

Applying the new WHO Classification of Lymphoid Neoplasms in Daily Practice
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SUMMARY

- The WHO Classification differs from previous classifications in its emphasis on defining real disease entities through a multimodality approach.
- New entities defined in the 4th edition require more extensive immunophenotyping and in some cases genetic information for classification.
- Panels of antibodies selected based on the morphological differential diagnosis and tumor location can be used in an algorithmic approach to aid diagnosis and classification.

Keywords: lymphoma, classification, immunophenotyping

Differences between the REAL/WHO Classification and earlier classifications

1. vs Working Formulation and Rappaport
 - a. Recognition of distinct disease entities in classification
 - b. Attempt to classify by normal counterpart when possible, but recognizing not always possible
 - c. No clinical groupings (low/int/high grade)
 - d. Use of immunophenotyping and genetic studies in diagnosis/classification
 - e. Involvement of clinicians and importance of clinical features in diagnosis/classification
 - f. Consensus among as broad a group as possible on definitions and terminology
2. vs Kiel classification
 - a. Recognizing that normal counterpart is not always known
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Differences between WHO 4th ed and WHO 3rd ed

1. More immunophenotypically and genetically defined categories of lymphoid neoplasms
2. Recognition of lineage plasticity –
 - a. Genetic abnormalities that may give rise to either or both myeloid and lymphoid neoplasms

