t(2;5)(p23;q35)

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Identity

t(2;5)(p23;q35) G-banding (left), and R-bandng (right); note tetraploid cells (left middle and bottom) - Courtesy Jean-Luc Lai and Alain Vanderhaegen.

Clinics and pathology

Disease
Translocations involving 2p23 are found in more than half cases of anaplastic large cell lymphoma (ALCL), a high grade non Hodgkin lymphoma (NHL). They involve ALK, and are therefore called ALK+ ALCL. The t(2;5) is the far most frequent 2p23 translocation in ALK+ ALCL.

Phenotype/cell stem origin
T-cell in 80% (or 100%?), or null-cell type; B-cell cases, if they exist, would represent cases of large B-cell lymphomas; CD30+; present with some overlapping features with Hodgkin’s disease: CD30 positivity and Reed-Sternberg like cells, but the t(2;5) is not found in Hodgkin's disease (it has long been debated).

Epidemiology
10% of NHL; found in children and young adults; median around 16 yrs).

Clinics
Involve lymph nodes and extra nodal sites such as lungs and gastro intestinal tract.
Cytology

t(2;5) is found in about 30-50% of anaplastic large cell NHL (also called ALCL); it was thought previously that the t(2;5) could be found in diffuse large cell NHL or immunoblastic NHL; however, cases may easily be misdiagnosed, as the malignant cells display a pleomorphic appearance.

Prognosis

Although t(2;5) is found in aggressive high grade tumours, a 80% five yr survival seems to be associated with this anomaly.

Additional anomalies

Sole anomaly in less than 20% of cases; often part of a complex karyotype, with various structural and/or numerical anomalies; recurrent numerical anomalies are: +7, found in 20% of cases, +9, and +X, in 5 to 10% of cases.

Variants

Closely related anomalies, also found in anaplastic large cell lymphoma, are: t(X;2)(q11;p23), t(1;2)(q25;p23), inv(2)(p23q35), t(2;3)(p23;q21), t(2;17)(p23;q23), t(2;19)(p23; p13.1) and t(2;22)(p23;q11.2). They all involve ALK in 2p23.

Genes involved and proteins

ALK

Location
2p23

Protein
After glycosylation, produces a glycoprotein; membrane associated tyrosine kinase receptor.

NPM1

Location
5q35

Protein
nuclear localisation; RNA binding nucleolar phosphoprotein involved in preribosomal assembly

Result of the chromosomal anomaly

Hybrid gene

Description
5’ NPM-3’ ALK on der(5).

Transcript
2.4 kb

Fusion protein

Description
80 kDa; 680 amino acids; the 116 N-term aminoacids from NPM are 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.

Expression / Localisation

Localisation: both in the cytoplasm and in the nucleus (nucleoplasm and nucleolus).

Oncogenesis

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

References


Wellmann A, Otsuki T, Vogelbruch M, Clark HM, Jaffe ES, Raffeld M. Analysis of the t(2;5)(p23;q35) translocation by reverse transcription-polymerase chain reaction in CD30- anaplastic large-cell lymphomas ('Ki-1 lymphoma') are associated with a chromosomal translocation involving 5q35. Blood. 1995 Sep 15;86(6):2321-8


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