Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Leukaemia Section

Mini Review

t(5;11)(q35;p15.5)

Lyndal Kearney

Leukaemia Research Fund Centre, Institute of Cancer Research, Chester Beatty Laboratories, 237 Fulham Road, London SW3 6JB, UK (LK)

Published in Atlas Database: March 2002

Online updated version : http://AtlasGeneticsOncology.org/Anomalies/t0511q35p15ID1209.html
DOI: 10.4267/2042/37872

Clinics and pathology

Disease

De novo acute non lymphocytic leukemia (ANLL).

Phenotype/cell stem origin

No specific subtype. Only 5 cases reported to date (1 ANLL-M1, 2 ANLL-M2, 2 ANLL-M4).

Epidemiology

All 5 reported cases were children or young adults (age range 3-18 years). Male: female ratio 1.5:1.

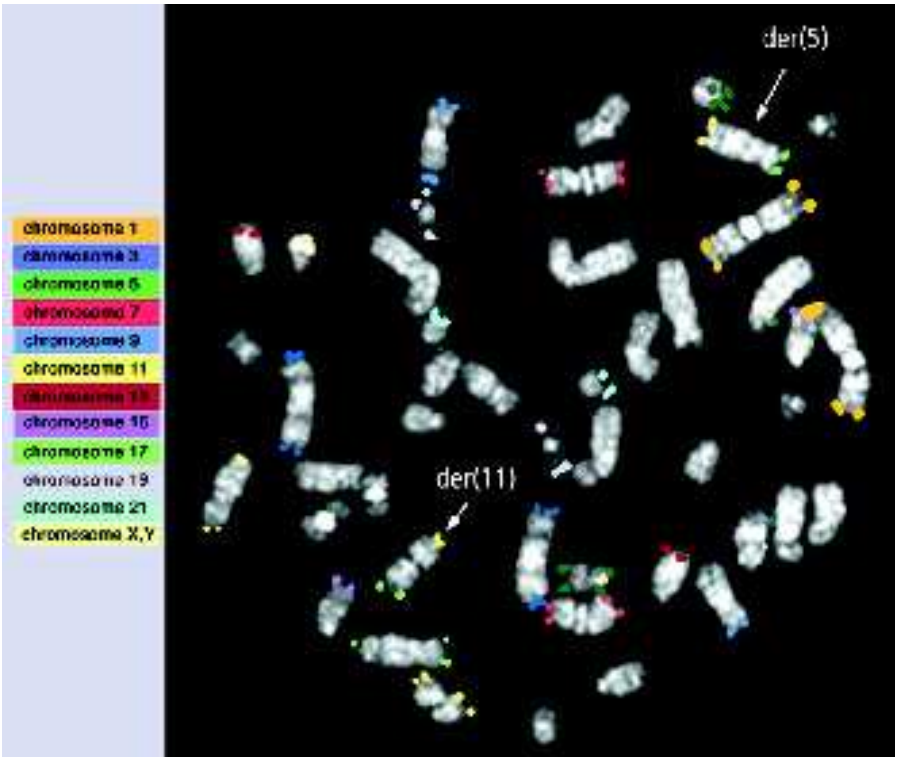

Fig 1. Identification of a cryptic t(5;11) using the M-TEL assay. Bone marrow metaphase from a normal karyotype ANLL child hybridized with the M-TEL1 probe set. Chromosomes 1, 3, 7, 9, 13, 15, 17, 19, 21 and X and Y probes were all correctly hybridized. However, one homologue of chromosome 5 has chromosome 11 material on the q arm (yellow), and the corresponding chromosome 11 homologue has chromosome 5 material on the p arm (green). This corresponds to a balanced translocation, t(5q;11p). The der(5) and der(11) are indicated by arrows.

Cytogenetics

Cytogenetics morphological

The t(5;11)(q35;p15.5) is not detectable by G-banding. Three cases were reported as cryptic t(5;11) associated with del(5q); a further two cases were identified in apparently normal karyotypes.

Cytogenetics molecular

In one FISH study using whole chromosome paints, three out of four cases of childhood ANLL with del(5q) as the sole cytogenetic abnormality were found to have a cryptic t(5;11). In a second study using chromosome-specific subtelomeric probes, two out of 31 children and young adults (19 years) with a normal G-banded karyotype were found to have a cryptic t(5;11).
Note: while the der(11) is detectable by single colour painting using chromosome 5 whole chromosome paint (WCP), the der(5) is not detectable using chromosome 11 WCP. Neither M-FISH or SKY can reliably detect the t(5;11).

Probes

Subtelomeric probes: PAC GS-240-G13 (5q), PAC GS-908-H22 (11p), both from Incyte Genomics NSD1 BAC: CTC HSP 2301A4 (available from Incyte Genomics); NUP98: PAC1173 K1, p9R1 (exons 10-12 of NUP98 gene), p6G2 (exons 13-14 of NUP98 gene).

Genes involved and proteins

NUP98

Location
11p15.5

Note
At least 8 different fusion partners for NUP98 in leukaemia.

DNA/RNA
Two major transcripts: 4.0 and 7.0 kb. The 4.0 kb transcript consists of 20 exons.

Protein
98 kD protein. Component of the nuclear pore complex, which regulates nucleocytoplasmic transport of protein and RNA. Contains multiple phenylalanine-glycine (FG) repeats which act as Œdocking' sites for transport receptors.

NSD1 (nuclear receptor-binding, SET domain-containing protein 1)

Location
5q35

DNA/RNA
At least 21 exons, cDNA is 8552 bp, open reading frame of 8088 bp.