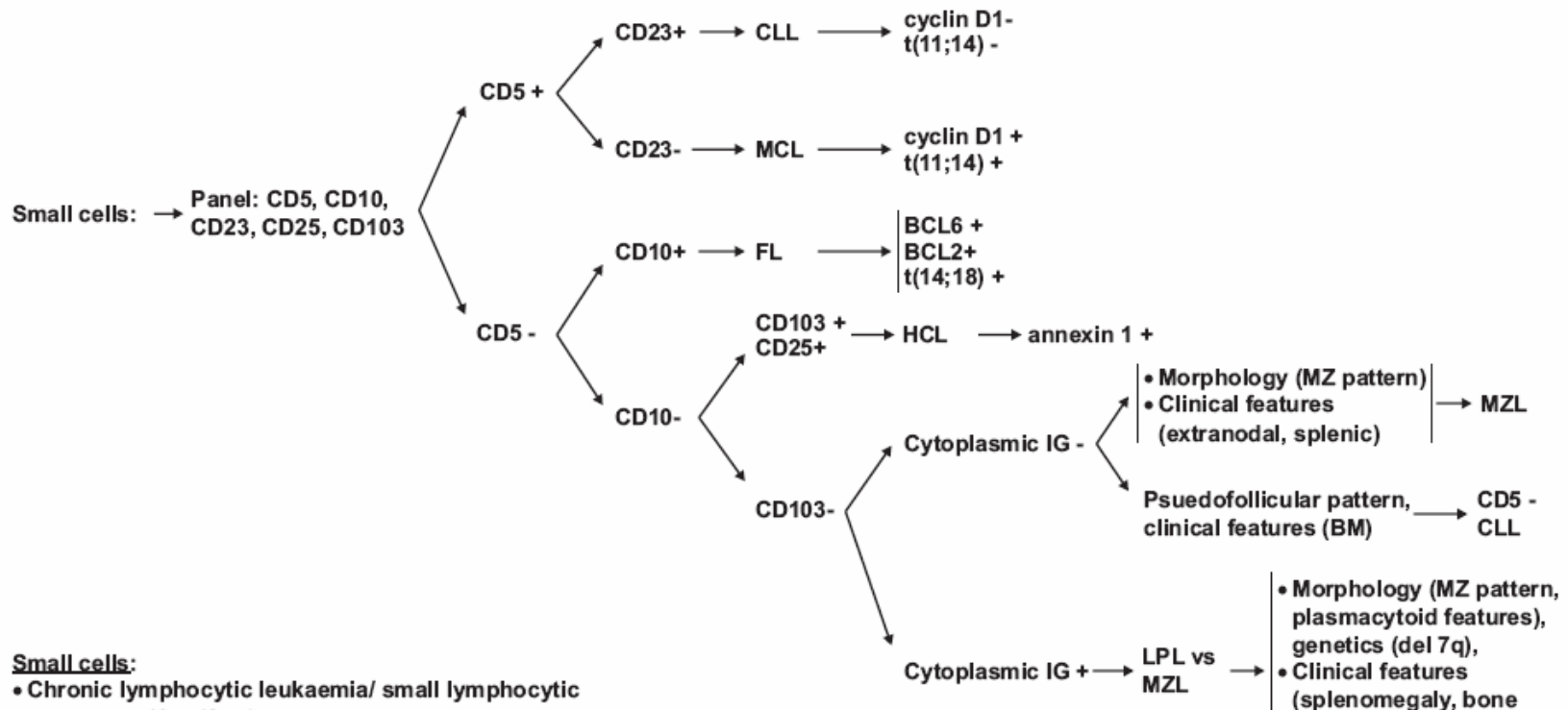
- i. Implication: new category – need to recognize by morphology and do appropriate testing
 - b. Development of histiocytic neoplasms in lymphomas
 - i. Implication – recognize that these may be clonally related; appropriate immunophenotyping
 - c. Overlap between DLBCL and CHL
 - i. Decide when to use these categories
- 3. B-cell neoplasms
 - a. Small clonal populations – MBL, MCL, MGUS, IGH/BCL2, FL (in-situ, FH clonal); new criteria for CLL, WM, MM
 - b. Unclassifiable splenic lymphomas
 - c. New subtypes of FL
 - d. Cutaneous BCL – importance of Mum1, Bcl2 in diagnosis
 - e. More categories of DLBCL
 - i. Molecular and immunophenotypic subgroups
 - 1. Do we need to do all these stains? Discuss with clinicians
 - ii. Virus-associated (PBL, PEL, LyG, HHV8, EBV+, Infection-assoc)
 - 1. Need immunophenotyping, staining for virus, clinical data (this needs to be done)
 - 2. Do we need EBER in all DLBCL? Probably in non-GCB types, especially if CD20-
 - 3. Do we need Bcl6, CD10, Mum1 in all DLBCL?
 - iii. Others – THRBCL, ALK+ - need to recognize as DLBCL, otherwise optional
 - f. Gray-zone categories (DLBCL/CHL; DLBCL/BL)
 - i. Recognize by morphology and immunophenotype
 - ii. Don't over-use!
 - iii. Importance of CG/FISH in diagnosis of BL/BLL
- 4. T/NK-cell neoplasms
 - a. EBV+ childhood T-LPD
 - i. Rare in non-Asians, but need to recognize, do EBV, TCR clonality
 - b. Cutaneous TCL
 - i. Need to recognize CD8+ aggressive; gamma-delta types
 - c. ALK- ALCL
 - i. Recognize by morphology; do appropriate stains
 - ii. Need to exclude LD variants of CHL – morphology and immunophenotype (Pax5! EBER)

