor et al. 1981). The breakpoints on chromosome 14 were found to be at 14q11.1 or 14q11.2 in all three cases with the 14q− chromosome from the t(X;14) translocations being half the size of the t(14;14) 14q− chromosome (0.25% of the genome versus 0.5%; Fig. 1) (Kennaugh et al. 1986; Hollis et al. 1987).

Localisation of the 14q11 breakpoint within the α chain gene

We have previously shown by in situ hybridisation that chromosome 14 in t(14;14) and t(X;14) clones from the same two A-T patients that are described here, was broken at a site 5′ to the constant region of the T cell receptor α chain gene (TCRCα) or proximal to it with respect to the centromere. Peaks of hybridisation were observed on the 14q+ and Xq+ chromosomes of these clones (from patients AT2BI and AT8BI respectively), but no hybridisation was observed on either of the 14q− chromosomes (Kennaugh et al. 1986; Hollis et al. 1987).

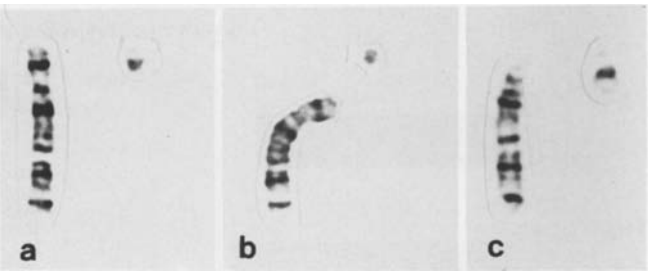

Fig. 1. a, b t(X;14)(q28;q11) translocation chromosomes from patients AT8BI and AT1CT respectively. **c** t(14;14)(q11;q32) translocation chromosomes from patient AT2BI. All three clones show the same breakpoint at 14q11.1–14q11.2. The t(X;14) 14q− chromosome is half the size of the t(14;14) 14q−

We examine here the site of the TCRVα locus in the translocation cells following 72 h culture, by in situ hybridisation using a DNA probe for the variable (TCRVα) region of the T cell receptor α chain gene.

An advantage of both types of translocation was that the Xq+, 14q+ and 14q− chromosomes were clearly recognisable in unbanded, denatured mitotic spreads by virtue of their length or shortness respectively. A disadvantage of measuring in situ hybridisation in the 14q− chromosome in the t(X;14) translocation, in particular, is its very small size (0.25% of the genome, compared with 1.8% for chromosome 21). The probability of obtaining a grain on such a small chromosome, and not just near it, is therefore reduced.

Metaphase chromosome spreads hybridised with [^{3}H]TdR-labelled probe were scanned to examine grain distribution over the Xq+, 14q+ and 14q− translocation chromosomes alone. In Table 1 the observed and expected grain counts on chromosomes Xq+, 14q+ and 14q− are shown. The distribution of hybridisation within the Xq+, 14q+ and 14q− chromosomes from the same metaphases are also shown in Fig. 2.

Table 1. In situ hybridisation of a TCRVα probe to Xq+, 14q+ and 14q− chromosomes in t(X;14) and t(14;14) translocation cells

Patient	Probe	No. of metaphases analysed	Total no. of grains	No. of grains on Xq+ or 14q+		No. of grains on 14q−	
				Observed	Expected[a]	Observed	Expected
AT8BI (t(X;14))	TCRVα	115	1239	46 (3.7%)	49 (3.95%)	22 (1.8%)	3 (0.25%)
AT1CT (t(X;14))	TCRVα	80	1622	71 (4.4%)	64 (3.95%)	23 (1.4%)	4 (0.25%)
AT2BI (t(14;14))	TCRVα(i)[b]	106	456	32 (7.1%)	14 (3.0%)	10 (2.2%)	2 (0.5%)
	TCRVα(ii)	65	1671	68 (4.1%)	50 (3.0%)	18 (1.1%)	8 (0.5%)

[a] The grain count expected (for a random distribution) in the number of cells analysed and calculated as length of chromosome/total length of all chromosomes x total number of grains. A single X chromosome represents 2.5% of the diploid genome and a single chromosome 14, 1.7%. The Xq+ and 14q− chromosomes of the t(X;14) translocation represent 3.95% and 0.25% of the diploid genome. The 14q+ and 14q− of the t(14;14) translocation represent 3.0% and 0.5% respectively

