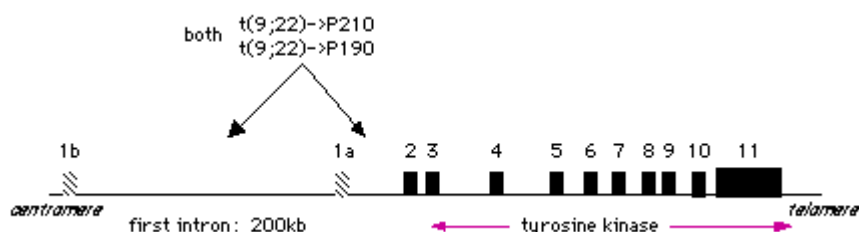


## ABL1 (v-abl Abelson murine leukemia viral oncogene homolog 1) (updated: old version not available)

### Identity

Other names **ABL**  
 Hugo **ABL1**  
 Location 9q34.1  
**CAN** is more telomeric, TAN1 even more in 9q34.3

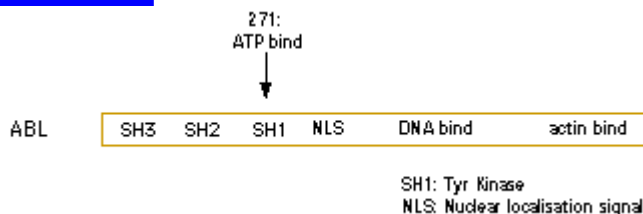
### DNA/RNA



DNA diagram

Description 12 exons; 230 kb  
 Transcription alternate splicing: 1a and 1b are 5' alternative exons; mRNA of 6 and 7 kb (with 1a and 1b respectively), giving rise to 2 protein of 145 kDa

### Protein



Protein diagram

Description 1130-1143 amino acids; 4 domains: of which are SH (SRC homology) domains; NH<sub>2</sub>-term -- domain 1: SH3 (where can bind the binding protein BP1, to inhibit SH1 activation) and SH2 (with high affinity towards BCR first exon) -- domain 2: SH1 (with a self-phosphorylable tyrosine) -- 'domain' 3: nuclear localization domain (DNA binding, but not during mitosis) -- domain 4: actin binding (cytoskeleton) --COOH-term; note: 1b (but not the 1a alternative) myristylable allowing anchorage to the membrane

Expression ubiquitously expressed , c-ABL K/O phenotype is lethal

Localisation nuclear and cytoplasmic

Function c-ABL exhibit a permanent nuclear and cytoplasmic shuttling activity, driven by 3 nuclear localisation signals (NLS) and a single nuclear export signal (NES) close to the C-terminal region. Recent data suggest that

nuclear and cytoplasmic ABL may have different functions.

1- Nuclear c-ABL plays a major role in the regulation of cell death after DNA damage. All DNA damage inducing agents activate nuclear c-ABL kinase in a ATM-dependent manner and in the presence of the p53-homolog p73 protein. The latter is physically associated with c-ABL after DNA damage through the SH3 domain of c-ABL. DNA damage also activates simultaneously p53 pathway, leading to the activation of Rb which induces growth arrest and protects cells from apoptosis. The exact mechanisms of apoptosis induced by c-ABL are unknown. The nuclear entrapment of BCR-ABL has also been shown to induce apoptosis in leukemic cells.

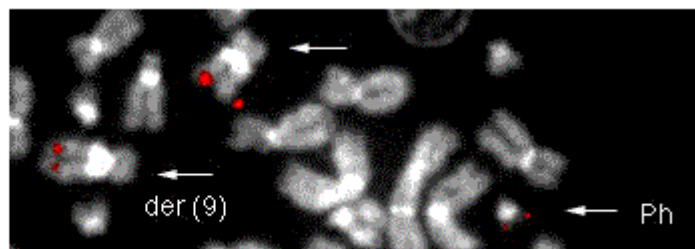
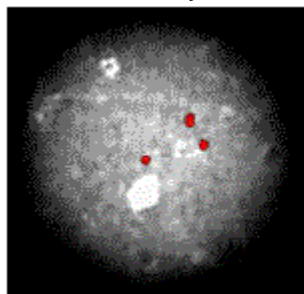
2- Cytoplasmic c-ABL : possible function in adhesion signalling as an efflux of c-ABL from nucleus to the cytoplasm is found in fibroblasts after adhesion.

