Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Leukaemia Section

Mini Review

t(4;11)(p12;q23)

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Clinics and pathology

Disease

Treatment related diseases.

Clinics

Four cases to date:
A 67 year old female patient with acute lymphoblastic leukemia (ALL) following breast adenocarcinoma treatment; latency was 5 years.
A 49 year old female patient with acute myeloid leukemia. The patient have had a non Hogkin lymphoma and a breast adenocarcinoma, 5 years and more before onset of the leukemia.
The third case was that of a 3 year old boy with juvenile myelomonocytic leukemia 17 months after treatment of a pre-B ALL with the typical t(12;21)(p13;q22) (ETV6/RUNX1).
The fourth case was a 4 year old boy; the t(4;11) was found from bone marrow surveillance, 18 months after diagnosis of a metastatic neuroblastoma; there was no other evidence of leukemia and the patient carried the t(4;11) and remained healthy for 37 months, before progression to myelodysplasia.

Prognosis

One patient died at 1 month, the 3 others reached complete remission and were alive at 13 months+, 19 months+, and 51 months+.

Cytogenetics

Additional anomalies

Sole anomaly in 3 cases, accompanied with major karyotypic anomalies in the remaining case: duplication of the der(4), t(1;7)(q10;p10), del(20q), +3, +6, +8, +19, +22.

Genes involved and proteins

FRYL

Location
4p12
Protein
FRYL, also called AF4p12, is the homolog of the Drosophilia melanogaster furry (Fry). Fry maintains the integrity of polarized cell extensions during morphogenesis (Cong et al., 2001; He and Adler, 2001). The morphogenesis of these cell extensions involves the activation of the actin and microtubule cytoskeletons (Tilney et al., 2000). Fry controls various aspects of dendritic outgrowth and branching via the Tricornered (Trc) kinase and Furry (Fry) Trc/Fry signaling pathway; in particular, it may regulate dendritic tiling (non-redundant coverage via dendritic repulsion) and dendritic self-avoidance (Emoto et al., 2004; Gao, 2007).

MLL

Location
11q23
Protein
Transcription regulator (yin/yang?), regulates, among others, HOX genes expression. --> hematopoiesis and embryogenesis regulation.

Result of the chromosomal anomaly

Hybrid gene

Description
In frame fusion between MLL exon 6 and FRYL exon 49 in one case, between MLL exon 8 and FRYL exon 51 in another case.

Fusion protein

Description

The 2074 or 2156 predicted amino acids of the fusion protein comprise the N-term AT hooks, speckled nuclear localisation signals and repression domains (methyl transferase domain) of MLL, and the leucine zipper domain from FRYL C-term.

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