[b] Results from two experiments (i) and (ii) with TCRVα

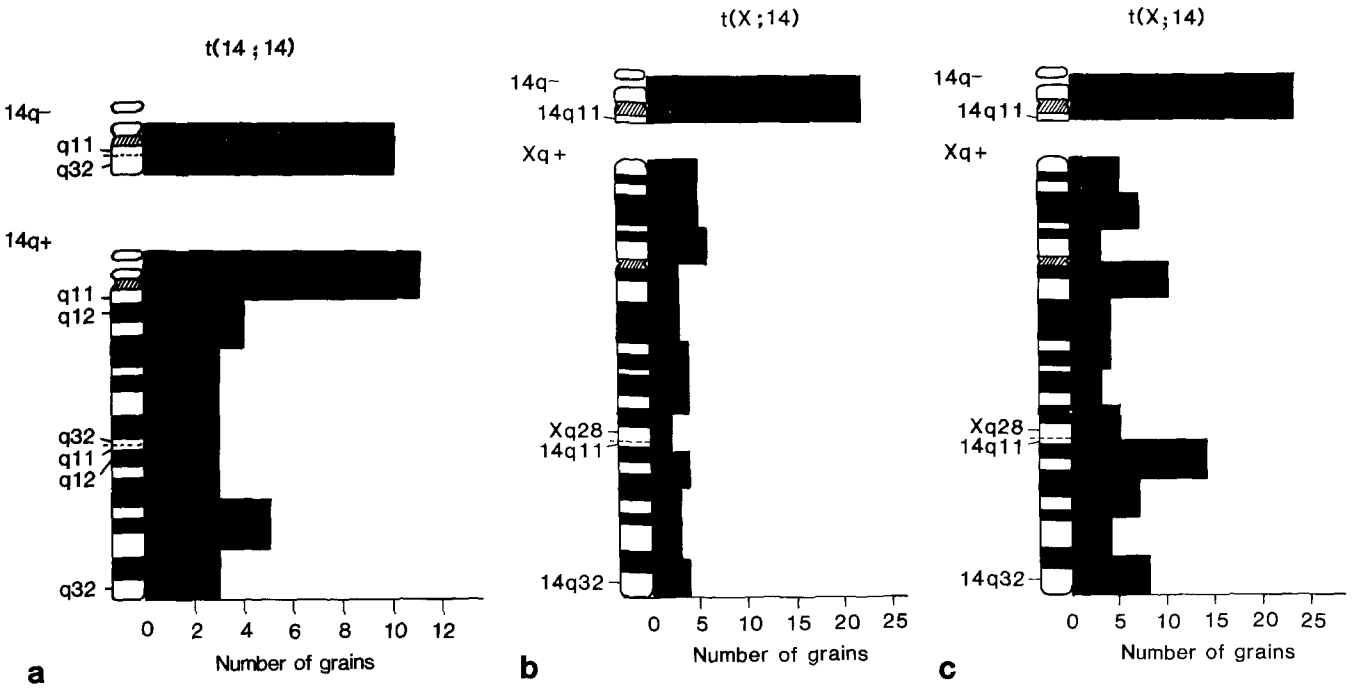

Fig. 2a–c. Distribution of autoradiographic silver grains over translocation chromosomes from three ataxia telangiectasia clones following in situ hybridisation with TCRVα. **a** 14q− and 14q+ from patient AT2BI with t(14;14)(q11;q32) (from experiment TCRVα(i) only). **b** 14q− and Xq+ from patient AT8BI with t(X;14)(q28;q11). **c** 14q− and Xq+ from patient AT1CT with t(X;14)(q28;q11)