ALGORITHMS FOR USE OF IMMUNOPHENOTYPING IN THE DIFFERENTIAL DIAGNOSIS OF LYMPHOID NEOPLASMS

1. Begin with a broad but limited panel of antibodies, based on the morphological differential diagnosis.
2. Add antigens in additional panels, based on initial results.
3. Avoid “shotgun” panels of unnecessary antibodies unless a clinically urgent situation warrants.

USE OF IMMUNOPHENOTYPING IN DIFFERENTIAL DIAGNOSIS
OF MATURE B-CELL AND T/NK-CELL NEOPLASMS¹

B-CELL ANTIGENS POSITIVE (CD19, CD20, CD79a, PAX5)



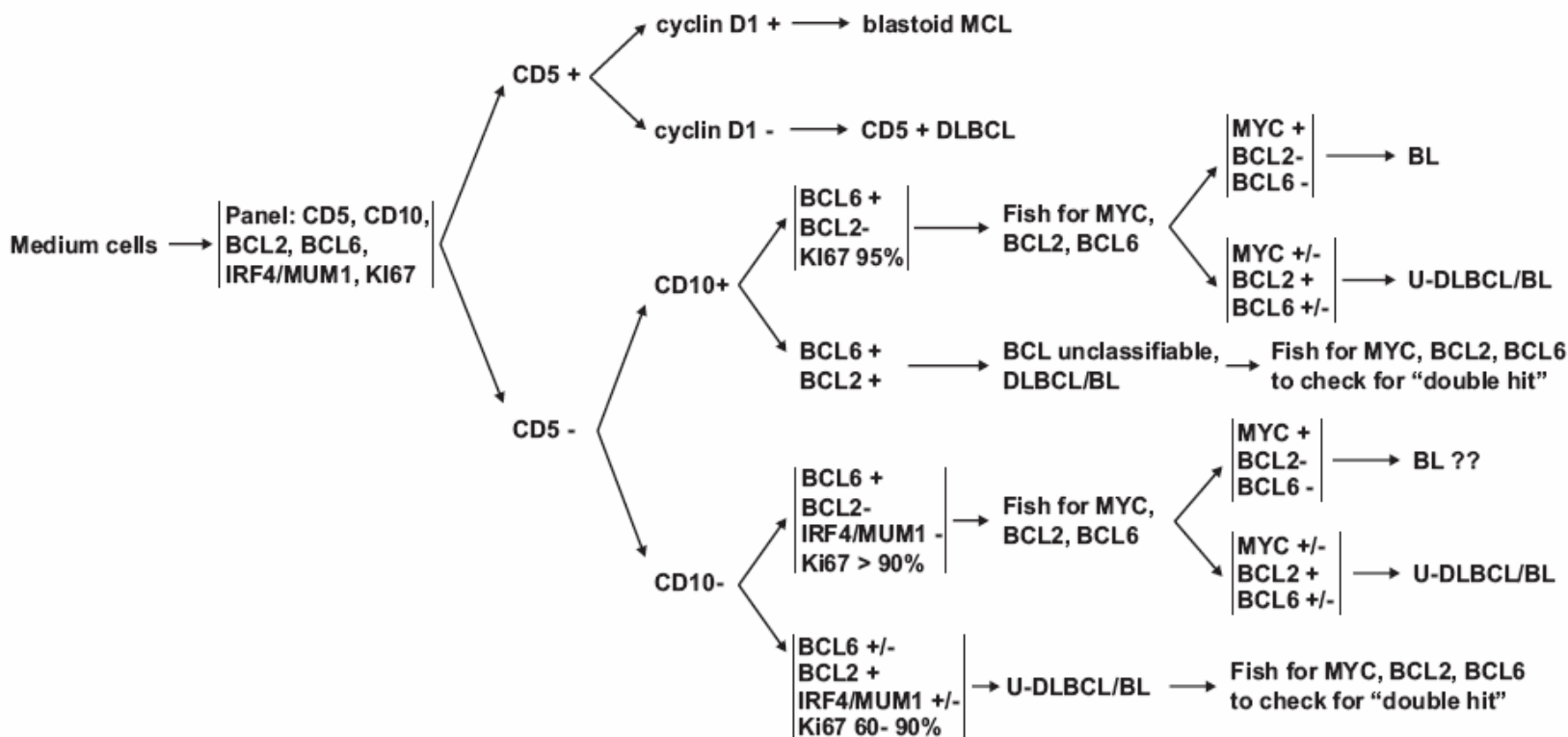
Small cells:

- Chronic lymphocytic leukaemia/ small lymphocytic lymphoma (CLL/SLL)
- Mantle cell lymphoma (MCL)
- Splenic marginal zone lymphoma
- Hairy cell leukaemia (HCL)
- Lymphoplasmacytic lymphoma (LPL)
- Extranodal marginal zone lymphoma (MALT lymphoma)
- Nodal marginal zone lymphoma
- Follicular lymphoma (FL)

