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Gene Section
Mini Review

NPM1 (nucleophosmin)

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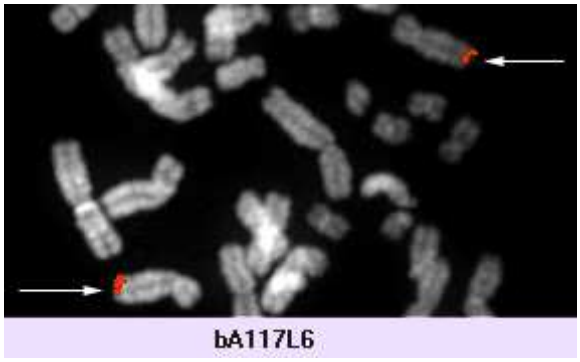
Identity

Other names: NPM; B23; Numatrin; NO38

HGNC (Hugo): NPM1

Location: 5q35



NPM1 (5q35) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

11 exons on 25 kb.

Transcription

in a centromeric --> telomeric orientation; transcription is cell-cycle regulated, reaching peaks at G1/S transition and being baseline at S/G2 1.6 kb mRNA.

Protein

Description

294 amino acids, 32.5 kDa; contains in C-term an oligomerization domain (residues 1-83), a metal binding site (residues 104-115), 2 domains rich in acidic amino acids (residues 120- 132 and 161-188), and 2 nuclear localisation signals in C-term; forms homo-hexameres; binds to single and double strand nucleic acids.

Expression

Wide

Localisation

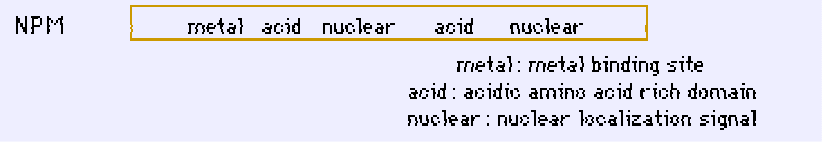
Nuclear, mainly in the nucleolus.

Function

RNA binding nucleolar phosphoprotein involved in preribosomal assembly; transport ribonucleoproteins between cellular compartments.

Homology

With nucleoplasmin.



DNA Diagram.

Implicated in

Anaplasic large cell lymphoma (ALCL) with t(2;5)(p23;q35) --> NPM1-ALK

Disease

ALCL are high grade non Hodgkin lymphomas; ALK+ ALCL are ALCL where ALK is involved in a fusion gene; ALK+ ALCL represent 50 to 60 % of ALCL cases (they are CD30+, ALK+;); 80% of ALK+ ALCL cases bear a t(2;5).

Prognosis

Nonetheless, a 80% five yr survival may be associated with this anomaly.

Cytogenetics

Additional anomalies are most often found.

Hybrid/Mutated gene

5' NPM1-3' ALK on der(5).

Abnormal protein

680 amino acids, 80 kDa; N-term 116 amino acids from NPM1 fused to the 563 C-term aminoacids of ALK (i.e. composed of the oligomerization domain and the metal binding site of NPM1,and the entire cytoplasmic portion of ALK); no apparent expression of the ALK/NPM1 counterpart; Characteristic localisation both in the cytoplasm and in the nucleus, due to heterooligomerization of NPM-ALK and normal NPM whereas the normal NPM protein is confined to the nucleus; constitutive activation of the catalytic domain of ALK.

Oncogenesis

Via the kinase function activated by oligomerization of NPM1-ALK mediated by the NPM1 part.

t(3;5)(q25;q34)/in myeloid malignancies --> NPM - MLF1

Disease

Acute non lymphocytic leukemia (ANLL), myelodysplasia (MDS), chronic myelogenous leukemia in blast crisis (BC-CML); trilineage involvement.

Prognosis

Very poor.

Cytogenetics

Location of breakpoints difficult to ascertain.

Hybrid/Mutated gene

5' NPM-3' MLF1 on der(5).

Abnormal protein

with the 175 N term amino acids of NPM1; nuclear protein.

t(5;17)(q34;q21)/M3-ANLL --> NPM1-RARa

Disease

Promyelocytic ANLL (M3-ANLL).

Cytogenetics

Variant translocation of the well known t(15;17).

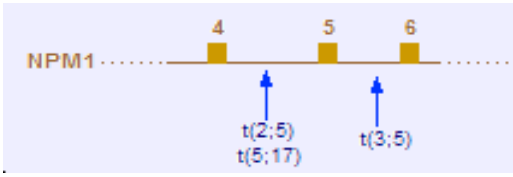
Hybrid/Mutated gene

5' NPM1-3' RARa on der(5).

Abnormal protein

With the 117 N term amino acids of NPM1.

Breakpoints



Note

Within the 4th intron in the cases of t(2;5) or t(5;17), within the 6th intron in case of t(3;5).

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