Leukaemia Section

Short Communication

t(1;19)(q22;p13.2) MEF2D/DAZAP1

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Abstract

Review on t(1;19)(q22;p13.2) MEF2D/DAZAP1, with data on the genes involved

Keywords
Chromosome 1 ; Chromosome 19 ; t(1;19)(q22;p13.3) ; MEF2D ; DAZAP1 ;

Clinics and pathology

Disease
B lymphoblastic leukemia

Epidemiology
Only one case to date: a 3-year-old female child (Yuki et al., 2004; Prima et al., 2005; Liu et al., 2016).

Cytogenetics
The cells carry t(1;19) but lack TCF3 (E2A) rearrangements and do not express E2A/ PBX1.

Genes involved and proteins

**MEF2D** (*Myocyte Enhancer Factor 2D*)

Location 1q22

Protein
MEF2D belongs to the MADS-box family of transcription factors; this molecule binds as a homo- or hetero-dimer to the MEF2 element present in the regulatory regions of numerous muscle-specific and growth-factor and stress-

induced genes.

A remarkable increase in expression levels of MEF2A and MEF2D has been reported during differentiation into monocytes using the promyeloid HL-60 cell line (Yuki et al., 2004).

In mouse models, MEF2D was identified as a candidate oncogene involved in the pathogenesis of leukemia.

It is assumed, that native MEF2D has latent transforming properties, which can be unmasked via aberrant protein expression (Prima et al., 2005).

**DAZAP1** (*Deleted in Azoospermia-Associated Protein 1*)

Location 19p13.3

Protein
DAZAP1 is an RNA binding protein, which contains two RNA-recognition motifs (RRMs), a proline-rich C-terminal portion and expressed most abundantly in the testis during spermatogenesis, and to a lower level, in the thymus.

Result of the chromosomal anomaly

Hybrid gene

Description
The genes were fused in-frame between exon 6 of MEF2D and exon 7 of DAZAP1 (MEF2D/DAZAP1), as well as, between exon 6 of DAZAP1 and exon 7 of MEF2D (DAZAP1/MEF2D). Sequencing of the RT-PCR products confirmed in-frame fusions between MEF2D (codon 222) and DAZAP1 (codon 155) in both chimeric transcripts (Yuki et al., 2004).
Both chimeric transcripts, MEF2D/DAZAP1 and DAZAP1/MEF2D, whose sequences indicated in-frame fusions between MEF2D and DAZAP1 were expressed in bone marrow cells (Yuki et al., 2004).

**Fusion protein**

Expression / Localisation

MEF2D/DAZAP1 and DAZAP1/MEF2D proteins were both located in the nucleus, MEF2D/DAZAP1 was able to form dimers with MEF2D and HDAC4. Furthermore, exogenous expression of MEF2D/DAZAP1 and DAZAP1/MEF2D promoted the growth of HeLa cells (Yuki et al., 2004).

Oncogenesis

MEF2D/DAZAP1 and/or DAZAP1/MEF2D contribute to leukemogenesis by altering signaling pathways normally regulated by wild-type MEF2D and DAZAP1. MEF2D/DAZAP1 binds avidly and specifically to DNA and is a substantially more potent transcriptional activator, than MEF2D and also may associate more strongly with other proteins involved in transcriptional regulation (e.g. HDAC4). MEF2D/DAZAP1 might immediately activate transcription of genes crucial for lymphocyte growth and/or survival such as IL2 (interleukin-2), a known transcriptional target of MEF2D in T-cells. As well, MEF2D/DAZAP1 could contribute to leukemogenesis via dysregulated activation of MAPK-mediated cell proliferation pathways.

These alterations may confer more potent transforming properties to MEF2D/DAZAP1, which can be further augmented by coexpression with the reciprocal DAZAP1/MEF2D chimera, which retains sequence-specific RNA binding properties (Prima et al., 2005).

**References**


This article should be referenced as such:

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