Homology SRC homology; like SRC, ABL is one of the tyrosine kinases which are not membrane receptors

### Implicated in

**Entity** [t\(9;12\)\(q34;p12\)/ALL](#) --> [ETV6](#)-ABL  
**Disease** common ALL; yet poorly known  
**Hybrid/Mutated Gene** 5' ETV6/TEL from 12p12 - 3' ABL from 9q34  
**Abnormal Protein** NH2-term Helix Loop Helix from ETV6(TEL) fused to Tyr Kinase from ABL COOH-term; localised in the cytoskeleton.  
**Oncogenesis** forms HLH-dependent oligomers, which may be critical for Tyr kinase activation; oncogenesis may be comparable to that induced by BCR/ABL

**Entity** [t\(9;22\)\(q34;q11\)/CML](#) --> [BCR](#)/ABL  
**Disease** all CML have a t(9;22), at least at the molecular level (BCR/ABL); phenotype and stem cell origin: multipotent progenitor: t(9;22) is found in all myeloid and B- lineage progenitors  
**Prognosis** median survival => 4 yrs; alphaIFN therapy or BMT are indicated  
**Cytogenetics** anomalies additional to the t(9;22) may be found either at diagnosis or during course of the disease, or at the time of acute transformation; mainly: +der(22), +8, i(17q), +19; +21, -Y, -7, -17,+17; variant translocations: t(9;22;V) and apparent t(V;22) or t(9;V), where V is a variable chromosome, karyotypes with apparently normal chromosomes 9 and 22, may be found



[Probe 1132H12](#) on a case of CML with t(9/22). Note the splitting of the probe, evident also on interphase nuclei - Courtesy Mariano Rocchi, [Resources for Molecular Cytogenetics](#)

Hybrid/Mutated Gene see below  
Abnormal Protein see below  
Oncogenesis see below

**Entity** [t\(9;22\)\(q34;q11\)/ALL](#) --> [BCR/ABL](#)  
Disease most often CD 10+ ALL; frequent CNS involvement  
Prognosis is very poor (BMT is indicated); the breakpoint in M-bcr or in m-bcr (see below) does not seem to have impact on prognosis  
Cytogenetics the chromosome anomaly t(9;22) disappear during remission, in contrast with BC-CML cases (CML in blast crisis); additional anomalies: +der(22), -7, del(7q) most often, +8, but not an i(17q), in contrast with CML and ANLL cases; complex karyotypes, often hyperploid; variants and complex translocations may be found as in CML

Hybrid/Mutated Gene see below  
Abnormal Protein see below  
Oncogenesis see below

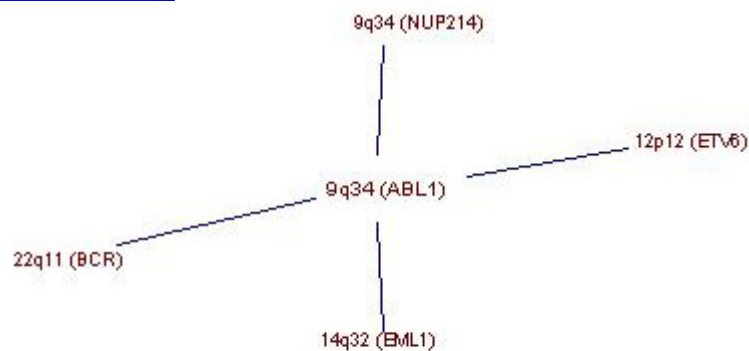
**Entity** [t\(9;22\)\(q34;q11\)/ANLL](#) --> [BCR/ABL](#)  
Disease ANLL mostly M1 or M2 ANL  
Prognosis is very poor  
Cytogenetics the chromosome anomaly t(9;22) disappear during remission, in contrast with BC-CML cases (CML in blast crisis); additional anomalies: similar to what is found in CML

Hybrid/Mutated Gene see below  
Abnormal Protein see below  
Oncogenesis see below

Hybrid/Mutated Gene BCR/ABL the crucial event lies on der(22), id est 5' [BCR](#) - 3' ABL hybrid gene is the crucial one, while ABL/BCR may or may not be expressed; breakpoint in ABL is variable over a region of 200 kb, often between the two alternative exons 1b and 1a, sometimes 5' of 1b or 3' of 1a, but always 5' of exon 2; breakpoint in BCR is either:  
1- in a region called M-bcr (for major breakpoint cluster region), a cluster of 5.8 kb, between exons 12 and 16, also called b1 to b5 of M-bcr; most breakpoints being either between b2 and b3, or between b3 and b4; transcript is 8.5 kb long; this results in a 210 KDa chimeric protein (P210); this is found in (most cases of) CML, and in half cases of ALL or ANLL  
HYBRID\_GENE  
2- in a 35 kb region between exons 1 and 2, called m-bcr (minor breakpoint cluster region), -> 7 kb mRNA, resulting in a 190 KDa protein (P190); this is found in half of the cases of ALL or ANLL  
3- A breakpoint in the exon 19 of BCR (designed as micro-bcr) with

