Leukaemia Section
Short Communication

t(X;17)(p11;q21) BCOR/RARA

Yukiya Yamamoto

Department of Hematology, Fujita Health University, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan (YY)

Published in Atlas Database: January 2012
Online updated version: http://AtlasGeneticsOncology.org/Anomalies/t0X17p11q21ID1594.html
DOI: 10.4267/2042/47344

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2012 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Epidemiology
Very rare. One case has been reported.

Clinics
A bone marrow sample was markedly hypercellular, containing 83% promyelocytes. Coagulopathy was present with an increased prothrombin time, an activated partial thromboplastin time, decreased fibrinogen, and mildly increased fibrin/fibrinogen degradation products.

Cytology
Bone marrow promyelocytes were strongly positive for Sudan black B, myeloperoxidase staining and naphthol AS-D chloroacetate staining and negative for alphonaphthyl butyrate staining. Flow cytometric analysis: HLA-DR-/CD13+/CD33+/CD56+.

Treatment
Conventional chemotherapy plus ATRA achieved complete remission, followed with consolidation therapies. However, 35 months after diagnosis, the patient relapsed and cord blood transplantation was performed with a myeloablative conditioning regimen. After engraftment was achieved, a bone marrow sample showed third CR. The patient demonstrated overt coagulopathy, sensitivity to ATRA, but resistance to arsenic trioxide.
Rectangular cytoplasmic bodies and round inclusions are found in some of hypergranular promyelocytes. May-Giemsa staining.

**Cytogenetics**

**Genes involved and proteins**

**BCOR**
- **Location**: Xp11.4
- **Protein**: The BCL6 co-repressor, BCOR, is a ubiquitously expressed nuclear protein which directly interfaces to proto-oncoprotein BCL6. BCOR also associates with HDACs, the polycomb group protein PCGF1/NSPC1 and the histone demethylase FBXL10, which implies that it could suppress gene transcription by epigenetic mechanisms.

**RARa**
- **Location**: 17q12-21
- **Protein**: Wide expression; nuclear receptor; binds specific DNA sequences: HRE (hormone response elements); ligand and dimerization domain; role in growth and differentiation.
Result of the chromosomal anomaly

Hybrid gene

Transcript
BCOR cDNA (isoform b; reference NM_001123384) from exons 1 to 12 to be fused to RARA exon 3. Full length chimeric fusion transcripts spanning from the start codon to 4948 nt of BCOR cDNA fused to RARA cDNA from exon 3 to the stop codon. A reciprocal chimeric cDNA of RARA-BCOR was not detected.

Fusion protein

Description
BCOR-RARA had a BCOR BBD (498–514 aa), three Ankyrin repeats (1410–1509 aa) of BCOR, a DNA binding domain (DBD) derived from RARA (1557–1622 aa) and a ligand binding domain of RARA (1669–1888 aa).

Expression / Localisation
BCOR-RARA localized as two patterns; (I) diffusely in the nucleus as well as PML-RARA, (II) diffusely in the nucleus and aggregately in the cytoplasm. The subcellular localization of BCOR-RARA was clearly distinguishable from the punctuate pattern shown in the nucleus of BCOR-expressing cells.

Oncogenesis
BCOR-RARA was found to possess common features with other RARA fusion proteins. These included: (I) the same break point in RARA cDNA; (II) self-association; (III) RXRA is necessary for BCOR-RARA to associate with the RARA responsive element; (IV) action in a dominant-negative manner on RARA transcriptional activation; (V) aberrant subcellular relocalization.

References

This article should be referenced as such: