t(3;9)(q27;p13) GRHPR/BCL6

Jean-Loup Huret

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

Published in Atlas Database: November 2012
Online updated version : http://AtlasGeneticsOncology.org/Anomalies/t0309q27p13ID2132.html
DOI: 10.4267/2042/48764
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Clinics and pathology

Disease
Non Hodgkin lymphoma

Clinics
The t(3;9)(q27;p13) was found in a case of follicular lymphoma transformed to diffuse aggressive lymphoma, from a study with no individual data (Akasaka et al., 2003), in a 71-year-old female patient with a diagnosis of diffuse large B-cell lymphoma (DLBCL) of stomach, which evolved to a nodular lymphocyte-predominant Hodgkin's lymphoma 3 years later, and to a nodal DLBCL nine years after the initial diagnosis (Wlodarska et al., 2004), in a 47-year-old male patient with Burkitt lymphoma, who died of progressive disease 2 months after diagnosis (Bacher et al., 2011), and in a female patient with a follicular lymphoma (Cheung et al., 2012).

Cytogenetics

Cytogenetics morphological
The Burkitt lymphoma case showed the characteristic t(8;14)(q24;q32) and a complex karyotype, the follicular lymphoma case showed the t(14;18)(q32;q21). In the DLBCL case, no specific translocation accompanied the t(3;9).

Genes involved and proteins

BCL6
Location 3q27.3
Protein 706 amino acids; composed of a NH2-term BTB/POZ domain (amino acids 1-130 (32-99 according to Swiss-Prot) which mediates homodimerization and protein-protein interactions with other corepressors (including HDAC1 and NCOR2/SMRT to constitute a large repressing complex, another transcription repression domain (191-386), PEST sequences (300-417) with a KKYK motif (375-379), and six zinc finger at the C-term (518-541, 546-568, 574-596, 602-624, 630-652, 658-681), responsible for sequence specific DNA binding. Transcription repressor; recognizes the consensus sequence: TTCCT(A/C)GAA (Albagli-Curiel, 2003). Role in germinal centers of lymphoid follicles. BCL6 prevents ATM and TP53 to induce apoptosis in response to DNA rearrangements such as somatic hypermutation and class switch recombination. Therefore essential for normal B cell development.

GRHPR
Location 9p13.2
Note GRHPR was found involved in the translocation reported in the Akasaka's case, and Wlodarska et al., 2004 also point to its possible involvement.
Protein GRHPR is an enzyme which catalyzes the reduction of hydroxy-pyruvate to D-glycerate, glyoxylate to glycolate and the oxidation of D-glycerate to hydroxypyruvate. Primary hyperoxaluria type 2 is an autosomal recessive disease caused by mutations in GRHPR (Cramer et al., 1999).

Result of the chromosomal anomaly

Hybrid gene
Description Breakpoint in BCL6 first intron.
References

Cramer SD, Ferree PM, Lin K, Milliner DS, Holmes RP. The gene encoding hydroxypyruvate reductase (GRHPR) is mutated in patients with primary hyperoxaluria type II. Hum Mol Genet. 1999 Oct;8(11):2063-6


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