

Classification of B-cell non-Hodgkin lymphomas (NHL)

Identity

Note B-cell NHL include a number of clinicopathologic subsets of lymphoid neoplasms having heterogeneous features. This situation is reflected by variations in the classification systems that were proposed over the last decade. Cytogenetic findings were recognized to help defining a rationale biologic ground for the nosologic classification of lymphomas. An outlook of the salient cytogenetic entities in this spectrum of disorders is presented herein; a complete illustration of the cytogenetic profile of each disease is provided in specific cards. Unless otherwise specified the WHO classification system will be used.
Legend for immunophenotypes (below): +: positive in >90% of the cases; +/-: positive in more than 50% of the cases; -/+: positive in less than 50% of cases; -: positive in <10% of the cases; pan-B markers include CD19; CD20; CD79a; R = rearranged; slg: surface immunoglobulins; cylg: cytoplasmic Ig; IgV genes: genes encoding for the variable portion of the Ig.

Clinics and Pathology

Disease [Small lymphocytic lymphoma \(SLL\)](#)
Phenotype / cell stem origin Histologic subset and Immunophenotype: Pan-B+; CD5+; CD23+; CD10-; slgM+ faint.
 Putative cell of origin: CD5+ virgin B-cell with germline IgV genes (as was recently demonstrated to be the case with chronic lymphocytic leukemia, the leukemic counterpart of SLL, it is likely that part of the cases may derive from post-germinal centre quiescent B-cells that harbour hypermutated IgV genes)
Clinics Indolent disease;
 leukemic involvement by lymphoid cells, including prolymphocytes and/or paraimmunoblasts Splenomegaly
Cytogenetics del(6)(q21-23) (20-30% of the cases)

Disease [Lymphoplasmacytic lymphoma](#)
Phenotype / cell stem origin Histologic subset and Immunophenotype: Pan-B+; CD5-; CD10-; cylgM+
 Putative cell of origin: Peripheral B-lymphocyte transforming into plasma cell with mutated IgV genes and ongoing mutations
Clinics Indolent low-grade disease. with possible clinical and/or histologic

progression

Cytogenetics [t\(9;14\)\(p13;q32\) PAX5/IgH](#) (50% of cases)

Disease [Follicle centre cell lymphoma](#)

Phenotype / cell stem origin Histologic subset and Immunophenotype: Pan-B+; CD10+/-; CD5-; slg+
Putative cell of origin: Centrocytes / centroblasts of germinal centre origin with somatic hypermutation of the IgV genes and ongoing mutations (antigen driven stimulation)

Clinics Indolent. Advanced stages predominate.
Conflicting data as to the prognostic significance of the t(14;18)/BCL2

Cytogenetics [t\(14;18\)\(q32;q21\) / BCL2](#) Rearr (70-80% of cases)

Disease [Diffuse large cell lymphoma](#)

Phenotype / cell stem origin Histologic subset and Immunophenotype: CD19+; CD22+; CD10-/+; Slg+
Putative cell of origin: Large transformed B-cells harbouring somatic hypermutation of the Ig genes (ongoing mutations in some cases)

Clinics Usually aggressive
Immunoblastic lymphoma (Kiel classification) do worse than centroblastic lymphomas
No convincing demonstration that any "primary" cytogenetic / molecular defect has prognostic significance; complex karyotype confers a shorter survival

Cytogenetics [t\(14;18\)](#) and [p53](#) mutations (20% of the cases)
[t\(3;V\)\(q27;V\) / BCL6](#) Rearr (6-30% of cases (% variations depending on detection methods: molecular genetics and FISH more sensitive than conventional cytogenetics))
or variants [c-MYC](#) Rearr (7-10% of cases)

Disease [Burkitt's lymphoma](#)

Phenotype / cell stem origin Histologic subset and Immunophenotype: Pan-B+; TdT-; CD10+; CD5-; slgM+
Putative cell of origin: Peripheral B-cells that have encountered the antigen and harbours somatic hypermutation of the Ig genes

Clinics Extremely aggressive disease
Specific treatment mandatory

Cytogenetics [t\(8;14\)\(q24;q32\) ID1050> or variants / R earr \(80% of the cases\)](#)
[GENES](#)

Disease [Burkitt-like lymphoma](#)

Phenotype / cell stem origin Histologic subset and Immunophenotype: Pan-B+; TdT-; CD10-/+ CD5-; slg+
Putative cell of origin: Peripheral B-cells that have encountered the

antigen

Clinics Aggressive disease
Cases with dual 8;14 and 14;18 translocations have a worse outcome (data requiring confirmation -1 study only)

Cytogenetics [t\(8;14\)](#) or variants (25% of cases)
[t\(8;14\)+ t\(14;18\)](#) (30% of cases)

Disease [Mantle cell lymphoma](#)

Phenotype / cell stem Histologic subset and Immunophenotype: Pan-B +; CD5+; CD23-;
CD10-/+; slgM+ bright

origin Putative cell of origin: CD5+ B-cells of the follicle mantle having germline IgV gene sequences

Clinics Advanced stages predominate
Response to chemotherapy often unsatisfactory
Short survival
Complex karyotype carries an unfavourable prognostic significance

Cytogenetics [t\(11;14\)\(q13;q32\)](#) / [BCL1](#) Rearr (50-90%) (molecular genetic methods have limited application due to variability of breakpoints; FISH is the most sensitive technique)

Disease [Marginal zone B-cell lymphoma](#) (MZBCL)

Phenotype / cell stem Histologic subset and Immunophenotype: pan-B+; CD5-/+; CD10-;
CD23-; CD11c+/-; cylg + (40% of the cells), slgM+ bright; slgD-

origin Putative cell of origin: Marginal zone lymphocytes harbouring hypermutated IgV genes

Cytogenetics [t\(11;18\)\(q21;q21\)](#) ID: 2022> / [PI2](#) / [MLT](#) fusion (30-50% of the low-grade MALT): Extra-nodal low-grade MALT lymphoma; indolent disease
[t\(1;14\)\(p21;q32\)](#): Extra-nodal MALT lymphoma
[del\(7\)\(q22-31\)](#) (40% of the cases): Splenic MZBCL
/+3q (30-70% of the cases): Nodal, extra-nodal and splenic MZBCL
GENES

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