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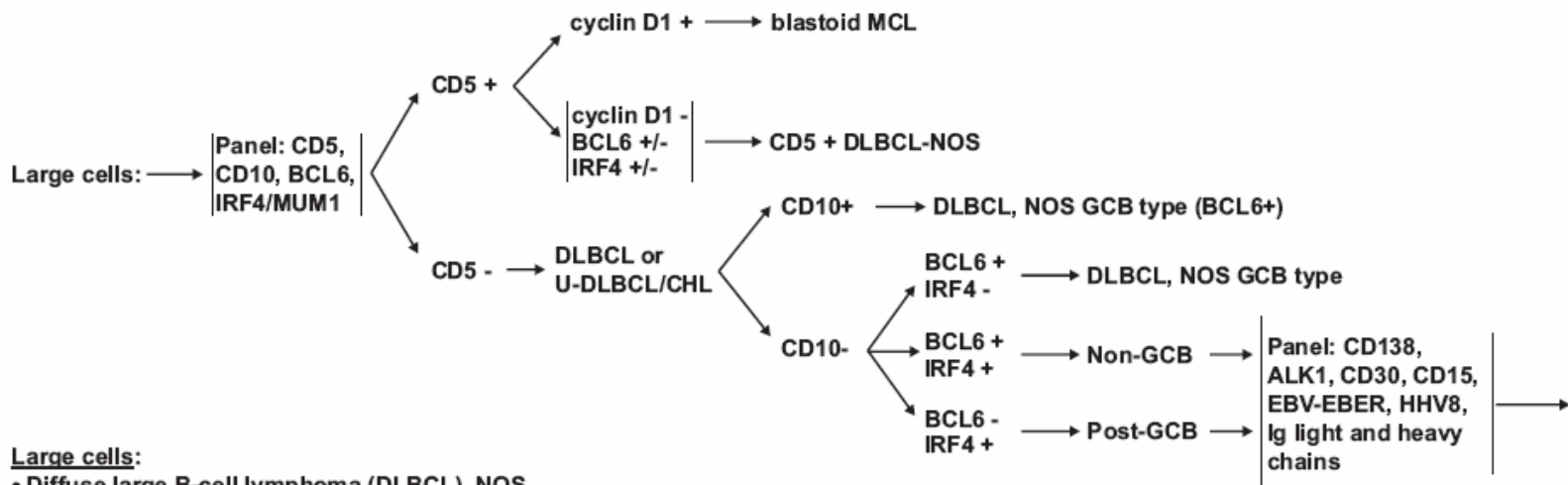
Medium cells

- Burkitt's lymphoma (BL)
- Diffuse large B-cell lymphoma (DLBCL)
- Mantle cell lymphoma (MCL), blastoid variant
- B-cell lymphoma, unclassifiable, intermediate between DLBCL and BL (U-DLBCL/BL)

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Large cells:

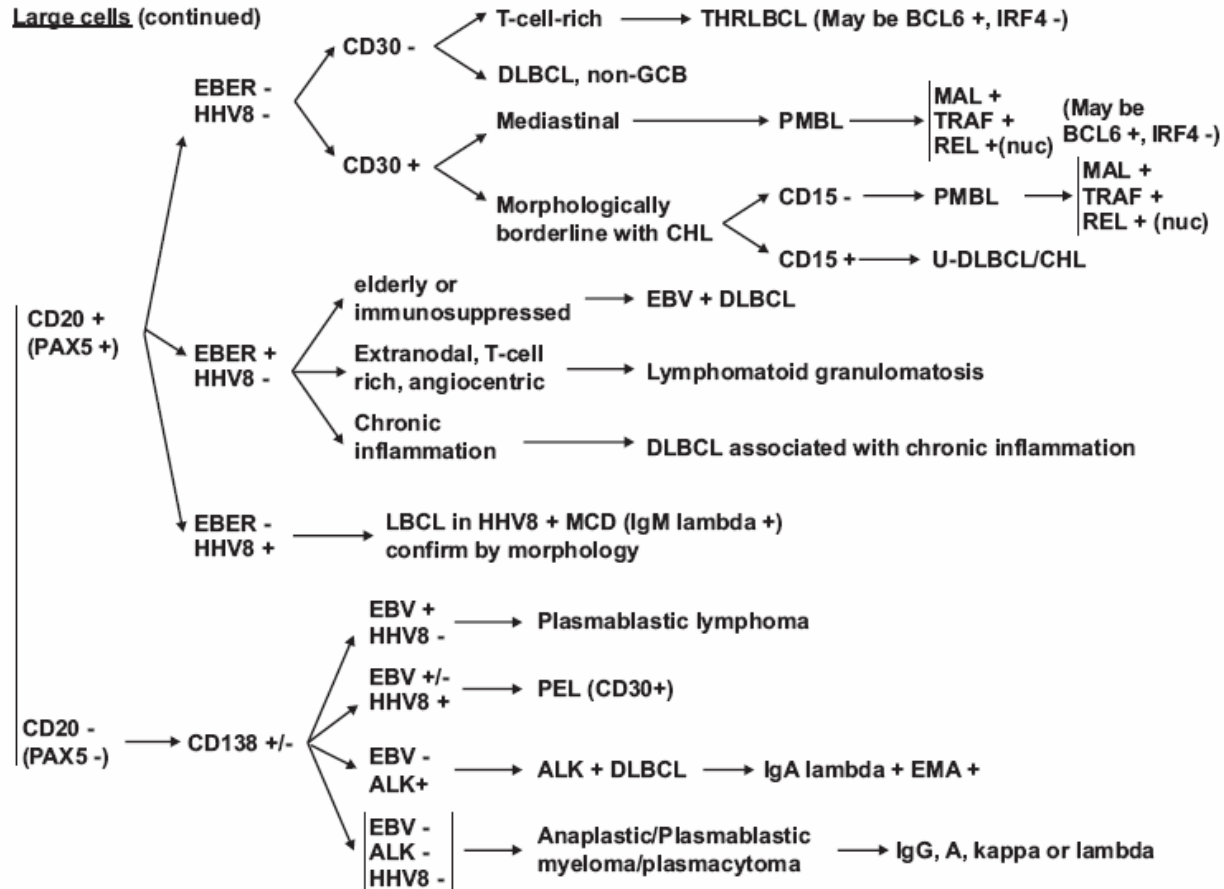
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 - T-cell/histiocyte rich large B-cell lymphoma (THRLBCL)
 - Primary DLBCL of the CNS
 - Primary cutaneous DLBCL, leg type
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GCB= Germinal center B-cell like

