calcium enrichment on tree stems during rain. This enrichment may be part of a general nutrient tropism caused by stem flow that would enhance root growth near the base of tree stems and that ultimately may cause root apogeotropism in these forests. This idea is supported by (i) increased depth of the root mat at the base of stems, (ii) increased rates of root growth with nutrient enrichments especially toward calcium sources, and (iii) the key role of calcium in initiating root apogeotropism.

Several intriguing questions remain concerning apogeotropic roots. The total number of species that produce these roots was not determined by this study. The mycorrhizal status of these roots is unknown. Apogeotropic roots of *Eperua purpurea* are abundant on stems of other species, but for unknown reasons, other species' roots are excluded from growing up stems of *Eperua purpurea*. Climbing roots have yet to be widely examined as a feature of nutrient cycling in tropical rain forests. There is anecdotal evidence, however, that roots in Asian tropical rain forests are capable of climbing nearby stems (*12*). I have observed apogeotropic roots in *Metrosideros* sp. forests in Hawaii Volcanoes National Park, Hawaii (19°31'N, 155°27'W), and in rain forests near La Selva Biological Station (10°25'N, 84°01'W) in Costa Rica in addition to those at San Carlos de Rio Negro.

Climbing roots have evolved in rain-forest tree species representing at least five families (Table 1). These roots appear to have evolved in environments with low soil nutrient availability, but where a reliable, relatively rich source of nutrients is available via stem flow. Species with climbing roots absorb stem flow nutrients before these nutrients enter the soil and become either generally available to the roots of all species or unavailable to plants because of leaching and strong adsorption on soil particles. Climbing roots form a nutrient cycling pathway in which nutrients entering tropical forests in the form of stem flow are absorbed and transported from one stem to another without entering the soil solution.

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Relationship Between the c-*myb* Locus and the 6q− Chromosomal Aberration in Leukemias and Lymphomas

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Deletions of the long arm of chromosome 6 (6q−) are frequently found in hematopoietic neoplasms, including acute lymphoblastic leukemias, non-Hodgkin lymphomas and (less frequently) myeloid leukemias. The c-*myb* proto-oncogene has been mapped to region 6q21–24, which suggests that it could be involved in the 6q− aberrations. By means of in situ chromosomal hybridization on cells from six hematopoietic malignancies, it was demonstrated that the c-*myb* locus is not deleted, but is retained on band q22, which is consistently bordered by the chromosomal breakpoints in both interstitial and terminal 6q− deletions. The deletion breakpoints were located at some distance from the *myb* locus since no rearrangement of c-*myb* sequences was found. In one case, however, amplification of the entire c-*myb* locus was detectable. Furthermore, in all cases tested that carry 6q− deletions, *myb* messenger RNA levels were significantly higher than in normal cells or in malignant cells matched for lineage and stage of differentiation but lacking the 6q− marker. These results indicate that 6q− deletions are accompanied by structural and functional alterations of the c-*myb* locus and that these alterations may be involved in the pathogenesis of leukemias and lymphomas.

NONRANDOM AND SPECIFIC CHROMOSOME aberrations have been described in several malignant disorders of animals and man (*1*). A role for these cytogenetic abnormalities in the pathogenesis of different tumors is supported by the findings that in some cases proto-oncogene loci are specifically involved in the chromosomal recombinations (*2*). This is the case for the c-*myc* and c-*abl* loci in the (8;14) and (9;22) translocations typical of undifferentiated B-cell lymphoma (UBL) and chronic myelogenous leukemia (CML), respectively (*3–4*).

A frequent, yet poorly characterized chromosomal abnormality is represented by an apparently heterogeneous group of deletions of part of the long arm of chromosome 6 (6q−), including both interstitial and terminal deletions with breakpoints at region 6q21–23. The 6q− abnormalities were originally reported as a relatively frequent observation in acute lymphoblastic leukemia (ALL) (*5*) and are included in the restricted catalog of chromosomal defects that can be found as single aberrations in a defined group of tumors (*6*). Recent studies involving large panels of cases have reported that 6q− deletions are found in 5 to 25% of ALL (*5, 7*), in 30% of non-Hodgkin lymphomas (NHL) (*8*), and, less frequently, in acute myelogenous leukemia (AML) and CML (*9*).