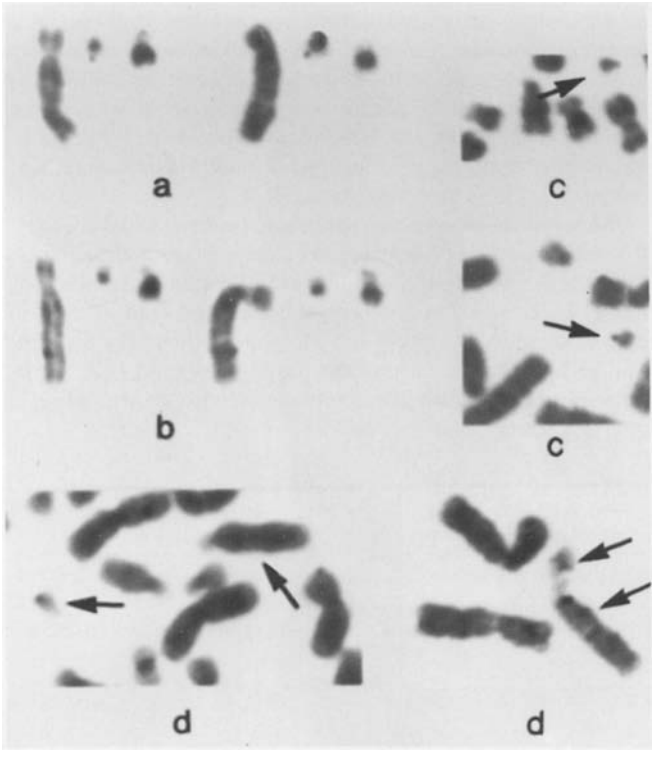

Fig. 3. a Autoradiographic grains showing hybridisation of TCRVα to 14q− in the t(X;14) clone from patient AT1CT. A G-group chromosome and the Xq+ are also shown for comparison. **b** Hybridisation of TCRVα to Xq+ at the translocation point in AT1CT. **c** Partial metaphase of cells from patients AT8BI showing hybridisation of TCRVα to 14q− of the t(X;14) translocation. **d** Partial metaphase of cells from patient AT2BI showing hybridisation of TCRVα to both 14q− chromosome and the 14q11 site not involved in the t(14;14) translocation

The TCRVα probe showed a peak of hybridisation on the 14q− chromosome in the t(14;14) clone and also at the centromeric region of the 14q+ chromosome (Fig. 3d). Table 1 shows results of two experiments with this patients (AT2BI) lymphocytes. The first (TCRVα(i)) had a low background and indicates a clear preferential hybridisation to 14q−, with 5 times the expected grain number (Fig. 2a). On 14q+ 32 grains were also observed compared with the 14 expected. Of these 32 grains, 11 hybridised to the centromeric region not involved in the translocation and therefore showing the normal site of TCRVα (Fig. 2a). The second result (TCRVα(ii)) has more background but even here an excess of grains was observed on both the 14q− and centromeric region of 14q+ (data not shown in Fig. 2).

In the two t(X;14) translocation clones from patients AT8BI and AT1CT the TCRVα probe again showed a peak of hybridisation on the 14q− (Fig. 3a, c) chromosome with 6 or 7 times the expected numbers of grains. No hybridisation of TCRVα was observed on the Xq+ chromosome in the AT8BI clone unlike the constant region probe which hybridised only to Xq+ (Hollis et al. 1987). In the t(X;14) clone from AT1CT there was a degree of hybridisation of TCRVα to Xq+ (Figs. 2c, 3b) suggesting the possibility of a break within TCRVα in this translocation.

These observations suggest that breakage of chromosome 14 at q11 occurred 3′ of the V region of TCRα (or distal to it with respect to the centromere) in both t(X;14) translocations and the t(14;14) translocation. Taken together with our previous results with TCRCα it is clear that both chromosomes 14 in the two clones from AT2BI and AT8BI are broken within TCRα between the variable and constant regions or in the case of AT1CT possibly within TCRVα. The orientation of TCRα; centromere, V region, C region, telomere was the

same as previously reported (Baer et al. 1985; Lewis et al. 1985).

Discussion

Here we have presented evidence to show that in three A-T patients, each with cytogenetically abnormal T cell clones, the chromosome translocation involved breakage within the α chain locus of the T cell receptor between the variable and constant regions. In two clones from patients AT2BI and AT8BI the segregation of TCRVα and TCRCα is compatible with a breakpoint in the Jα region. In the third clone from patient AT1CT there was some degree of hybridisation of TCRVα to Xq+. This may be indicative of the translocation breakpoint being within TCRVα, as has previously been shown for a t(8;14)(q24;q11) translocation (Bernard et al. 1988). Alternatively the breakpoint could still have occurred in Jα provided there was a prior VαJα inversion or simultaneous VαJα inversion at the time of translocation involving the several Vα segments to which the Vα probe will hybridise (Shima et al. 1986). A similar possible rearrangement of the VαJα region in the SKW-3 line has been previously discussed (Shima et al. 1986).

