

the *AML1* gene of chromosome 21, to produce a fusion gene. Expression of the fusion gene results in a fusion protein (218,219). The fusion product is named TEL-AML1 (also known as ETV6-RUNX1). TEL is also known as ETV6, while AML1 is also known as RUNX1. The chromosomal abnormality is named t(12;21), which refers to the fact that it is a translocation, and that the translocation involves chromosomes 12 and 21. The TEL-AML1 (ETV6/RUNX1) translocation appears to be a necessary, first step in the development of ALL, but this mutation alone is not sufficient to cause leukemia (220,221).

In B-cell precursor ALL, hyperdiploidy (more than 50 chromosomes) and TEL-AML1 fusion, which account for 25% and 23% of childhood cases but only 7% and 2% of adult cases, respectively, are associated with a favorable prognosis (222).

d. Cytogenetics for Diagnosis and Prediction—CML

Philadelphia chromosome encodes a mutant protein, that is, a fusion protein

(*BCR/ABL1*), that is responsible for causing CML.

The BCR/ABL1 fusion protein is essential for initiation, maintenance, and progression of CML (223).

Where a patient's cells contain Philadelphia chromosome, the genotype is called Ph-positive.

However, in about 1% of patients with CML, the bone marrow cells appear to be Ph-negative, although the *BCR/ABL1* fusion gene still exists, where it may be located on chromosomes 22q11, 9q34, or even on a third chromosome (224). The failure to observe Philadelphia chromosome in Ph-negative CML patients has been explained by a scenario where a first translocation forms Philadelphia chromosome, resulting in generation of the *BCR/ABL1* fusion gene, followed by a second translocation that restores what appears to be of the original, normal chromosomes. Virgili et al. (225) have identified the locations of the *BCR/ABL1* fusion gene in a number of Ph-negative CML patients.

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