The c-*myb* proto-oncogene has been localized on chromosome 6 in the approximate region 6q21–24 (*10*). The possible relationship between the 6q− abnormality found in hematopoietic neoplasms and the c-*myb* gene is particularly intriguing, in view of the apparent hematopoiesis-specific expression of this gene. In fact, c-*myb* messenger RNA (mRNA) has primarily been found in hematopoietic cells, where relatively high levels are detectable in immature myeloid and lymphoid precursors (*11*). Expression of c-*myb* is induced in proliferating immature hematopoietic cells (*12*) and suppressed in terminally differentiated cells (*10, 13*), suggesting that this gene may be involved in the

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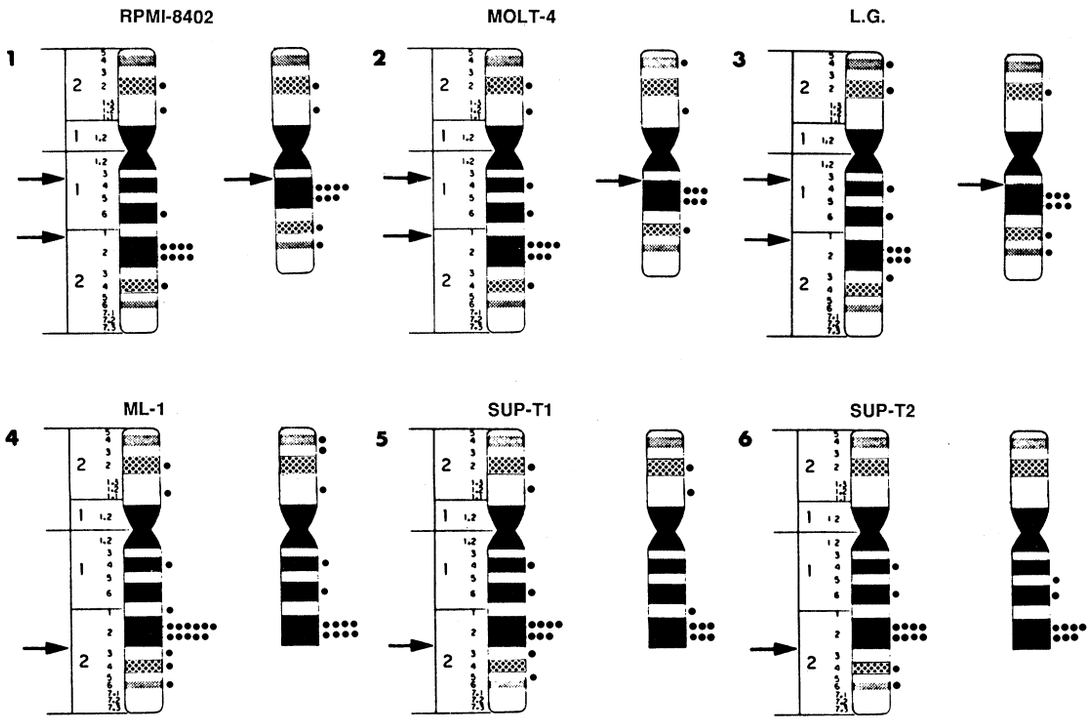


Fig. 1. Distribution of c-*myb* labeled sites on normal 6 and 6q− chromosomes. In each case the normal and 6q− chromosomes are illustrated on the left and right side, respectively. The arrows identify the approximate position of the breakpoints.

control of proliferation and/or differentiation of hematopoietic cells. The expression of *myb* is also associated with hematopoietic transformation, since v-*myb* is responsible for the ability of avian myeloblastosis virus (AMV) to cause myeloblastic leukemia in chickens and to transform avian myelomonocytic cells in culture (*14*). Furthermore, truncations of cellular *myb* sequences by viral insertional mutagenesis appear to be associated with the pathogenesis of some mouse hematopoietic tumors (*15*), while c-*myb* gene amplification may be involved in the pathogenesis of human AML (*16*).

