Leukaemia Section
Short Communication

**t(X;9)(q21;p13) PAX5/DACH2**

Jean-Loup Huret

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

Published in Atlas Database: January 2014

Online updated version : http://AtlasGeneticsOncology.org/Anomalies/tX09q21p13ID1595.html

DOI: 10.4267/2042/54018

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.

© 2014 Atlas of Genetics and Cytogenetics in Oncology and Haematology

**Abstract**

Short communication on t(X;9)(q21:p13) PAX5/DACH2, with data on clinics, and the genes implicated.

**Clinics and pathology**

**Disease**
Acute lymphoblastic leukemia (ALL)

**Epidemiology**
Only one case to date, a 4-year old boy with a pre-B ALL (Coyaud et al., 2010).

**Prognosis**
No data.

**Cytogenetics**

**Cytogenetics morphological**
The t(X;9)(q21:p13) was the sole abnormality.

**Genes involved and proteins**

**PAX5**

**Location**
9p13.2

**Protein**
391 amino acids; from N-term to C-term, PAX5 contains: a paired domain (aa: 16-142); an octapeptide (aa: 179-186); a partial homeodomain (aa: 228-254); a transactivation domain (aa: 304-359); and an inhibitory domain (aa: 359-391). Lineage-specific transcription factor; recognizes the concensus recognition sequence GNCCANTGAAGCGTGAC, where N is any nucleotide. Involved in B-cell differentiation. Entry of common lymphoid progenitors into the B cell lineage depends on E2A, EBF1, and PAX5; activates B-cell specific genes and repress genes involved in other lineage commitments. Activates the surface cell receptor CD19 and repress FLT3. Pax5 physically interacts with the RAG1/RAG2 complex, and removes the inhibitory signal of the lysine-9-methylated histone H3, and induces V-to-DJ rearrangements. Genes repressed by PAX5 expression in early B cells are restored in their function in mature B cells and plasma cells, and PAX5 repressed (Fuxa et al., 2004; Johnson et al., 2004; Zhang et al., 2006; Cobaleda et al., 2007; Medvedovic et al., 2011).

**DACH2**

**Location**
Xq21.2

**DNA/RNA**
7 splice transcript variants.

**Protein**
599 amino acids and shorter forms; from N-term to C-term, contains a Poly-Gly (amino acids (aa) 56-61), a Dachshund domain motif N (aa 69-155), which interact with HDAC3 (histone deacetylase 3, 5q31), NCOR1 (nuclear receptor corepressor 1, 17p11.2), and SIX6 (SIX homeobox 6, 14q23.1), a Poly-Ala (aa 350-353), a Dachshund Domain motif C, which interact with EYA2 (eyes absent homolog 2 (Drosophila), 20q13.1), and a Coiled coil domain (aa 459-554) (Swiss-Prot). DACH2 is a transcriptional repressor of MYOG (myogenin, 1q32.1).
PAX3 (paired box gene 3, 2q36.1) and DACH2 positively regulate each other, and support the existence of a PAX3/SIX1/EYA2/LBX1/DACH2 network in regulating the myogenic differentiation program (Mennerich and Braun, 2001; Kardon et al., 2002).

Histone deacetylase (HDAC4) activity, imported into the nucleus, suppresses DACH2 gene expression in denervated muscle (Tang and Goldman, 2006; Cohen et al., 2007). DACH2 represses SIX1 (SIX homeobox 1, 14q23.1), and SIX1 overexpression has been described in gliomas. DACH1 (13q22) and DACH2 are required for Müllerian duct development. DACH2 is abundantly expressed in fallopian tubes, and it has been implicated in premature ovarian failure syndrome (Bione et al., 2004; Suzumori et al., 2007). In ovarian cancer, DACH2 is expressed, and a significantly reduced overall survival was found for tumours expressing high levels of DACH2 in the subgroup of serous carcinoma, but not in other subgroups (Nodin et al., 2012).

**Result of the chromosomal anomaly**

**Hybrid gene**

**Description**
Fusion of PAX5 exon 5 to DACH2 exon 3.

**Fusion protein**

**Description**
587 amino acids. The predicted fusion protein contains the DNA binding paired domain of PAX5 (the 201 N-term aa) and the DACHbox-C of DACH2 (the 386 C-term aa).

**References**

Mennerich D, Braun T. Activation of myogenesis by the homeobox gene Lbx1 requires cell proliferation. EMBO J. 2001 Dec 17;20(24):7174-83


Tang H, Goldman D. Activity-dependent gene regulation in skeletal muscle is mediated by a histone deacetylase (HDAC)-Dach2-myogenin signal transduction cascade.


