Leukaemia Section
Mini Review

t(2;14)(p13-16;q32)
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Identity

(A) Partial karyotype showing the t(2;14)(p13;q32) Top - Courtesy Adriana Zamecnikova; Middle and below - Courtesy Melanie Zenger and Claudia Haferlach. (B) Fluorescence in situ hybridization with LSI IgH/MYC and LSI ALK probe showing the juxtaposition of ALK (fusion signal) from 2p23 to the region proximal to IgH locus (green signal) on chromosome 14 and translocation of IgH segments to der(2) chromosome resulting in a green signal on rearranged chromosome 2 - Courtesy Adriana Zamecnikova.
Clinics and pathology

Disease
Identified predominantly in B-cell malignancies, including CLL/SLL, found in 20 cases of chronic lymphocytic leukemia (CLL), 1 B-prolymphocytic leukemia, 1 diffuse, mixed small/large cell non Hodgkin lymphoma (NHL); 8 cases of acute lymphocytic leukemia (ALL); one T-ALL and 7 B-ALL (two in association with t(1;19), one in Ph+ ALL, one with 3-way translocation); two AML (Ph+ M1 and inv(16)) cases and in one Ph+ CML case. CLL cases are characterized by marrow involvement, absolute lymphocytosis, lymphadenopathy, atypical morphologic features; prolymphocytes may be increased. Serum lactate dehydrogenase and betamicroglobulin levels are elevated, ZAP70 is expressed. Ig VH genes are unmutated; most cases are positive for CD5, CD19 and CD23; weak intensity of immunoglobuline and CD20, weak or negative CD79b, CD22, absence of FMC-7.

Epidemiology
Sex ratio: CLL cases 10 males and 6 females patients, 4 unknown; adults: aged 40-68 years, and 3 children aged 6, 10 and 15 years; ALL cases (3 males, 5 females) were 1 adult 37 years old and 7 children aged 1-17 years; 2 AML cases (1 male, 1 female) were 34 and 45 years old; the CML case was a 21 years old male patient.

Prognosis
8 CLL cases were dead after 27-145 months survival; from available data on 3 ALL cases: they were all dead (one after 15 months, 2 after bone marrow transplantation).

Cytogenetics

Cytogenetics morphological
Sole anomaly in 8 documented cases; found in complex karyotypes; associated with t(14;19)(q32;q13) in 2 CLL cases, del(6)q in 4 cases, il(9)(q10) in 2 cases, +12 in 3 cases. In two pediatric ALL cases, it was associated with t(1;19) and in 3 cases it was associated with Ph+ leukemia.

Genes involved and proteins

BCL11A
Location
2p16.1
DNA/RNA
Originally assigned to region 1, band 3, 2p13; it has subsequently been reassigned to 2p16.1.
Protein
BCL11A/EVI9 is a zinc-finger protein, containing 6 Krüppel C2H2 zinc fingers as well as a proline-rich domain between zinc fingers 1 and 2 and an acidic domain between 3 and 4. 835 amino acids; 91197 Da, alternative splicing: 6 isoforms, sharing a common N-terminus. Originally named EV19 human homolog BCL11A; high level of conservation across a wide range of species; highly homologous to another gene (BCL11B) on chromosome 14q32.1; like BCL11A, BCL11B is remarkable in having a large 5’ CpG island. Predominantly expressed in brain and hematopoietic cells, expression is tightly regulated during B-cell development; low-level or undetectable BCL11A RNA expression in most adult tissues. BCL11A is a DNA sequence-specific transcriptional repressor, an essential factor in lymphopoiesis, required for B-cell formation in fetal liver.

IgH
Location
14q32

Result of the chromosomal anomaly

Fusion protein
Oncogenesis
Juxtaposition of IgH enhancer elements leading to inappropriate overexpression of the partner gene product. BCL11A may be activated through chromosomal translocation or amplification, leading to myeloid leukemias in mice and lymphoid malignancies in humans; the conserved N-terminus of BCL11A. deregulated expression of BCL11A may play a major role in the pathogenesis; gains and amplifications of the region of chromosome 2p13-16 have been reported in B-cell malignancies, REL, a NF-kappaB gene family member, mapping within the amplified region is coamplified with BCL11A in B-NHL cases and HD lymphoma cell lines; with gains and amplifications, BCL11A interacts directly with BCL6, that serves a crucial role in lymphocyte development, also involved in IG translocations.

The structure of the t(2;14) translocation is a “head-to-head” arrangement, with the breakpoints falling centromeric to the first exon adjacent to a large CpG island at the 5’ end; BCL11A is deregulated as a consequence of the translocation, suggesting that BCL11A may be involved in lymphoid malignancies through either chromosomal translocation or amplification.

References
t(2;14)(p13-16;q32) Zamecnikova A


Yin CC, Lin KI, Ketterling RP, Knudson RA, Medeiros LJ, Barron LL, Huh YO, Luthra R, Keating MJ, Abruzzo LV. Chronic lymphocytic leukemia With t(2;14)(p16;q32) involves the BCL11A and IgH genes and is associated with atypical morphologic features and unmutated IgVH genes. Am J Clin Pathol. 2009 May;131(5):663-70

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