Chromosomal deletions in region 6q21–23 could result in the total or partial loss of the c-*myb* locus, in its translocation to another chromosome, or in its retention on chromosome 6 in variable proximity to the deletion breakpoint(s). To distinguish among these possibilities, we performed in situ chromosomal hybridization of human c-*myb* probes to metaphase chromosomes prepared from leukemia and lymphoma cells carrying 6q− deletions. In all six cases, c-*myb* probes specifically hybridized to both the normal 6 and 6q− chromosomes, but not to other chromosomes (Table 1), indicating that c-*myb* was neither lost nor translocated. On the normal chromosome 6 the hybridization consistently appeared on band q22. On chromosome 6q− the hybridization signal, which we assume to identify band q22 even though this band was not always morphologically identifiable, was located either terminally (ML-1, SUP-T1, and SUP-T2) or interstitially (RPMI-8402, MOLT-4, and L.G.), as shown schematically in Fig. 1. We interpreted these results as evidence for the existence of both terminal (q23–qter) and interstitial (q13–q21) 6q− deletions, occurring at either side of band q22 and c-*myb*; toward the centromere in the interstitial deletions and toward the telomere in the terminal deletions. In ML-1 cells, which carry an amplified c-*myb*, the hybridization signal on 6q−, but not on the normal 6 chromosome, was frequently represented by clusters of two to three grains. This observation may reflect the five- to tenfold c-*myb* amplification detectable in this case (*16*) and indicates its occurrence on the 6q− chromosome.

To investigate whether parts of c-*myb* or of its immediately flanking sequences were directly affected by the chromosomal breakpoints, we performed Southern blot hybridization analysis of genomic DNA from malignancies carrying the 6q− deletion and from analogous cases lacking this marker (*17*). By means of a set of complementary DNA (cDNA) and genomic probes in combination with several different restriction enzymes, the entire c-*myb* locus, spanning over 40 kb (*17*), plus 12 kb upstream from the putative 5′ end and 6 kb downstream of the polyadenylation signal, can be explored (Fig. 2B) (*17*). There was no divergence from the normal restriction enzyme pattern in the six cases carrying the 6q− abnormality (Fig. 2A) and in an additional 16 ALL, 24 NHL, and 20 AML cases lacking this chromosomal marker. However, amplification of *myb* sequences was detectable in two cases (Fig. 2A, lanes 2 and 6). One of these was the cell line ML-1 for which amplification and the 6q− marker were already reported (*16*). The second case represents a novel observation of c-*myb* amplification in primary AML cells for which, however, no cytogenetic data indicating the presence or absence of the 6q− marker were available.

Table 1. Results of in situ hybridization (*27*) of human c-*myb* probe to metaphase cells carrying 6q− chromosomes. The probe was a 2.8-kb Eco RI cDNA fragment (*17*) (Fig. 2) that had been labeled to a specific activity of 3×10^7 to 4×10^7 dpm/μg with ^{3}H-dTTP. L.G. was a primary cell culture; cell lines were as described (*28*).

Cells	Diagnosis	Total number of labeled sites	6*		6q−*	
			Total	q22	Total	q22
RPMI-8402	T-ALL	115	12 (10.4)†	8 (6.95)	11 (9.56)†	7(6)
MOLT-4	T-ALL	115	12 (10.4)†	7 (6.1)	9 (7.8)†	6 (5.2)
L.G.	T-NHL	106	11 (10.37)†	6 (5.66)	9 (8.49)†	6 (5.66)
ML-1	AML	102	18 (17.6)†	11 (10.78)	13 (12.74)†	8 (7.84)‡
SUP-T1	T-NHL	102	13 (12.7)†	7 (6.8)	9 (8.8)†	6 (5.8)
SUP-T2	T-ALL	110	12 (10.9)†	8 (7.2)	9 (8.18)†	7 (6.36)

*Data are shown as number of labeled sites (percent of labeling over entire genome). †The χ^2 value corresponds to $P < 0.0005$. The χ^2 analysis tests the hypothesis that labeling is random over all chromosomes. ‡Grains were arranged in clusters of two to three grains per cluster in three out of eight labeled sites.