In ataxia telangiectasia patients, there appear to be two types of chromosome translocation in T cells involving the T cell receptor loci (Hollis et al. 1987). One translocation type appears to involve sites of two T cell receptor loci e.g. β and γ chain genes (inv(7) and t(7;7)), α and β chain genes (t(7;14)(q35;q11)) or α and γ chain genes (t(7;14)(p13;q11)). The second type appears to involve the α chain gene only with an unknown gene e.g. inv(14), t(14;14) and t(X;14). The available evidence suggests that, of the different rearrangements observed, only t(14;14), t(X;14) and inv(14) give rise to large clones and only the t(14;14) and inv(14) rearrangements in the second group have been reported to become malignant (McCaw et al. 1975; Sparkes et al. 1980; Taylor and Butterworth 1986).

It has been suggested that TCRα may play a role in the pathogenesis of T cell tumours analogous to the role of immunoglobulin genes in B cell lymphomas. Here we have presented evidence to show that a translocation involving this locus is present in non-malignant proliferating cells and may not be sufficient by itself to cause malignant transformation. Particular loci involved in both the t(14;14) rearrangement and inv(14) inversion are the TCRα chain locus and an unknown gene at 14q32 outside the IgH gene and 3′ to it (Kennaugh et al. 1986; Baer et al. 1987) which also seems to be involved in T-CLL and T-PLL (T cell prolymphocytic leukaemia) in non-A-T patients with inv(14) and t(14;14) respectively (Mengle-Gaw et al. 1987). An ordered sequence of events starting with the rearranged 14 but including additional chromosome rearrangements may be required for this particular pathway to T cell malignancy. We have observed such a sequence of events in an A-T patient (AT5BI), who developed T cell chronic lymphocytic leukaemia in a clone containing an inv(14) inversion (Taylor and Butterworth 1986) with breakpoints in TCRJα and 3′ to the IgH locus (Baer et al. 1987). Over several years, further chromosome abnormalities noted; first an 11p− chromosome, followed by the development of a complex clone with karyotype, 45 XY, inv(14), 6q−, i(8q), 11p−, −16, ring (16), 19p+, −20, t(21;21) + mar 1, still retaining the inv(14) (Taylor and Butterworth 1986). A diagnosis of T cell lymphocytic leukaemia was made after the complex clone had occupied 100% of the mitogen-stimulated T cell compartment for over a year. Progression to the malignant phenotype appeared to occur as a result of the consecutive development of subclones of the original inv(14) clone. Clones with the t(X;14) translocation may also have the potential for becoming malignant. We have noted that in patient AT1CT, with the t(X;14) clone, several subclones have arisen with further translocations including one with an isochromosome 8 (i8q) similar to that described in the previous patient (AT5BI) with a T cell tumour (Taylor and Butterworth 1986).

There is more than one chromosome translocation associated with human T cell leukaemogenesis. These include t(8;14) involving TCRα and c-*myc*, and both t(11;14) and t(10;14) involving TCRα with unknown genes on chromosome 11, and 10 respectively. In some of these translocations there is apparently no requirement for further complex chromosomal rearrangements in the leukaemic cells (Erikson et al. 1985; Williams et al. 1984; Kagan et al. 1987). In all T cell tumours both in A-T patients and non-A-T patients the initial chromosome rearrangement e.g. t(14;14), inv(14) or t(8;14) may determine the subsequent phenotype of the tumour that develops. A-T patients may be more prone to T-CLL by being more likely to produce inv(14) or t(14;14) rearrangements, possibly as a result of a defective immune system gene rearrangement, or as a result of failure to remove cells with these rearrangements. The same sequence of events may also occur at a much lower frequency in non-A-T patients with T cell tumours associated with inv(14) inversions.

