Leukaemia Section
Short Communication

t(8;21)(q22;q22) RUNX1/RUNX1T1

Wilma Kroes, Marian Stevens-Kroef

Department of Clinical Genetics, Leiden University Medical Center, Leiden; Department of Human Genetics, Radboud university medical center, Nijmegen, The Netherlands. w.g.m.kroes@lumc.nl; Marian.Stevens-Kroef@radboudumc.nl

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Abstract

Review on t(8;21)(q22;q22) RUNX1/RUNX1T1, with data on clinics, and the genes involved.

Identity

See figure below.

G- banding (left) - Courtesy Jean-Luc Lai and Alain Vanderhaegen (top) and Diane H. Norback, Eric B. Johnson, Sara Morrison-Delap; R- banding (middle) - above: Jean Loup Huret; 2nd row: - Courtesy Christiane Charrin; 3rd and 4th row: - Courtesy Roland Berger. Right: FISH - Courtesy Hossein Mossafa.
Translocation t(8;21) is found in 5-12% of AML. Among the non-random chromosomal aberrations observed in AML, t(8;21)(q22;q22) is one of the best known and usually correlates with AML M2, with well defined and specific morphological features. The common morphological features include the presence of large blast cells with abundant basophilic cytoplasm, often containing numerous azurophilic granulations; few blasts in some cases show very large granules (pseudo-Chediak-Higashi granules), suggesting abnormal fusion. Auer rods are frequently found. In addition to the large blast cells, there are also some smaller blasts, predominantly found in the peripheral blood. Promyelocytes, myelocytes and mature granulocytes with variable dysplasia are seen in the bone marrow. These cells may show abnormal nuclear segmentation and/or cytoplasmic staining defects including homogeneous pink colored cytoplasm - Text and iconography Courtesy Georges Flandrin 2001.

Clinics and pathology

**Disease**
Acute myeloid leukemia (AML) with t(8;21)(q22;q22) is part of the Group of AML with recurrent genetic abnormalities.

**Phenotype/cell stem origin**
M2 mostly, rarely: M1 or M4

**Epidemiology**
Annual incidence: 1/10^6; 5% of AML, 10% of prior AML M2 (FAB classification). The most frequent anomaly in childhood AML; seen in children and adults: mean age 30yrs, rare in elderly patients.

**Clinics**
Myeloid sarcomas may be present at presentation.

**Prognosis**
Complete remission (CR) in most cases (90%) with relatively long disease-free survival when treated with high dose chemotherapy.

**Cytology**
See figure and legend.

t(8;21)(q22;q22): cohybridization experiments using dJ155L8 (RUNX1T1) and dJ1107L6 (RUNX1 ); note the splitting of RUNX1 and colocalization on der(8) with RUNX1T1 - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.
RUNX1 and RUNX1T1 breakpoints in the t(8;21) / 5' RUNX1 - 3' RUNX1T1 fusion gene, and FISH - Courtesy Hossein Mossafa.

**Cytogenetics**

**Cytogenetics molecular**
Cases with cryptic molecular translocation have been detected --> FISH use may be relevant.

**Additional anomalies**
Sole anomaly in only 20-30%; additional anomalies: loss of Y or X chromosome in half cases (1 X must be present), del(7q) or -7, +8, del (9q): 10% each.

**Variants**
Complex t(8;21:Var) involving a (variable) third chromosome have been described in 3%; part from chromosome 21 goes on der(8), part of the 8 on der (Var), and part of Var on der(21); therefore, the crucial event lies on der(8).

**Genes involved and proteins**

**RUNX1T1 (runt-related transcription factor 1; translocated to, 1 (cyclin D-related))**

**Location**
8q21.3

**DNA/RNA**
Transcription is from telomere to centromere.

**Protein**
3 proline rich domains, 2 Zn fingers, and in C-term, a PEST region; tissue restricted expression; nuclear localisation; putative transcription factor.
**RUNX1 (run-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene))**

**Location**
21q22.12

**DNA/RNA**
Transcription is from telomere to centromere.

**Protein**
Contains a Runt domain and, in the C-term, a transactivation domain; forms heterodimers; widely expressed; nuclear localisation; transcription factor (activator) for various hematopoietic-specific genes.

**Result of the chromosomal anomaly**

**Hybrid gene**
**Description**
5' RUNX1 - 3' RUNX1T1; breakpoints: at the very 5' end of RUNX1T1, between exons 5 and 6 in RUNX1.

**Detection**
Karyotyping, RT-PCR and FISH for cases of typical cell morphology, but apparently without the t(8;21); RT-PCR for minimal residual disease detection

**Fusion protein**
**Description**
The N-term runt domain from RUNX1 is fused to the 577 C-term residues from RUNX1T1; reciprocal product not detected; probable DNA binding role; the fusion protein retains the ability to recognize the RUNX1 concensus binding site (→ negative dominant competitor with the normal RUNX1) and to dimerize with the CBFb subunit.

**Oncogenesis**
Probable altered transcriptional regulation of normal RUNX1 target genes.

**References**


Ohki M. Molecular basis of the t(8;21) translocation in acute myeloid leukaemia. Semin Cancer Biol. 1993 Dec;4(6):369-75


This article should be referenced as such: