GENETIC ALTERATIONS IN ACUTE LYMPHOBLASTIC LEUKEMIA
Elena Esperanza Cebollada

Introduction
Acute Lymphoblastic Leukemia (ALL) is a neoplasm of immature lymphoid progenitors, characterized by clonal expansion of leukemic cells in the bone marrow (BM). It can affect both children and adults, but is more prevalent between ages of 2 and 5 years. The majority of ALL cases are aneuploidy or harbor recurring chromosomal rearrangements that are important in initiating events in leukemogenesis and which subdivide by the subtypes B and T, but that are insufficient to explain the biology and heterogeneity of ALL. For that reason it is necessary a thorough study about genetics of the disease.

Clinical diagnostic

- ALL-L1
- ALL-L2
- ALL-L3
- ALL-B: CD10, CD20, CD22, CD5, CD19, CD7, CD103, and CD104
- ALL-T: CD2, CD3, CD5, CD1a, CD4, and CD7

Conventional cytogenetics
- Molecular cytogenetics
- PCR and CGH

Techniques

- 1956 The human chromosome number is 46
- 1985 Invention of polymerase chain reaction (PCR)
- 1982 Fluorescence in situ hybridization (FISH) was developed
- 1992 Comparative genomic hybridization (CGH) was developed

Methods and objectives
Bibliographic search of reviews and original articles in databases such as PubMed (NCBI) has been made in order to accomplish the following goals: present the current situation of the disease and how the genetic study has allowed us to understand the disease as well as the risk stratification, and develop new therapies.

GENETIC ALTERATIONS

<table>
<thead>
<tr>
<th>Cytogenetic alterations</th>
<th>Genetic lesion</th>
<th>Associated clinical features and specific treatments</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in chromosome Number 25%</td>
<td>Hyperdiploidy (&gt;50)</td>
<td>High frequency of BM puberty and IKAROS family mutations</td>
<td>Good prognosis</td>
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<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>B-ALL</td>
<td>Associated with t(9;22) and t(12;21) deletions. Treatment with tyrosine kinase inhibitors like imatinib but resistance develops rapidly.</td>
<td>Poor prognosis</td>
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<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>BCR-ABL (t(9;22))</td>
<td>Type of rhabdoid tumors in some rearrangements. Treatment with PLTJ inhibitors like sorafenib or crizotinib</td>
<td>Poor prognosis</td>
</tr>
<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>MLL rearrangements</td>
<td>Rearrangements of MLL, use of cytokines in some rearrangements. Treatment with PLTJ inhibitors like sorafenib or crizotinib</td>
<td>Improved outcome</td>
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<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>AML</td>
<td>Intensive chemotherapy that includes cytarabine. Sometimes present with multiple copies of RUNX1. Current development of treatment in the UK</td>
<td>Good prognosis</td>
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<td>T-ALL</td>
<td>E2A-PAX1 (t(1;19))</td>
<td>Increased incidence in African Americans. Intensive chemotherapy</td>
<td>Genetically excellent prognosis</td>
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<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>T-ALL</td>
<td>Susceptible tumors, gain of function that activates JAK/STAT pathway</td>
<td>Good prognosis</td>
</tr>
<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>NOTCH1 (t(4;12))</td>
<td>Reduced expression of NOTCH1 inhibition of NOTCH1 and NOTCH2 phosphatases</td>
<td>NOTCH1 T-ALL has better prognosis than other T-ALL molecular</td>
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<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>ALL1 (t(11;21))</td>
<td>Dimerizes E2A and HEB transcription factors, blocking T cell differentiation</td>
<td>Good and poor outcomes</td>
</tr>
<tr>
<td>Structural abnormalities chromosome 50%</td>
<td>LIN2 (t(14;20))</td>
<td>Dimerizes E2A and HEB transcription factors, blocking T cell differentiation</td>
<td>Good and poor outcomes</td>
</tr>
</tbody>
</table>

Novel alteration

- CRLF2
- PAX5
- JAK1/2

Novel perspectives

- There is no consensus on what constitutes an optimal treatment
- Develop less toxic treatments while preserving earlier gains in efficacy
- Studies have begun to identify a number of polyomorphisms, such as ARID1B, IRF4, RBM6, and CDKN2A

New epigenetic studies

ALL is the most common and heterogeneous neoplasm in childhood and its also affects adults. Early diagnosis is important to perform a good treatment and get complete remission.

Genetics have allowed us to identify a large number of chromosomal alterations that are associated with biological features. The genetics alterations has been used to define B-ALL and T-ALL, prognostic and risk stratification.

Conventional cytogenetic analysis should be a mandatory routine examination. Further genetic study must be carried out to understand the disease and create specialized treatments.

References