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References

Al Saadi A, Palutke M, Krishna Kumar G (1980) Evolution of chromosomal abnormalities in sequential cytogenetic studies of ataxia telangiectasia. Hum Genet 55:23–29

Aurias A, Dutrillaux B (1986) Probable involvement of immunoglobulin superfamily genes in most recurrent chromosomal rearrangements from ataxia telangiectasia. Hum Genet 72:210–214

Aurias A, Dutrillaux B, Buriot D, Lejeune J (1980) High frequencies of inversion and translocation of chromosomes 7 and 14 in ataxia telangiectasia. Mutat Res 69:369–374

Baer R, Chen K-C, Smith SD, Rabbitts TH (1985) Fusion of an immunoglobulin variable gene and a T-cell receptor constant gene in the chromosome 14 inversion associated with T cell tumours. Cell 43:705–713

Baer R, Heppell A, Taylor AMR, Rabbitts PH, Boullier B, Rabbitts TH (1987) The breakpoint of an inversion chromosome 14 in a T cell leukaemia; sequences downstream of the immunoglobulin heavy chain locus implicated in tumorigenesis. Proc Natl Acad Sci USA 84:9069–9073

Barton P, Malcolm S, Murphy C, Ferguson-Smith MA (1982) Localisation of the human α-globin gene cluster to the short arm of chromosome 16 (16p12-16pter) by hybridisation in situ. J Mol Biol 156:269–278

Bernard O, Larsen C-J, Hampe A, Mauchauffe M, Berger R, Mathiew-Mahul D (1988) Molecular mechanisms of a t(8;14)(q24;q11) translocations juxtaposing c-*myc* and TCRα genes in a T cell leukaemia: involvement of a Vα internal heptamer. Oncogene 2: 195–200

Caccia N, Bruns GAP, Kirsch IR, Hollis GF, Bertner V, Mak TW (1985) T cell receptor α chain genes are located on chromosome 14 at 14q11–14q12 in humans. J Exp Med 101:1255–1260

Croce CM, Nowell PC (1986) Molecular genetics of human B cell neoplasia. Adv Immunol 38:245–274

Erikson J, Williams DC, Finan J, Nowell PC, Croce CM (1985) Locus of the α chain of the T cell receptor is split by a chromosome translocation in T cell leukaemias. Science 229:784–786

Erikson J, Finger L, Sun L, ar-Rushdi A, Nishikura K, Minowada J, Finan J, Emanuel BS, Nowell PC, Croce CM (1986) Deregulation of c-*myc* by translocation of the α locus of the T cells receptor in T cell leukemias. Science 232:884–886

Hecht F, Morgan R, Kaiser-McCaw Hecht B, Smith SD (1984) Common region on chromosome 14 in T cell leukaemia and lymphoma. Science 226:1445–1447

Hollis RJ, Kennaugh AA, Butterworth SV, Taylor AMR (1987) Growth of chromosomally abnormal T cell clones in ataxia telangiectasia patients is associated with translocation at 14q11 – a model for other T cell neoplasia. Hum Genet 76:389–395

Isobe M, Erikson J, Emanuel BS, Nowell PC, Croce CM (1985) Location of gene for β subunit of human T cell receptor at band 7q35, a region prone to rearrangements in T-cells. Science 228:280–282

Kagan J, Finan J, Letofsky J, Besa EC, Nowell PC, Croce CM (1987) α chain locus of the T cell antigen receptor is involved in the t(10;14) chromosome translocation of T cell acute lymphocytic leukaemia. Proc Natl Acad Sci USA 84:4543–4546

Kennaugh AA, Butterworth SV, Hollis R, Baer R, Rabbitts TH, Taylor AMR (1986) The chromosome breakpoint at 14q32 in an ataxia telangiectasia t(14;14) T cell clone is different from the 14q32 breakpoint in Burkitt's and an inv(14) T cell lymphoma. Hum Genet 73:254–259

Le Beau MM, McKeithan TW, Shima EA, Goldman-Leikin RE, Chan SJ, Bell GI, Rowley JD, Diaz MO (1986) T cell receptor α-chain gene is split in a human T-cell leukaemia cell line with a t(11;14)(p15;q11). Proc Natl Acad Sci USA 83:9744–9758

Lewis WH, Michalpoulos EE, Williams DL, Minden MD, Mak TW (1985) Breakpoints in the human T-cell antigen receptor α chain locus in two T cell leukaemia patients with chromosomal translocations. Nature 317:544–546

