+21 or trisomy 21

Franck Viguié

Laboratoire de Cytogénétique - Service d'Hématologie Biologique, Hôpital Hôtel-Dieu, 75181 Paris Cedex 04, France (FV)

Published in Atlas Database: August 2001
Online updated version: http://AtlasGeneticsOncology.org/Anomalies/tri21ID1041.html
DOI: 10.4267/2042/37795

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2001 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Note
Acquired trisomy 21 is not to be confused with constitutional trisomy 21 (Down syndrome, DS) which is a factor of predisposition to childhood acute leukemia but whose significance and clinical context are quite different.

Clinics and pathology

Disease
Acute non lymphocytic leukemia (ANLL) / myelodysplastic syndromes (MDS)

Phenotype/cell stem origin
No specific phenotype but possibly a slight higher incidence in mononuclear phenotypes (ANLL-M4 and - M5, chronic myelomonocytic leukemia (CMML)). ANLL-M7 with acquired +21 is exceptional, whereas ANLL-M7 is frequent in Down Syndrome.

Epidemiology
+21 is the second more frequent acquired trisomy, after trisomy 8, in adult ANNL/MDS. It is rarely observed as the sole abnormality. According to large series, +21 was observed in 3% to 7% of cases, out of which 0.3-0.4% of cases with +21 as the only abnormality.

The more frequent association is with -5/5q- and -7/7q-, followed by trisomy 8 and structural rearrangements t(8;21), t(15;17) and inv(16).

Alternatively to +21 and in the same clinical context, tetrasomy or pentasomy 21 can be observed, as well as single or multiple copies of a structurally rearranged chromosome 21, such as i(21q), psu dic(21q) or r(21). In some of these der(21), a chromosome 21 segment can be tandemly amplified as homogeneous staining region (HSR).

Prognosis
+21 as sole abnormality has an unfavorable prognosis, none of the published patients could achieve a long-term disease-free survival.

When associated with other recurrent chromosome changes, it does not modify the prognosis of these abnormalities.

Disease
Acute lymphocytic leukemia (ALL).

Phenotype/cell stem origin
Essentially B-cell lineage.

Epidemiology
+21 is the more frequent aneuploid observed in both adult and childhood ALL. Its overall incidence would be around 15% of cases.

As the sole clonal abnormality (excepting DS patients), +21 accounts for 2% of pediatric and less than 1% of adult ALL cases.
In childhood ALL, the incidence of +21 is approximately of 40% and of 80%, respectively, in the 47-50 chromosomes and in the >50 chromosomes ploidy groups.

The main association is with t(12;21)(p13;q22) in childhood (15% of cases at diagnosis), followed by 6q abnormalities. Association also with t(1;19)(q23;p13), t(4;11)(q21;q23) and 14q abnormalities.

The main association with a second aneuploidy is with +X, +16 or -20.

In adults, +21 is associated the most frequently with t(9;22)(q34;q11): about 50% of cases.

**Prognosis**

+21 as sole abnormality has a favorable prognosis.

In the group 47-50 chromosomes, +21 has a rather good prognosis in children, when it is not associated with a bad prognosis structural rearrangement. In the same ploidy group, +21 has no prognostic impact in adults.

**Genetics**

**Note**

Gene(s) involved in trisomy 21 associated leukemia is (are) unknown.

The 21q22 region seems crucial. Der(21) containing an HSR have constantly multiple copies tandemly amplified of the AML1 gene, both in ANLL and in ALL, but there is no proof that this gene is directly implicated.

The overexpression of cystathionine-b-synthetase (CBS; 21q22.3) would be linked to increased sensitivity of myeloblasts to ara-C and daunorubicin in DS ANLL patients. This has not been confirmed in acquired trisomy 21.

**References**


Wan TS, Au WY, Chan JC, Chan LC, Ma SK. Trisomy 21 as the sole acquired karyotypic abnormality in acute myeloid leukemia and myelodysplastic syndrome. Leuk Res. 1999 Nov;23(11):1079-83

This article should be referenced as such: