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Leukaemia Section

Short Communication

t(3;7)(q26;q21) CDK6/MECOM

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Abstract

Review on t(3;7)(q26;q21), with data on clinics, and the genes involved.

Keywords

chromosome 3; t(3;7)(q26;q21); MECOM

Clinics and pathology

Disease

Myeloid malignancies.

Phenotype/cell stem origin

Fifteen cases are available (Tien et al., 1989; Henzan et al., 2004; Storlazzi et al., 2004; Madrigal et al., 2006; Bobadilla et al., 2007; Colovic et al., 2011; Haferlach et al., 2012). There were 4 chronic myelogenous leukemia in blast crisis (CML-BC), one myelodysplastic syndrome (MDS) and 10 acute myeloid leukemia (AML) cases.

Epidemiology

t(3;7)(q26;q21) represented about 1% of a cohort of 606 AML and 377 MDS patients with normal karyotypes (n = 594) or chromosome 7 alterations (-7/7q-; n = 389). Median age was 51 years (range 47-70) (Haferlach et al., 2012). In 6 other patients, ages were, 18, 41, 56, 58, 61 and 71 years. Of 7 cases with data on the patient'sex; there were 6 male and 1 female patient.

Cytogenetics

Cryptic rearrangement.

Prognosis

Poor prognosis. Survival outcomes in 22 patients with cryptic MECOM rearrangements (der(7)t(3;7)(q26;q21), inv(3)(p24q26), and t(3;21)(q26;q11), altogether) were compared with inv(3)(q21q26)/t(3;3)(q21;q26) cases. Median overall survival was 9.4 months in the subgroup with cryptic MECOM rearrangements which was not significantly different from the 21.8 months in patients with an inv(3)(q21q26)/t(3;3)(q21;q26) (Haferlach et al., 2012). The 3 other patients with t(3;7)(q26;q21) and survival data died 4, 6, and 26 months after diagnosis.

Cytogenetics

Cytogenetics morphological

There were 6 cases of balanced form t(3;7)(q26;q21) (the 4 CML-BC and 2 AMLs), and 9 cases of unbalanced form der(7)t(3;7)(q26;q21) (1 MDS, and 8 AMLs). CML-BC cases also showed the typical t(9;22)(q34;q11). No other additional chromosome abnormality was found in any documented case.

Genes involved and proteins

MECOM (Ecotropic Viral Integration Site 1 (EVI1) and Myelodysplastic Syndrome 1 (MDS1-EVI1)

Location

3q26.2

Note

MECOM is a nuclear transcription factor that plays an essential role in the proliferation and maintenance of hematopoietic stem cells and can inhibit myeloid differentiation. Two alternative forms exists, one generated from EVI1, the other MECOM (MDS1

and EVI1 complex locus) through intergenic splicing with MDS1 (myelodysplasia syndrome 1), a gene located 140 kb upstream of EVI1.

Protein

The protein encoded by this gene is a transcriptional regulator involved in cell differentiation and proliferation, and apoptosis. The encoded protein can interact with transcriptional coactivators (P/CAF, CBP) and corepressors (CTBP1, HDAC) as well as other transcription factors (GATA1, Smad3) (de Braekeleer et al., 2012)

CDK6 (cyclin dependent kinase 6)

Location

7q21.2

Protein

Serine/threonine-protein kinase; it was regarded as a mere homolog of CDK4 with overlapping functions in the initiation of the cell cycle. CCND1 (cyclin D1) is an activator of CDK4/ CDK6. CDK4 and CDK6 associate with D-type cyclins, to go through from the G1 phase to the S phase. CDK6 is overexpressed and/or amplified in leukemias and lymphomas, glioblastoma and pancreatic cancer. CDK6 can regulate transcription independently of its kinase activity (Tigan et al., 2016).

Result of the chromosomal anomaly

Fusion protein

Oncogenesis

Increased MECOM expression was noted.

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