t(7;9)(q11.2;p13.2) PAX5/AUTS2

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Abstract

Short Communication on t(7;9)(q11.2;p13.2) PAX5/AUTS2, with data on clinics, and the genes implicated.

Clinics and pathology

Disease

B-cell precursor acute lymphoblastic leukemia (BCP-ALL)

Epidemiology

This unbalanced chromosomal rearrangement was found in three pediatric patients with B-cell precursor acute lymphoblastic leukemia (Kawamata et al., 2008; Coyaud et al., 2010a; Denk et al., 2012).

Clinics

All three patients achieved a complete remission (CR) after completion of induction therapy; however, two of the patients experienced an early relapse and both patients died, one from an infectious complication in second CR and one from progressive leukemia after a further relapse. The third patient remains in first CR for more than two years after diagnosis (Denk et al., 2012).

Genes involved and proteins

PAX5

Location
9p13.2

DNA/RNA
10 exons, alternatively spliced transcript variants encoding different isoforms.

Protein

PAX5 is a transcription factor harboring a conserved paired box DNA-binding domain.

It is a master regulator of B-cell commitment and maintenance and within the hematopoietic system is expressed in B-cells from the pro-B cell to the mature B-cell stage and repressed upon plasma cell differentiation (Cobaleda et al., 2007; Medvedovic et al., 2011).

In BCP-ALL PAX5 is a frequent target of somatic mutations, comprising deletions, point mutations, and structural rearrangements resulting in the expression of fusion transcripts (Mullighan et al., 2007).

To date, 16 different in-frame PAX5 fusions genes have been reported in B-ALL (Cazzaniga et al., 2001; Bousquet et al., 2007; Mullighan et al., 2007; Nebral et al., 2007; Kawamata et al., 2008; Nebral et al., 2009; Coyaud et al., 2010b; Lee et al., 2012). The PAX5 fusion partners comprise a heterogeneous group of genes that encode transcription factors, structural proteins, kinases, as well as several genes with so far unknown functions.

AUTS2

Location
7q11.22

DNA/RNA
19 exons, alternatively spliced transcript variants encoding different isoforms.
Protein
AUTS2, is a highly conserved nuclear protein with so far unknown function, contains several putative N-terminal nuclear localization signals (NLS), two proline alternating with two histidine-rich regions, and two potential serine phosphorylation sites. It is strongly expressed in fetal and adult brain, particularly in the frontal, parietal, and temporal lobes. Mutations in the gene have been associated with autism and mental retardation (Oksenberg and Ahituv, 2013).

Result of the chromosomal anomaly

Hybrid gene
Transcript
In-frame fusions between PAX5 exon 6 and AUTS2 exon 4, 5 or 6 have been described (Kawamata et al., 2008; Coyaud et al., 2010; Denk et al., 2012).

Fusion protein
Description
The putative consensus chimeric protein contains the DNA-binding paired domain, the octapeptide, and the partial homeodomain of PAX5 fused to the C-terminal regions of AUTS2.

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