	fusion to abl sequences (a2) has been in neutrophilic CML, with presence of a larger protein (P230).
Abnormal Protein	BCR/ABL P210 comprises the first 902 or 927 amino acids from BCR, P190 only the 427 N-term from BCR; BCR/ABL has a cytoplasmic localization, in contrast with ABL, mostly nuclear
Oncogenesis	BCR/ABL has a cytoplasmic localization role and all three BCR-ABL fusion proteins have been shown to exhibit oncogenic potential. All three hybrid proteins have increased protein kinase activity compared to ABL: 3BP1 (binding protein) binds normal ABL on SH3 domain, which prevents SH1 activation; with BCR/ABL, the first (N-terminal) exon of BCR binds to SH2, hiding SH3 which, as a consequence, cannot be bound to 3BP1; thereof, SH1 is activated; oncogenesis 1- proliferation is induced through activation by BCR/ABL of RAS signal transduction pathway, PI3-K (phosphatidyl inositol 3' kinase) pathway, and MYC; 2- BCR/ABL inhibits apoptosis; 3- BCR/ABL provokes cell adhesive abnormalities

## Breakpoints



ABL1 and partners. Editor 07/2005

## External links

	<b>Nomenclature</b>
<a href="#">Hugo</a>	<a href="#">ABL1</a>
<a href="#">GDB</a>	<a href="#">ABL1</a>
<a href="#">Entrez Gene</a>	<a href="#">ABL1</a> <a href="#">25</a> v-abl Abelson murine leukemia viral oncogene homolog 1
	<b>Cards</b>
<a href="#">Atlas</a>	<a href="#">ABL</a>
<a href="#">GeneCards</a>	<a href="#">ABL1</a>
<a href="#">Ensembl</a>	<a href="#">ABL1</a>
<a href="#">CancerGene</a>	<a href="#">ABL1</a>
<a href="#">Genatlas</a>	<a href="#">ABL1</a>
<a href="#">GeneLynx</a>	<a href="#">ABL1</a>
<a href="#">eGenome</a>	<a href="#">ABL1</a>
<a href="#">euGene</a>	<a href="#">25</a>
	<b>Genomic and cartography</b>
<a href="#">GoldenPath</a>	<a href="#">ABL1 - 9q34.1</a> <a href="#">chr9:130740007-130792614 + 9q34.12</a> (hg17-May_2004)

