t(2;19)(p12;q13) IGK/BCL3, t(14;19)(q32;q13) IGH/BCL3, t(19;22)(q13;q11) BCL3/IGL

Jean-Loup Huret
Genetics, Dept Medical Information, University of Poitiers, CHU Poitiers Hospital, F-86021 Poitiers, France (JLH)

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Identity
Note: The t(14;19)(q32.3;q13.2) -as well as the variants t(2;19) and t(19;22)- is a recurrent translocation found in patients with chronic B-cell lymphoproliferative disorders.
This abnormality is cytogenetically identical but molecularly distinct from the t(14;19)(q32;q13) with IGH and CEBPA (or CEBPG) involvements, seen in acute B-cell lymphoblastic leukaemia.

Clinics and pathology
Disease
Chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CLL/SLL); most are the atypical form (at times reported as variant CLL, or transformed CLL), because of an atypical morphology and phenotype (Michaux et al., 1996; Michaux et al., 1997), but also for the presence of lymphocytosis (Soma et al., 2006), the frequency of
lymphadenopathy (Huh et al., 2007), young age (median 50-60 years), male predominence (about 2M/1F), and an aggressive course of the disease (Michaux et al., 1997).

Other diseases: marginal zone lymphoma (MZL), splenic marginal zone lymphoma (SMZL), diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma, low grade B-cell non Hodgkin lymphoma (NHL) not otherwise specified, aggressive B-cell NHL, and even one case of biphenotypic (B/M) acute leukemia.

A recent study reascertained and split the entity into the following subgroups herein below described; the accuracy of this proposal remains to be confirmed by further studies, inasmuch as there is a real problem of classification of t(14;19)(q32;q13) in chronic B-cell lymphoproliferative disorders, as has been pointed out (Soma et al., 2006; Huh et al., 2007):

"7q rearrangements cluster": 15% of cases: diagnosis of MZL/SMZL or aggressive B-cell NHL mostly. Medium complexity of the karyotype. IgVH mutated. Aggressive diseases. Median age 65 (49-85).

"Deletion 17p cluster": 10% of cases: diagnosis of CLL frequent. Complex karyotypes. IgVH mutated. Median age 54.

"1q rearrangements, deletions 6q and 13q cluster": 30% of cases: diagnosis of DLBCL or MZL and MZL in transformation, less often, CLL. Complex karyotypes. IgVH mutated. Median age 65.

"Trisomy 12 cluster": 45% of cases: diagnosis of CLL in most cases, low complexity of the karyotype. IgVH mutation rate low. This is the only cluster with an unequal sex ratio: 14M/4F; median age 65 (35-95).

**Phenotype/cell stem origin**

Chronic B-cell lymphoproliferation.

**Epidemiology**

103 published cases (40 reviewed in Soma et al., 2006; 7 cases in Huh et al., 2007; and 56 cases in Martin-Subero et al., 2007). Annual incidence 30/10^6. The t(14;19) occurs in less than 0.2 % of B-cell malignancies.

**Clinics**

Often a slow evolutive disease.

**Prognosis**

 Highly variable according to the staging: from staging A: where the survival is not reduced compared to age matched population, to staging C: with a median survival of 2 yrs. t(14;19) is often associated with rapidly progressive disease, and overall prognosis is poor compared to the expected survival in chronic lymphocytic leukemia and low-grade B-cell lymphoma. The prognosis has to be reascertained according to new (or further) sub-classification of the disease.

**Cytogenetics**

**Cytogenetics morphological**

The t(14;19)(q32.3;q13.2) is reciprocal and results in 14q+ and a 19q- derivative chromosomes.

**Cytogenetics molecular**

FISH is useful for identifying variant translocations.

**Additional anomalies**

The t(14;19) is rarely the sole cytogenetic aberration. Trisomy 12 is the most frequent associated abnormality, and is observed in 50% of cases. del(6q), del(7q), del(13q), del(17p) and additional 14q32 rearrangements can be found. Other chromosomes involved in structural aberrations are 1q, 3p, 3q, 6p, 7q, 11q, 12p.

**Variants**

t(2;19)(p12;q13) IGK/BCL3 and t(19;22)(q13;q11) BCL3/IGL, variants of the t(14;19)(q32;q13) IGH/BCL3, have been described; they are found in the same proportions as for the variants of the t(8;14)(q24;q32).

**COMPLEX TRANSLOCATIONS:** Three way "variants" are relatively frequent, compared to variants in other recurrent translocations. t(14;17;19) and t(7;19;14) were described.

**Genes involved and proteins**

**IgH**

**Location**

14q32

**Note**

IgK or IgL can replace IgH (see above).

**BCL3**

**Location**

19q13

**DNA/RNA**

9 exons, spanning 11.5 kb, BCL3 mRNA is expressed in a variety of tissues, particularly in spleen, liver and lung.

**Protein**

Encodes a protein which contains seven ankyrin repeats. Similar repeats are described in the structural protein ankyrin, as well as in proteins involved in cell cycle control and lineage determination (SW14, SW16, lin2).

BCL3 is a member of the IkappaB family, whose proteins regulate the NFkappaB family of transcription factors. NFkappaB plays a major role in B-cell development.
Result of the chromosomal anomaly

Hybrid gene
Description
The breakpoint is located in the 5' untranslated region of the BCL3 gene. BCL3 is juxtaposed to the immunoglobulin heavy chain gene locus on chromosome 14 (often in the switch alpha region) in a "head-to-head" configuration.

Fusion protein
Oncogenesis
No fusion protein. The translocation does not interrupt the transcriptional integrity of BCL3, but is associated with increased production of a BCL3 RNA of normal size. The immunoglobulin enhancer is not present on the same derivative chromosome as BCL3, suggesting other mechanisms for overexpression. The genes affected by overexpression of BCL3 remain to be identified.

References


This article should be referenced as such:
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