

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

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

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).

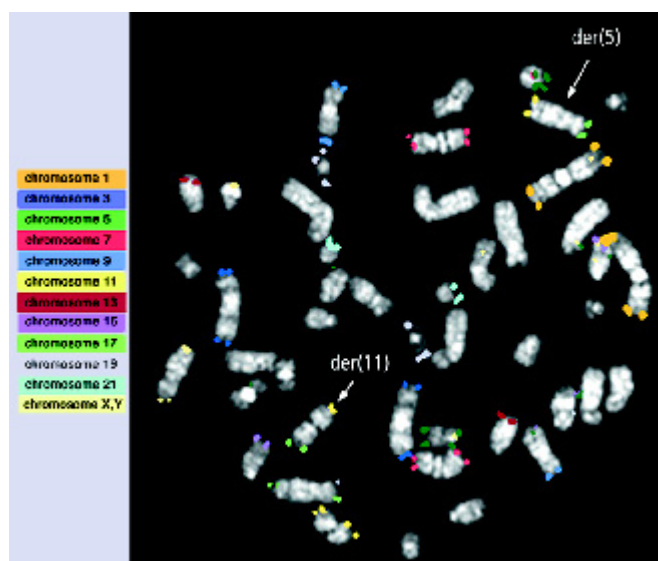


Fig 1. Identification of a cryptic t(5;11) using the M-TEL assay. Bone marrow

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.

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

Gene Name [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 'docking' sites for transport receptors.

Gene Name [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 proteinfinger 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

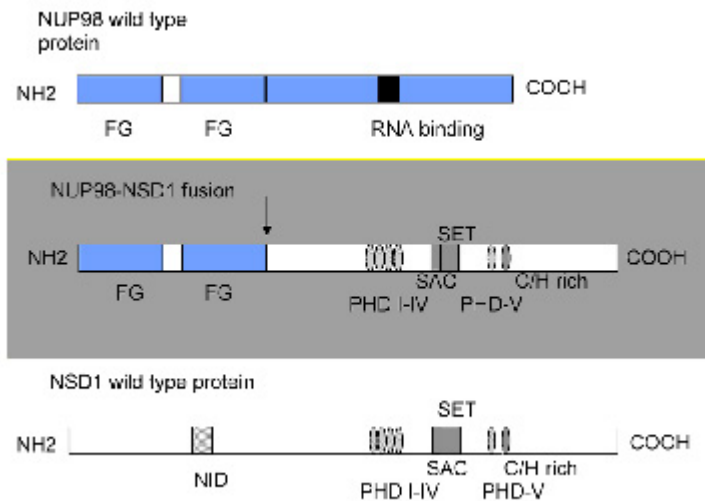


Fig 2. Schematic representation of the NUP98-NSD1 fusion protein. The wild type NUP98 and NSD1 proteins are also shown. The putative NUP98-NSD1 fusion protein would retain the NH2 terminal region of NUP98 containing the phenylalanine-glycine (FG) repeat domains and the COOH terminal region of NSD1 containing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

External links

Other database [t\(5;11\)\(q35;p15.5\)](#) [Mitelman database \(CGAP - NCBI\)](#)

Other database [t\(5;11\)\(q35;p15.5\)](#) [CancerChromosomes \(NCBI\)](#)

To be noted

Additional cases are needed to delineate the epidemiology of this rare entity:
you are welcome to submit a paper to our new [Case Report section](#).

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