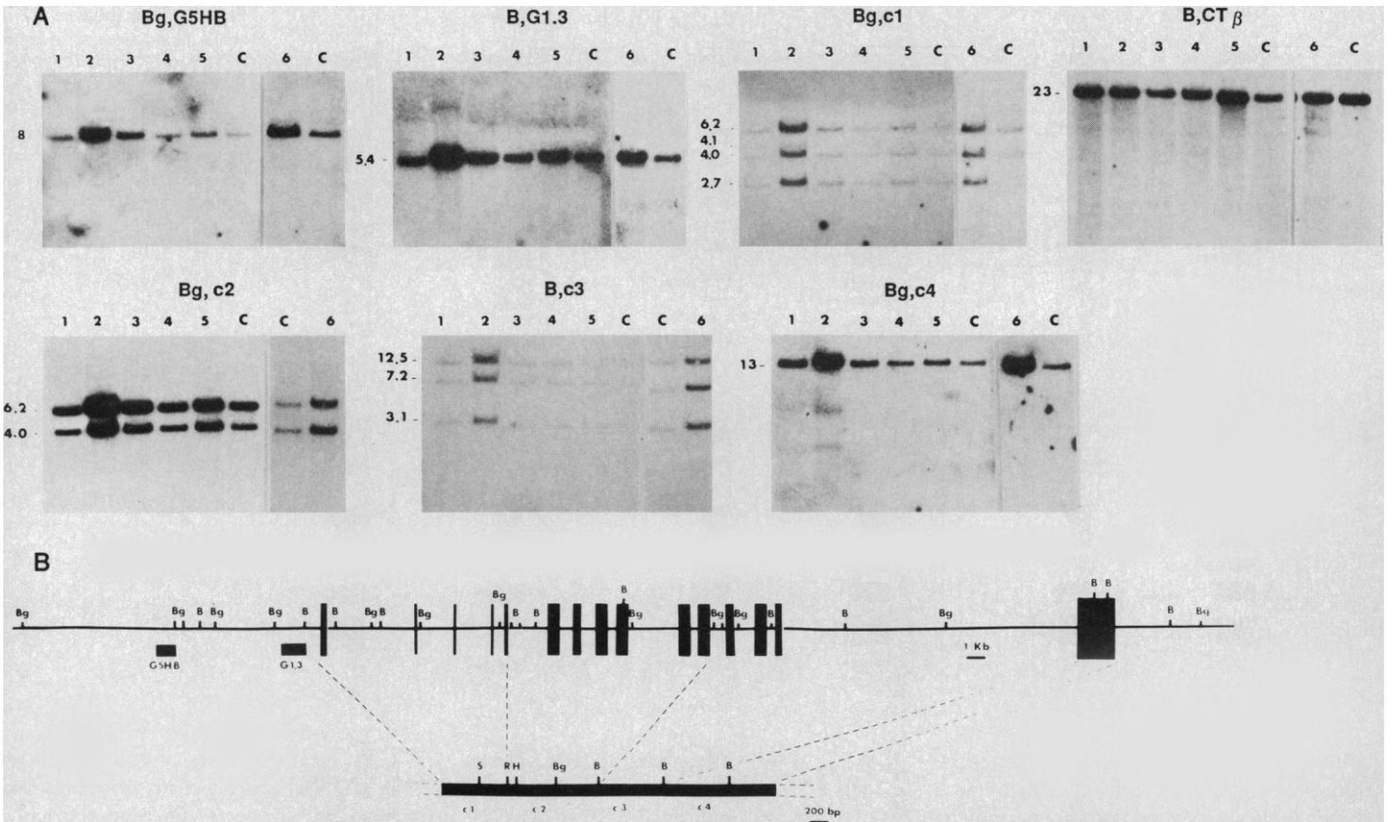


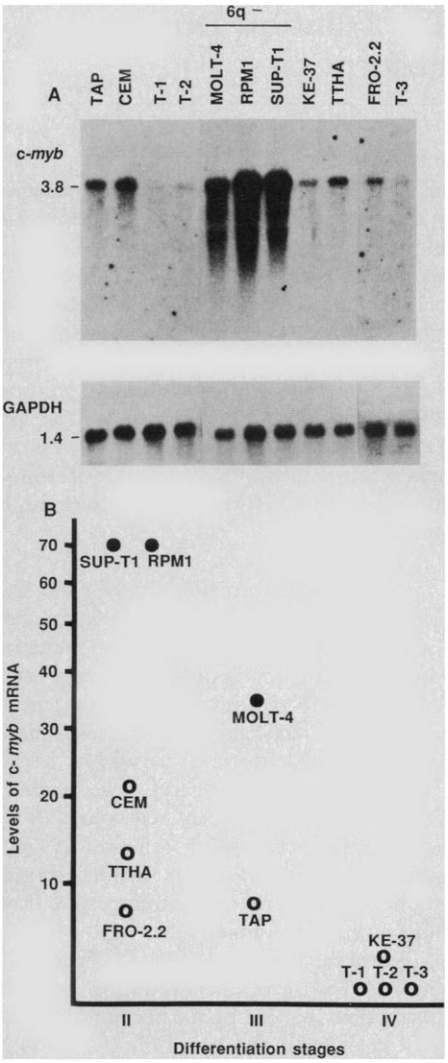
Fig. 2. Analysis of the genomic organization of the c-*myb* locus in cells carrying 6q− deletions. (**A**) Southern blot hybridization analysis of genomic DNA extracted from: (lanes 1) RPMI-8402 cell lines; (lanes 2) ML-1 cell line; (lanes 3) L.G., fresh T-NHL cells; (lanes 4) MOLT-4 cell line; (lanes 5) SUP-T1 cell line; (lanes 6) S.S., fresh AML cells; and (lanes c) HeLa cell line. DNAs were digested with the indicated restriction enzymes (Bg, Bgl II; B, Bam HI) and hybridized to the indicated probes. (Enzymes and probes are indicated above each gel.) Hybridization to the CT_β probe [constant region of human T-cell receptor β-chain gene (*20*)] was performed as control for the amount of DNA present on filters. Sizes are shown in kilobases. (**B**) Schematic representation of the human c-*myb* locus (top), of a human cDNA clone (*17*), and of the probes used for Southern blot analysis. Each probe is indicated either as a black box below the genomic map (G5HB, G1.3) or as c1–c4 below the cDNA map. Black boxes in the genomic map indicate the approximate position of c-*myb* exons (*17*). R, Eco RI; H, Hind III; S, Sst I; B, Bam HI; Bg, Bgl II.

In both AML cases, the amplification unit appears to contain the entire c-*myb* as presently identified (*17*) as well as 5′ and 3′ flanking sequences, since all the restriction fragments detected by the probes appear to be equally increased in copy number. These data together indicate that the chromosomal breakpoints of the 6q− deletion are not located within a presently measurable distance from the c-*myb* gene in all the six cases. Since the 5′ terminus of c-*myb* has not been functionally identified and is only tentatively assigned (*17*) to