Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Leukaemia Section

Mini Review

t(12;13)(p13;q14)

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Clinics and pathology

Disease

Acute lymphoblastic leukemia (ALL) and myeloid malignancies.
Note: This translocation is likely to be molecularly heterogeneous.

Epidemiology

Only one case to date with identification of ETV6 and TTL as genes involved in the translocation: a 46 year-old male patient with ALL (blasts were CD10+/-, CD19+) (Qiao et al., 2003).

Clinics

Altogether, 15 cases are available:
Pre-B or early pre-B ALL cases, with an unbalanced sex ratio (7M/2F), and a median age of 6 years (range: 2-46), 7 of 9 patients being children (Raimondi et al., 1989; Pui et al., 1991; Raimondi et al., 1991; Chan et al., 1994; Kobayashi et al., 1994; Raimondi et al., 1997; Coignet et al., 1999; Qiao et al., 2003).
Myeloid cases: 1 chronic myelomonocytic leukaemia (CMML), 1 chronic myelogenous leukaemia in blast crisis (BC-CML), 1 M3 acute myeloid leukaemia (AML), 1 M0-AML, and 2 treatment related AML (t-AML). In contrast with lymphoid cases, the sex ratio was balanced (3M/3F), and median age was 58 years (range (51-70) (Zitzelsberger et al., 1990; Abeliovich et al., 1993; Fugazza et al., 1997; Tosi et al., 1998; Castro et al., 2000; Temperani et al., 2000).

Prognosis

The patient with ETV6/TTL hybrid gene attained complete remission, but relapsed and died of refractory disease 4 years after diagnosis.

Cytogenetics

Additional anomalies

The t(12;13) accompanied a del(5q) in two (t-AML) cases, del(7q) in one of these two cases, +8 in one myeloid case, t(9;22)(q34;q11) in the BC-CML case, a PML / RARA hybrid without any apparent t(15;17) in the M3 case, an additional 21 in two ALL cases (+21 once, i(21q) once). The t(12;13) was the sole anomaly in four cases (2 ALL and two AML).

Genes involved and Proteins

Note: ETV6 was found implicated in 4 ALL cases and 1 AML case; most other cases have been published before ETV6/TEL was known.

ETV6

Location: 12p13

Protein

HLH domain responsible for hetero- and homodimerization in N-term, and an ETS domain responsible for sequence specific DNA-binding in C-term. Transcriptional regulator; involved in bone marrow hematopoiesis.

TTL

Location: 13q14

Protein

This gene/protein remains poorly known: there has been no study on it since the princeps paper by Qiao et al. (2003).

Results of the chromosomal anomaly

Hybrid gene

Description

Both reciprocal transcripts, TTL/ETV6 and ETV6/TTL, were detected. ETV6/TTL fusion transcript comprises 5' ETV6 exon 1, fused to TLL exon 9, resulting in a potential 31 amino acids peptid.
The other transcript, TTL/ETV6, comprises 5' TTL exons 1 to 5 or to 8a, fused to ETV6 from exon 2. The predicted 530 amino acids fusion protein consists mostly of ETV6 with both HLH and ETS domains, and could have modified transcriptional activities. On the other hand, a loss of function of ETV6 and/or of TTL could play the critical role in leukemogenesis.

References

Raimondi SC, Peiper SC, Kitchingman GR, Behm FG, Williams DL, Hancock ML, Mirro J Jr. Childhood acute lymphoblastic leukemia with chromosomal breakpoints at 11q23. Blood 1989 May 1;73(6):1627-34.

Zitzelsberger H, Bauchinger M, Wilmanns W, Strauss PG. Cytogenetic and molecular analysis of a 'masked' Philadelphia chromosome in chronic and blastic phases of chronic myeloid leukemia. Cancer Genet Cytogenet 1990 Jul 15;47(2):219-25.

Pui CH, Raimondi SC, Head DR, Schell MJ, Rivera GK, Mirro J Jr, Crist WM, Behm FG. Characterization of childhood acute leukemia with multiple myeloid and lymphoid markers at diagnosis and at relapse. Blood 1991 Sep 1;78(5):1327-37.

Raimondi SC, Privitera E, Williams DL, Look AT, Behm F, Rivera GK, Crist WM, Pui CH. New recurring chromosomal translocations in childhood acute lymphoblastic leukemia. Blood 1991 May 1;77(9):2016-22.

Abeliovich D, Yehuda O, Ben-Neriah S, Matzner Y. Therapy-related myelodysplastic syndrome. Two cytogenetically unrelated abnormal clones in a patient with multiple myeloma. Cancer Genet Cytogenet 1993 Oct 15;70(2):117-9.

Chan LC, Ha SY, Ching LM, Lee CP, Lau YL, Yuen P, Leung NK. Cytogenetics and immunophenotypes of childhood acute lymphoblastic leukemia in Hong Kong. Cancer Genet Cytogenet 1994 Sep;76(2):118-24.

Kobayashi H, Maseki N, Homma C, Sakurai M, Kaneko Y. Clinical significance of chromosome abnormalities in childhood acute lymphoblastic leukemia in Japan. Leukemia 1994 Nov;8(11):1944-50.

Fugazza G, Cerri R, Bruzzone R, Patrone F, Sessarego M. Duplication of the der(13)t(12;13)(p13;q14) in chronic myelomonocytic leukemia. Haematologica 1997 May-Jun;82(3):336-7.

Raimondi SC, Shurtleff SA, Downing JR, Rubnitz J, Mathew S, Hancock M, Pui CH, Rivera GK, Grosveld GC, Behm FG. 12p abnormalities and the TEL gene (ETV6) in childhood acute lymphoblastic leukemia. Blood 1997 Dec 1;90(11):4559-66.

Tosi S, Giudici G, Mosna G, Harbott J, Specchia G, Grosveld G, Privitera E, Kearney L, Biondi A, Cazzaniga G. Identification of new partner chromosomes involved in fusions with the ETV6 (TEL) gene in hematologic malignancies. Genes Chromosomes Cancer 1998 Mar;21(3):223-9.

Coignet LJ, Lima CS, Min T, Streubel B, Swansbury J, Telford N, Swanton S, Bowen A, Nagai M, Catovsky D, Fonatsch C, Dyer MJ. Myeloid- and lymphoid-specific breakpoint cluster regions in chromosome band 13q14 in acute leukemia. Genes Chromosomes Cancer 1999 Jul;25(3):222-9.

Castro PD, Liang JC, Nagarajan L. Deletions of chromosome 5q13.3 and 17p loci cooperate in myeloid neoplasms. Blood 2000 Mar 15;95(6):2138-43.

Temperani P, Luppi M, Giacobbi F, Medici V, Morselli M, Barozzi P, Marasca R, Torelli G, Emilia G. Late-appearing PML/RARalpha fusion transcript with coincidental t(12;13)(p13.2;q14) in acute promyelocytic leukemia lacking the t(15;17) cytogenetic anomaly. Cancer Genet Cytogenet 2000 Jun;119(2):121-6.

Qiao Y, Ogawa S, Hangaishi A, Yuji K, Izutsu K, Kunisato A, Imai Y, Wang L, Hosoya N, Nannya Y, Sato Y, Maki K, Mitani K, Hirai H. Identification of a novel fusion gene, TTL, fused to ETV6 in acute lymphoblastic leukemia with t(12;13)(p13;q14), and its implication in leukemogenesis. Leukemia 2003 Jun;17(6):1112-20.

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