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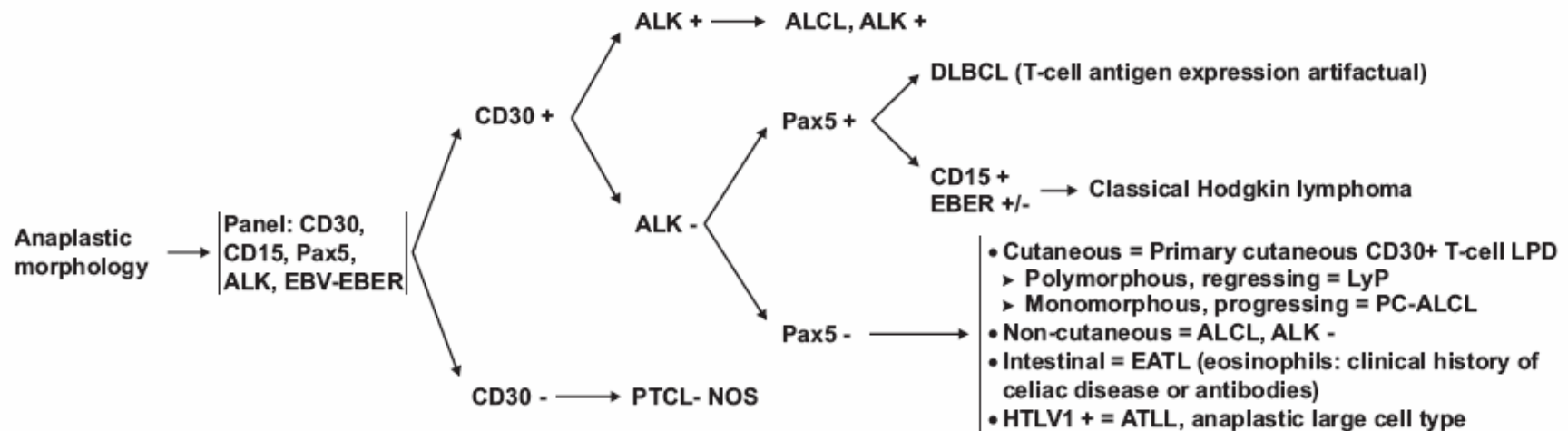
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