the first exon shown in Fig. 2B, the possibility remains that additional, hitherto unidentified, exons of the c-*myb* locus (or their flanking sequences) may be involved in the breakpoints. Indeed, a new exon has been recently identified >50 kb 5′ to the previously characterized c-*abl* sequences (*18*).

In view of the observation that the structure and function of c-*myb* are altered in UBL cells carrying a chromosomal breakpoint more than 50 kb distant from the 5′ or 3′ limit of the *myc* locus (*19*), we next examined the levels of c-*myb* mRNA expression in hematopoietic neoplasms carrying the 6q− abnormality and in normal and leukemic controls. Steady-state mRNA levels were studied by Northern blot hybridization with a human c-*myb* cDNA probe (Fig. 2). In addition to AML cells carrying c-*myb* amplification and the 6q− chromosome (*16*), very high levels are also detectable in three T-cell ALL (T-ALL), two T-NHL, and one B-NHL carrying the 6q− abnormality and a single copy gene (Fig. 3). These levels were >50-fold higher than those detectable in normal human T lymphocytes grown in vitro in the presence of interleukin-2 (IL-2) (Fig. 3). Furthermore, since it is known that c-*myb* expression is higher in immature hematopoietic cells and decreases during differentiation (*11*), we compared *myb* mRNA levels in 6q− T-cell malignancies and in analogous cells (T-ALL or T-NHL) that lacked the 6q− marker and were matched for stage of T-cell differentiation as determined by cell-surface marker analysis (stages I to IV) (*20*). Each 6q− case contained significantly more *myb* RNA than the respective controls (Fig. 3). Thus, the presence of the 6q− marker in T-ALL and T-NHL correlates with increased expression of c-*myb* in both immature and mature malignant T cells.