<a href="#">Ensembl</a>	<a href="#">ABL1 - 9q34.12 [CytoView]</a>
<a href="#">NCBI</a>	<a href="#">Genes Cyto</a> <a href="#">Gene Seq</a> [Map View - NCBI]
<a href="#">OMIM</a>	<a href="#">Disease map [OMIM]</a>
<a href="#">HomoloGene</a>	<a href="#">ABL1</a>
<b>Gene and transcription</b>	
<a href="#">Genbank</a>	<a href="#">K00009</a> [SRS] <a href="#">K00009</a> [ENTREZ]
<a href="#">Genbank</a>	<a href="#">M13099</a> [SRS] <a href="#">M13099</a> [ENTREZ]
<a href="#">Genbank</a>	<a href="#">M25949</a> [SRS] <a href="#">M25949</a> [ENTREZ]
<a href="#">Genbank</a>	<a href="#">S69223</a> [SRS] <a href="#">S69223</a> [ENTREZ]
<a href="#">Genbank</a>	<a href="#">U07563</a> [SRS] <a href="#">U07563</a> [ENTREZ]
<a href="#">RefSeq</a>	<a href="#">NM_005157</a> [SRS] <a href="#">NM_005157</a> [ENTREZ]
<a href="#">RefSeq</a>	<a href="#">NM_007313</a> [SRS] <a href="#">NM_007313</a> [ENTREZ]
<a href="#">RefSeq</a>	<a href="#">NT_086756</a> [SRS] <a href="#">NT_086756</a> [ENTREZ]
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<a href="#">TRASER</a>	<a href="#">ABL1</a> Traser - Stanford
<a href="#">Unigene</a>	<a href="#">Hs.431048</a> [SRS] <a href="#">Hs.431048</a> [NCBI] <a href="#">HS431048</a> [spliceNest]
<b>Protein : pattern, domain, 3D structure</b>	
<a href="#">SwissProt</a>	<a href="#">P00519</a> [SRS] <a href="#">P00519</a> [EXPASY] <a href="#">P00519</a> [INTERPRO]
<a href="#">Prosite</a>	<a href="#">PS00107</a> <a href="#">PROTEIN KINASE ATP</a> [SRS] <a href="#">PS00107</a> <a href="#">PROTEIN KINASE ATP</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS50011</a> <a href="#">PROTEIN KINASE DOM</a> [SRS] <a href="#">PS50011</a> <a href="#">PROTEIN KINASE DOM</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS00109</a> <a href="#">PROTEIN KINASE TYR</a> [SRS] <a href="#">PS00109</a> <a href="#">PROTEIN KINASE TYR</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS50001</a> <a href="#">SH2</a> [SRS] <a href="#">PS50001</a> <a href="#">SH2</a> [Expasy]
<a href="#">Prosite</a>	<a href="#">PS50002</a> <a href="#">SH3</a> [SRS] <a href="#">PS50002</a> <a href="#">SH3</a> [Expasy]
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<a href="#">Interpro</a>	<a href="#">IPR000719</a> <a href="#">Prot kinase</a> [SRS] <a href="#">IPR000719</a> <a href="#">Prot kinase</a> [EBI]
<a href="#">Interpro</a>	<a href="#">IPR000980</a> <a href="#">SH2</a> [SRS] <a href="#">IPR000980</a> <a href="#">SH2</a> [EBI]
<a href="#">Interpro</a>	<a href="#">IPR001452</a> <a href="#">SH3</a> [SRS] <a href="#">IPR001452</a> <a href="#">SH3</a> [EBI]
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<a href="#">Pfam</a>	<a href="#">PF00069</a> <a href="#">Pkinase</a> [SRS] <a href="#">PF00069</a> <a href="#">Pkinase</a> [Sanger] <a href="#">pfam00069</a> [NCBI-CDD]
<a href="#">Pfam</a>	<a href="#">PF00017</a> <a href="#">SH2</a> [SRS] <a href="#">PF00017</a> <a href="#">SH2</a> [Sanger] <a href="#">pfam00017</a> [NCBI-CDD]
<a href="#">Pfam</a>	<a href="#">PF00018</a> <a href="#">SH3</a> [SRS] <a href="#">PF00018</a> <a href="#">SH3</a> [Sanger] <a href="#">pfam00018</a> [NCBI-CDD]
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<a href="#">Smart</a>	<a href="#">SM00326</a> <a href="#">SH3</a> [EMBL]
<a href="#">Smart</a>	<a href="#">SM00219</a> <a href="#">TyrKc</a> [EMBL]
<a href="#">Prodom</a>	<a href="#">PD000001</a> <a href="#">Prot kinase</a> [INRA-Toulouse]
<a href="#">Prodom</a>	<a href="#">P00519</a> <a href="#">ABL1_HUMAN</a> [Domain structure] <a href="#">P00519</a> <a href="#">ABL1_HUMAN</a> [sequences sharing at least 1 domain]
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<a href="#">Blocks</a>	<a href="#">P00519</a>
<a href="#">PDB</a>	<a href="#">1AB2</a> [SRS] <a href="#">1AB2</a> [PdbSum], <a href="#">1AB2</a> [IMB]
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### Polymorphism : SNP, mutations, diseases

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### General knowledge

[Family Browser](#) [ABL1](#) [UCSC Family Browser]  
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[Amigo](#) [function|ATP binding](#)  
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[Amigo](#) [process|protein amino acid phosphorylation](#)  
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### Other databases

#### Probes

[Probe](#) [ABL \(9q34\) in normal cells \(Bari\)](#)  
[Probe](#) [ABL1 Related clones \(RZPD - Berlin\)](#)

#### PubMed

[PubMed](#) [70 Pubmed reference\(s\) in LocusLink](#)

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### **The molecular biology of chronic myeloid leukemia.**

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Medline [11071626](#)

### **Regulation of cell death by the Abl tyrosine kinase.**

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Medline [11114745](#)

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### **Contributor(s)**

**Written**      10-1997 Jean-Loup Huret

**Updated**      04-2001 Ali G Turhan

### **Citation**

*This paper should be referenced as such :*

**Huret JL** . ABL1 (v-abl Abelson murine leukemia viral oncogene homolog 1). Atlas Genet Cytogenet Oncol Haematol. October 1997 .

URL : <http://www.infobiogen.fr/services/chromcancer/Genes/ABL.html>

**Turhan AG** . ABL1 (v-abl Abelson murine leukemia viral oncogene homolog 1). Atlas Genet Cytogenet Oncol Haematol. April 2001 .

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