Protein
Predicted protein of 2696 amino acids. Contains at least 6 functional domains: su(var)3-9, enhancer-of-zeste, trithorax (SET), proline-tryptophan-tryptophan-proline (PWWP-I, PWWP-II), plant homeodomain protein-finger domains (PHD-I, PHD-II, PHD-III) and ten putative nuclear localization signals.

Result of the chromosomal anomaly

Hybrid gene

Note
Reciprocal NSD1-NUP98 fusion also present in all cases tested.

Description
The NUP98 and NSD1 mRNA are fused in-frame joining nucleotides 1552 of NUP98 to nucleotide 3506 of NSD1. The reciprocal transcript fuses NSD1 and NUP98 mRNA in-frame joining nucleotide 3505 of NSD1 to nucleotide 1553 of NUP98.

Detection
RT-PCR with sense NUP98-5 (5'-TCTTGGTACAGGAGCCTTTG-3', and antisense NSD1-1 (5'TCCAAAAGCCACTTGCTTGGC-3') primers.

Fusion protein

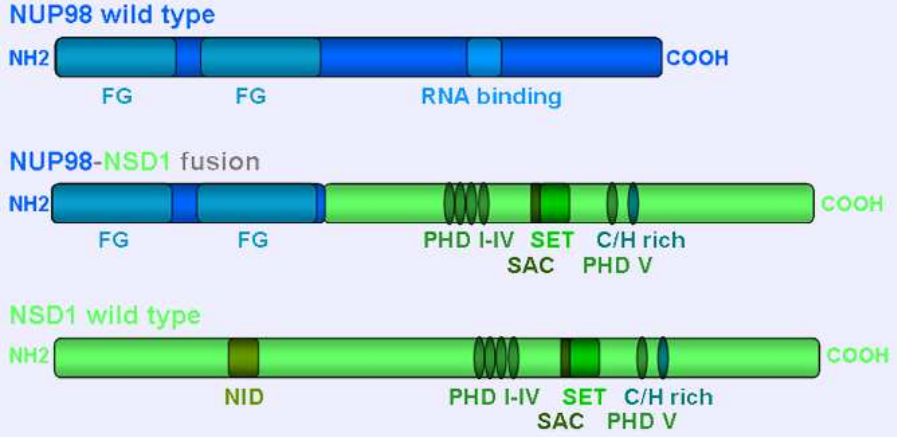

Fig 2. Schematic representation of the NUP98-NSD1 fusion protein. The wild type NUP98 and NSD1 proteins are also shown. The putative NUP98-NSD1 fusion protein would retain the NH2 terminal region of NUP98 containing the phenylalanine-glycine (FG) repeat domains and the COOH terminal region of NSD1 containing the SET, SET domain associated cysteine-rich (SAC) and PHD finger domains.

References

Huang N, vom Baur E, Garnier JM, Lerouge T, Vonesch JL, Lutz Y, Chambon P, Losson R. Two distinct nuclear receptor interaction domains in NSD1, a novel SET protein that exhibits characteristics of both corepressors and coactivators. EMBO J. 1998 Jun 15;17(12):3398-412

Jaju RJ, Haas OA, Neat M, Harbott J, Saha V, Boultwood J, Brown JM, Pirc-Danoewinata H, Krings BW, Müller U, Morris SW, Wainscoat JS, Kearney L. A new recurrent translocation, t(5;11)(q35;p15.5), associated with del(5q) in childhood acute myeloid leukemia. The UK Cancer Cytogenetics Group (UKCCG) Blood. 1999 Jul 15;94(2):773-80

Ahuja HG, Felix CA, Aplan PD. Potential role for DNA topoisomerase II poisons in the generation of t(11;20)(p15;q11) translocations. Genes Chromosomes Cancer. 2000 Oct;29(2):96-105

Knight SJ, Lese CM, Precht KS, Kuc J, Ning Y, Lucas S, Regan R, Brenan M, Nicod A, Lawrie NM, Cardy DL, Nguyen H, Hudson TJ, Riethman HC, Ledbetter DH, Flint J. An optimized set of human telomere clones for studying telomere integrity and architecture. Am J Hum Genet. 2000 Aug;67(2):320-32

Brown J, Saracoglu K, Uhrig S, Speicher MR, Eils R, Kearney L. Subtelomeric chromosome rearrangements are detected using an innovative 12-color FISH assay (M-TEL). Nat Med. 2001 Apr;7(4):497-501

Jaju RJ, Fidler C, Haas OA, Strickson AJ, Watkins F, Clark K, Cross NC, Cheng JF, Aplan PD, Kearney L, Boultwood J, Wainscoat JS. A novel gene, NSD1, is fused to NUP98 in the t(5;11)(q35;p15.5) in de novo childhood acute myeloid leukemia. Blood. 2001 Aug 15;98(4):1264-7

Kurotaki N, Harada N, Yoshiura K, Sugano S, Niikawa N, Matsumoto N. Molecular characterization of NSD1, a human homologue of the mouse Nsd1 gene. Gene. 2001 Nov 28;279(2):197-204

Lam DH, Aplan PD. NUP98 gene fusions in hematologic malignancies. Leukemia. 2001 Nov;15(11):1689-95

Brown J, Jawad M, Twigg SR, Saracoglu K, Sauerbrey A, Thomas AE, Eils R, Harbott J, Kearney L. A cryptic t(5;11)(q35;p15.5) in 2 children with acute myeloid leukemia with apparently normal karyotypes, identified by a multiplex fluorescence in situ hybridization telomere assay. Blood. 2002 Apr 1;99(7):2526-31

This article should be referenced as such:

Kearney L. t(5;11)(q35;p15.5). Atlas Genet Cytogenet Oncol Haematol. 2002; 6(3):206-208.