NPM1 (nucleophosmin)

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Identity

Other names: NPM; B23; Numatrin; NO38
HGNC (Hugo): NPM1
Location: 5q35

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.
Implicated in

**Anaplastic 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**

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<td>t(2;5)</td>
<td>t(5;17)</td>
<td>t(3;5)</td>
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**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).

**References**

- Delsol G, Raatki K, Stein H, Wright D, Jaffe E. Anaplastic large cell lymphomas, Primary systemic (T/Null cell type), WHO Classification of Tumors. Pathology and Genetics of tumours of Haematopoietic and Lymphoid Tissues . 2001 pp 230-235.

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