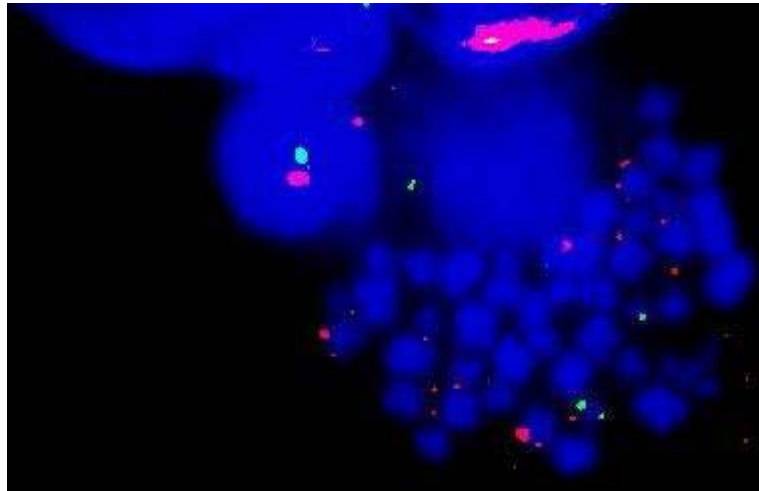


## amplified NUP214/ABL1

### Identity

Other names NUP214/ABL1 fusion gene on amplified episomes



Episomal amplification of ABL detected by FISH with the commercial probe LSI BCR-ABL ES.

### Clinics and Pathology

**Disease** T-cell acute lymphoblastic leukemia (T-ALL)

**Phenotype / cell stem origin** Immature T-cell leukemia (CD3+, CD2+ and CD7+). Not seen in B-cell ALL.

**Epidemiology** In about 6% of T-ALL. Mainly observed in T-ALL associated with the mutually exclusive overexpression of the oncogenes HOX11 and [HOX11L2](#). Found in pediatric T-ALL and adults T-ALL.

**Cytology** lymphoblasts

**Prognosis** Present data suggests that NUP214-ABL1 fusion gene amplification in T-ALL is associated with poor outcome. NUP214-ABL1 is sensitive to the tyrosine kinase inhibitor imatinib mesylate. Targeting therapies may improve outcome.

### Cytogenetics

**Note** Mechanism of gene amplification  
The main hypothesis for genomic amplification mechanism is that it is

a dynamic process. Molecular chronology of genomic amplification has been schematically described as follows. The first step is the production of submicroscopic, acentric, circular, extrachromosomal DNA molecules which replicate autonomously, called episomes. These DNA molecules are made of amplified genes. 2 mechanisms for the formation of episomes have been proposed: Conservative which preserves the original DNA sequence at the native chromosomal locus and non conservative which leads to the deletion of the original sequence at the native locus. The second step corresponds to an increase in copy number resulting from unequal mitotic segregation and an increase in size. They enlarge over time to form progressively heterogeneously sized structures, microscopically visible, called double minutes (dmin). In a later step they may integrate into chromosomes to generate intrachromosomally amplified structures (HSR). In some cases dmins or HSRs may form directly without precursors.

**Cytogenetics** Cryptic extrachromosomal amplification of the fusion NUP214-ABL.  
**Morphological** Rearrangement invisible by conventional cytogenetics. No dmins observed.

**Cytogenetics** FISH using commercially available ABL1 probe shows multiple  
**Molecular** extrachromosomal sites on metaphases and multiple signals in interphase nuclei. The extrachromosomal amplification of ABL1 appears to be pathognomonic for the presence of NUP214-ABL1 fusion in T-ALL.  
 There may be a corresponding deletion of the ABL1 probe on one of the chromosomes 9 (see note below concerning mechanisms of gene amplification).

**Additional anomalies** Associated with an apparently normal karyotype with banding techniques or variable additional abnormalities.

## Genes involved and Proteins

<b>Gene Name</b>	<a href="#">ABL1</a>
Location	9q34.1
Dna / Rna	Alternate splicing. mRNA of 6 and 7 kb
Protein	145 kDa; Localization: nuclear and cytoplasmic; Tyrosine kinase; Ubiquitously expressed
<b>Gene Name</b>	<a href="#">NUP214 (nuclear pore complex protein 241 kDa) or CAN, CAIN, Nucleoporin</a>
Location	9q34.3, more telomeric than ABL1.
Dna / Rna	7.5 kb mRNA
Protein	214 kDa; dimerization domains (2 leucine zippers) and a repeated motif; forms homodimers. Nuclear membrane localisation. Component of the Nuclear Pore Complex. Mediate nucleocytoplasmic transport.

## Result of the

## chromosomal anomaly

**Hybrid gene** Molecular analysis delineated the amplicon as a 500 kb region from chromosome band 9q34 containing the genes ABL1, LAMC3 and NUP214. The genomic region from ABL1 to NUP214 circularizes to generate the NUP214-ABL1 fusion gene = New mechanism for generation of a fusion gene. The breakpoint within ABL1 occurs in intron1 (coincides with ABL1 breakpoint in the Philadelphia chromosome). Whilst the breakpoint in NUP214 is variable (ranging from intron 23 to intron 34).

**Description**

**Detection** RT-PCR

**Fusion Protein** The NUP214-ABL transcript encodes a 239-333 kDa protein. NUP214-ABL retains the N-terminal region of NUP 214 which includes the predicted coiled-coil domains that serve as oligomerisation motifs. NUP214-ABL contains SH3, SH2 and kinase domains of ABL1. NUP214-ABL is a constitutively activated tyrosine kinase that activates similar pathways as BCR\_ABL1.

**Description**

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