Our results indicate the need for a reevaluation of the architecture of the 6q− chromosomal deletions, the breakpoint of which have been reported by different authors to occur in a region spanning almost the entire 6q chromosome arm (*5, 7–9*). These apparent discrepancies may reflect actual heterogeneity of these aberrations or, as recently suggested (*21*), technical limitations in the cytogenetic analysis of the 6q− chromosome. The retention of c-*myb* in the 6q− chromosomes provides a marker for this chromosomal region allowing the definition of at least two types of 6q− deletions—terminal (6q23–qter) and interstitial (6q13–q21) with a common breakpoint cluster on band q22. Approximately the same region, 6q21–23, can be involved, although rarely, in gene amplification in AML. Also, this region is proximal to the breakpoints of reciprocal translocations involving different chromosomes in different ALL and NHL cases (*8*). When deletions and translocations are considered together, breakpoints on bands q21–23, most likely on q22, are present in as many as 50% of NHL cases (*8*). These observations suggest that the gene(s) critical for the putative

Fig. 3. Increased expression of c-*myb* mRNA in malignant cells carrying 6q− chromosomes. (**A**) Total RNA (20 μg) from the indicated T-ALL and T-NHL cell lines or normal human T lymphocytes (T-1, T-2, and T-3) grown in the presence of IL-2, was analyzed by Northern blot hybridization with the c-*myb* cDNA probe (clone c2, in Fig. 2). In order to provide a control for the amounts of RNA on the filter, the c-*myb* signal was removed from the same filter by boiling for 10 minutes in distilled water and rehybridized to a probe for the human glyceraldehyde-3-phosphate-dehydrogenase (GAPDH) gene, which is assumed to be equally expressed in all these cells (*29*). (**B**) Values of relative c-*myb* mRNA expression, obtained by densitometric screening of the filter in (A) and normalized against GAPDH values, are expressed as multiples of the *myb* RNA value detected in T-1, which is arbitrarily defined as 1. The *myb* RNA values for each case are grouped according to the differentiation stage of their respective NHL or ALL cells as determined by cell surface marker analysis (*20*). TAP (T-ALL), CEM (T-ALL), KE-37 (T-ALL), TTHA (T-ALL), FRO-2.2 (T-ALL), and SUP-T1 and SUP-T2 cell lines have been described (*28*). Sizes are shown in kilobases.



pathogenetic role of this abnormality is likely to be located in proximity to the conserved breakpoint rather than in the deleted or translocated regions which vary in different cases.

The present study provides further support for the hypothesis that c-*myb* is the critical element of the 6q− abnormalities by showing that: (i) c-*myb* is located in close cytogenetic proximity to the conserved breakpoint region; (ii) c-*myb* is involved in amplifications which, as shown for c-*myc* (*22*) and c-*abl* (*23*) as well as for other genes (*24*), occasionally accompany nearby chromosomal recombinations; and (iii) the levels of *myb* mRNA expression are significantly increased in malignant cell cases carrying a 6q−. A causal link between breakpoint locations and structure/function alterations cannot be presently demonstrated since the 5′ end of c-*myb* has not been conclusively identified. However, even if the breakpoints were located at some distance 3′ or 5′ from c-*myb* this would not preclude an effect of the breakpoint on c-*myb* structure and function. In fact, this situation would be reminiscent of the (2;8), (8;22), and some of the (8;14) translocations in UBL, where the breakpoints are located more than 50 kb upstream or downstream from c-*myc* (*19*) and are invariably accompanied by mutations within c-*myc* regulatory sequences (*19*). A relationship between nearby genomic recombinations and somatic mutations has been demonstrated in other systems as well (*25*). The increased expression of c-*myb* in 6q− cases may occur as the result of structural alterations caused by nearby chromosomal breakpoints or, alternatively, as the result of functional alterations of general mechanisms of gene regulation (such as chromatin arrangement, which may be locally altered in the rearranged 6q− region).

Regardless of the mechanism involved, the altered expression of c-*myb* observed in 6q− malignancies can have a significant role in the pathogenesis of hematopoietic neoplasms. The expression of this gene appears to correlate directly with proliferation and inversely with differentiation, since the gene is active in mature proliferating cells (*11, 12*) and is switched off in terminally differentiated, nonproliferating cells (*11, 13*). It has been proposed that the leukemogenic effect of v-*myb* sequences in AMV may be caused by its unregulated expression, which blocks the differentiation of immature myeloid precursors (*26*). Our data, showing that *myb* expression is maintained at high levels in both immature and relatively mature cells carrying the 6q− chromosome, suggest that the high constitutive expression of this gene may be involved in malignant transformation by promoting the continuous proliferation of these cells and by preventing further progression along the differentiation pathway.

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