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Leukaemia Section
Short Communication

t(6;20)(q13;q12) LMBRD1/CHD6

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Abstract

Short communication on t t(6;20)(q13;q12) LMBRD1/CHD6, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

Myelodysplastic syndrome/myeloproliferative disorder (MDS/MPD) in transformation (Acute myelocytic leukemia - AML)

Epidemiology

No cases registered in the Mitelman database.

Clinics

A 78-year-old woman seen because of worsening of cytopenias two years following diagnosis of MDS/MPD. No further investigations.

Evolution

Patient deceased soon after diagnosis of AML.

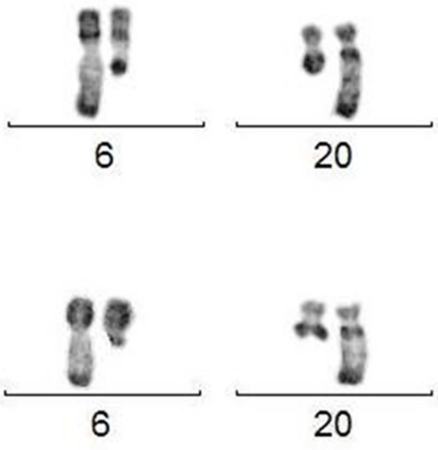
Cytogenetics

Note

The t(6;20)(q13;q12) involves two genes, the LMBRD1 and CHD6 genes, that have never been shown to form a fusion gene.

Cytogenetics morphological

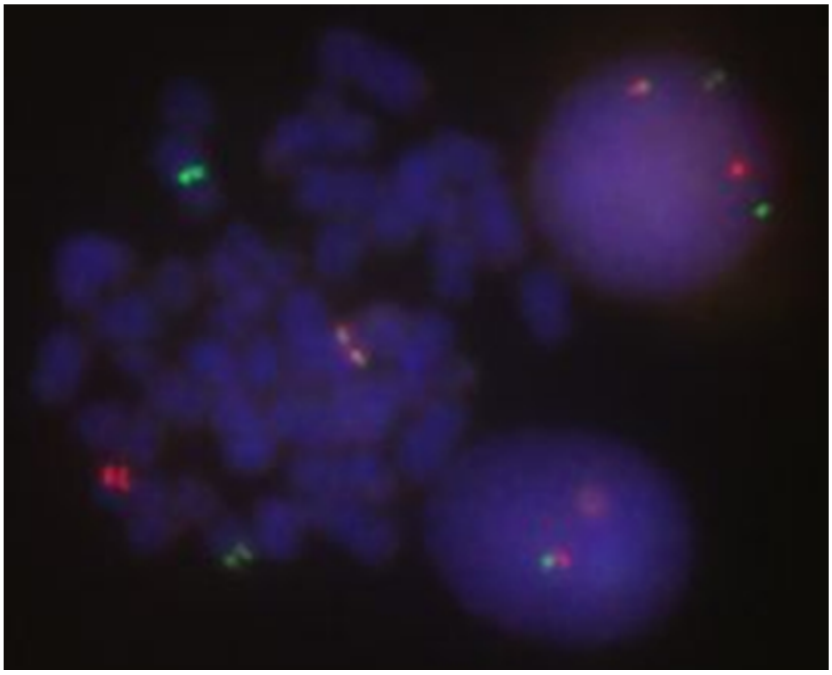
t(6;20)(q13;q12) is identified by banding cytogenetics.



RHG banding showing chromosomes 6 and 20 and the derivatives der(6) and der(20).

Cytogenetics molecular

To determine the position of the breakpoints on chromosomes 6 and 20, BACs located in the bands of interest were used as probes in FISH experiments. Analysis with RP11-359N1 showed that one signal hybridized to the normal chromosome 6, and the other split and hybridized to both der(6) and der(20). Analysis with RP11-257H6 showed that one signal hybridized to the normal chromosome 20, and the other split and hybridized to both der(6) and der(20). Co-hybridization with both BAC clones showed two fusion signals. RP11-359N1 contains the LMBRD1 gene and RP11-257H6 the CHD6 gene.



FISH with BACs RP11-359N1 (spectrum green, located in 6q13 and containing LMBRD1) and RP11-257H6 (spectrum orange, located in 20q12 and containing CHD6) showing co-hybridization.

Genes involved and proteins

LMBRD1

Location
6q13

Note
Mutations in the LMBRD1 gene is responsible for methylmalonic aciduria and homocystinuria type cblF (autosomal recessive disorder). It is a disorder of cobalamin metabolism characterized by decreased levels of the coenzymes adenosylcobalamin and methylcobalamin due to accumulation of free cobalamin in lysosomes, thus preventing its conversion to cofactors.
Clinical features include poor feeding, failure to thrive, developmental delay, stomatitis, glossitis, seizures, macrocytic anemia, neutropenia, thrombocytopenia and methylmalonic aciduria responsive to vitamin B12.

DNA/RNA
The LMBRD1 gene contains 15 exons, spanning 115 kb. Three transcripts (splice variants) are known, two being protein coding.

Protein
The protein has 540 amino acids (61.4 kDa) and localizes to the lysosome membrane. It contains nine transmembrane helices and six putative glycosylation sites with an N terminus in the lysosomal interior and a cytoplasmatic C terminus. It is a probable lysosomal cobalamin transporter, being required to export cobalamin from lysosomes, which in turn allows its conversion to cofactors.
It also appears to play a key role in mediating and regulating the endocytosis of the insulin receptor. Isoform 3 coding the nuclear export signal interacting protein (NESI) may play a role in the assembly of hepatitis delta virus.

CHD6

Location
20q12

Note
The CHD6 gene, located 403 kb centromeric to STS marker D20S108 is constantly deleted in MDS and MPD associated with del(20q) or ider(20q).

DNA/RNA
The CHD6 gene contains 37 exons of which 36 are coding, spanning 216 kb. Nine transcripts are known.

Protein
The gene encodes a member of the SNF2/RAD54 helicase protein family. The protein has 2715 amino acids (305 kDa) and localizes to the nucleus. It contains two chromodomains, a helicase domain, and an ATPase domain.
The protein is thought to be a core member of one or more of chromatin remodelling complexes. It may function as a transcriptional repressor.
It is involved in the cellular repression of influenza virus replication and in transcriptional repression of papillomavirus.

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