Mathieu-Mahul D, Sigaux F, Chen Z, Bernheim A, Mauchauffe M, Daniel M-T, Berger R, Larsen C-J (1986) A t(8;14)(q24;q11) translocation in a T-cell leukaemia (L1-ALL) with c-*myc* and TcR-alpha chain locus rearrangements. Int J Cancer 38:835–840

McCaw BK, Hecht F, Harnden DG, Teplitz RL (1975) Somatic rearrangement of chromosome 14 in human lymphocytes. Proc Natl Acad Sci USA 72:2071–2075

McKeithan TW, Shima EA, Le Beau MM, Minowada J, Rowley JD, Diaz MO (1986) The molecular cloning of the breakpoint junction of a human chromosomal 8;14 translocation involving the T cell receptor α chain gene and sequences of the 3′ side of *myc*. Proc Natl Acad Sci USA 83:6636–6640

Mengle-Gaw L, Willard HF, Smith CIE, Hammarstrom L, Fischer P, Sherrington P, Lucas G, Thompson PW, Baer R, Rabbitts TH (1987) Human T cell tumours containing chromosome 14 inversion or translocation with breakpoint proximal to immunoglobulin joining regions at 14q32. EMBO J 6:2273–2280

Mure C, Waldmann RA, Morton CC, Bongiovanni KF, Waldmann TA, Shows TB, Seideman JG (1985) Human γ chain genes are rearranged in leukaemic T cells and map to the short arm of chromosome 7. Nature 316:549–552

O'Connor RD, Brown MG, Francke U (1982) Immunologic and karyotypic studies in ataxia telangiectasia; specificity of breakpoints on chromosome 7 and 14 in lymphocytes from patients and relatives. In: Bridges BA, Harnden DG (eds) Ataxia telangiectasia. A cellular and molecular link between cancer, neuropathology and immune deficiency. Wiley, Chichester, pp 251–270

Shima EA, Le Beau MM, McKeithan TW, Minowada J, Showe LC, Mak TW, Minden MD, Rowley JD, Diaz MO (1986) Gene encoding the α chain of the T cell receptor is moved immediately downstream of c-*myc* in a chromosomal 8;14 translocation in a cell line from a human T-cell leukemia. Proc Natl Acad Sci USA 83:3439–3443

Shtivelman E, Lifshitz B, Gale RP, Canaani E (1985) Fused transcript of *abl* and *bcr* genes in chronic myelogenous leukaemia. Nature 315:550–554

Sparkes RS, Como R, Golde DW (1980) Cytogenetic abnormalities in ataxia telangiectasia with T cell chronic lymphocytic leukaemia. Cancer Genet Cytogenet 1:329–336

Spector BD, Filipovich AH, Perry GS, Kersey JH (1982) Epidemiology of cancer in ataxia telangiectasia. In: Bridges BA, Harnden DG (eds) Ataxia telangiectasia. A cellular and molecular link between cancer, neuropathology and immune deficiency. Wiley, Chichester, pp 103–138

Taylor AMR (1982) Cytogenetics of ataxia telangiectasia. In: Bridges BA, Harnden DG (eds) Ataxia telangiectasia. A cellular and molecular link between cancer, neuropathology and immune deficiency. Wiley, Chichester, pp 53–82

Taylor AMR, Butterworth SV (1986) Clonal evolution of T cell chronic lymphocytic leukaemia in a patient with ataxia telangiectasia. Int J Cancer 37:511–516

Taylor AMR, Oxford JM, Metcalfe JA (1981) Spontaneous cytogenetic abnormalities in lymphocytes from thirteen patients with ataxia telangiectasia. Int J Cancer 27:311–319

Williams DL, Look AT, Melvin SL, Roberson PK, Dahl G, Flake T, Stass S (1984) New chromosomal translocations correlate with specific immunophenotypes of childhood acute lymphoblastic leukaemia. Cell 36:101–109

Yanagi Y, Chan A, Chin B, Minden M, Mak TW (1985) Analysis of cDNA clones specific for human T cells and the α and β chains of the T cell receptor heterodimer from a human T cell line. Proc Natl Acad Sci USA 82:3430–3434

Zech L, Godal T, Hammarstrom K, Mellstedt H, Smith CIE, Totterman T, Went M (1986) Specific chromosome markers involved with chronic T lymphocyte tumours. Cancer Genet Cytogenet 21:67–77

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