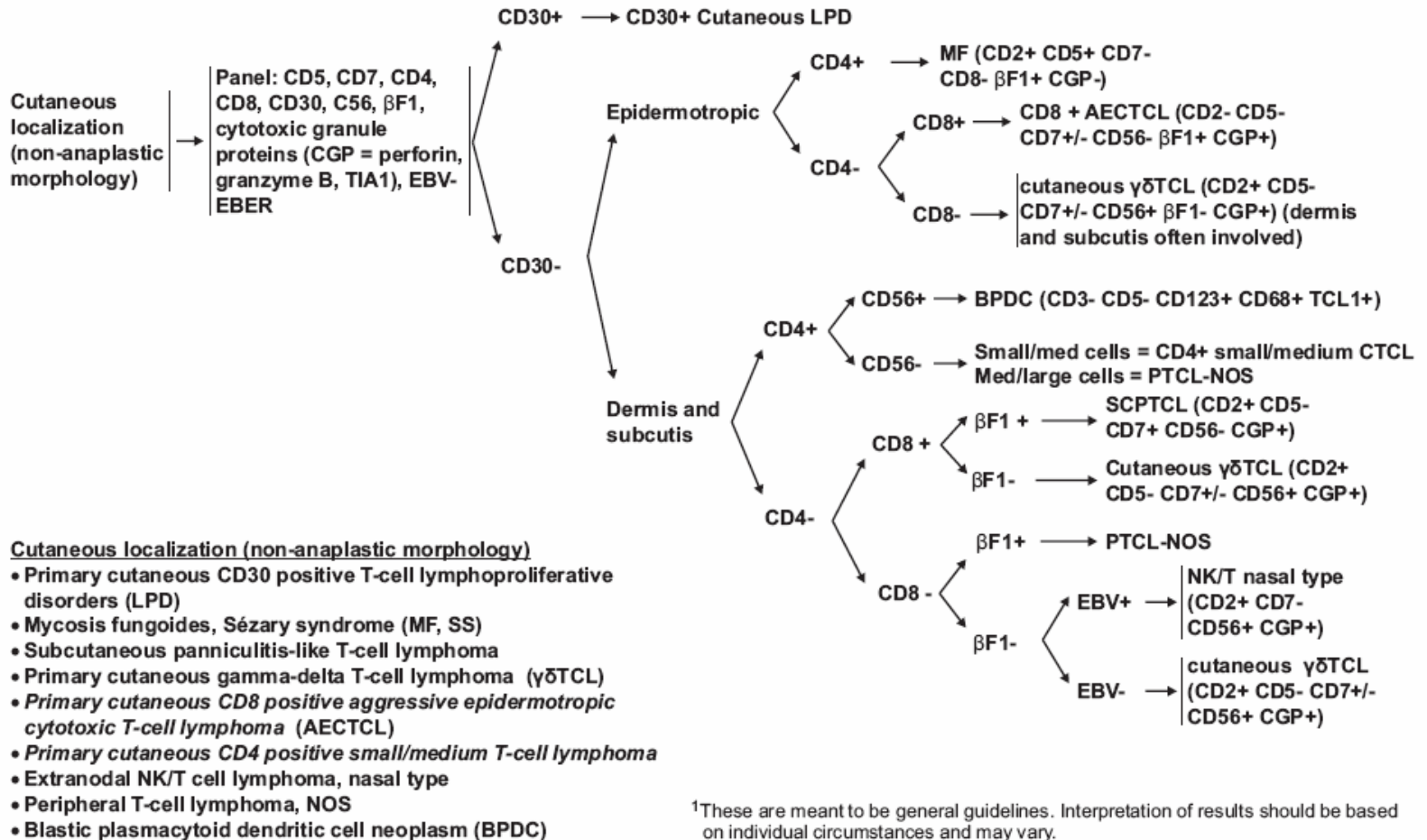
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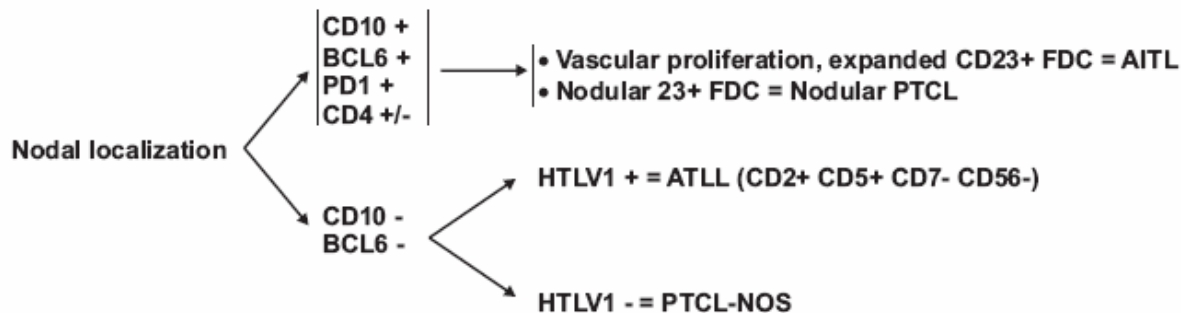
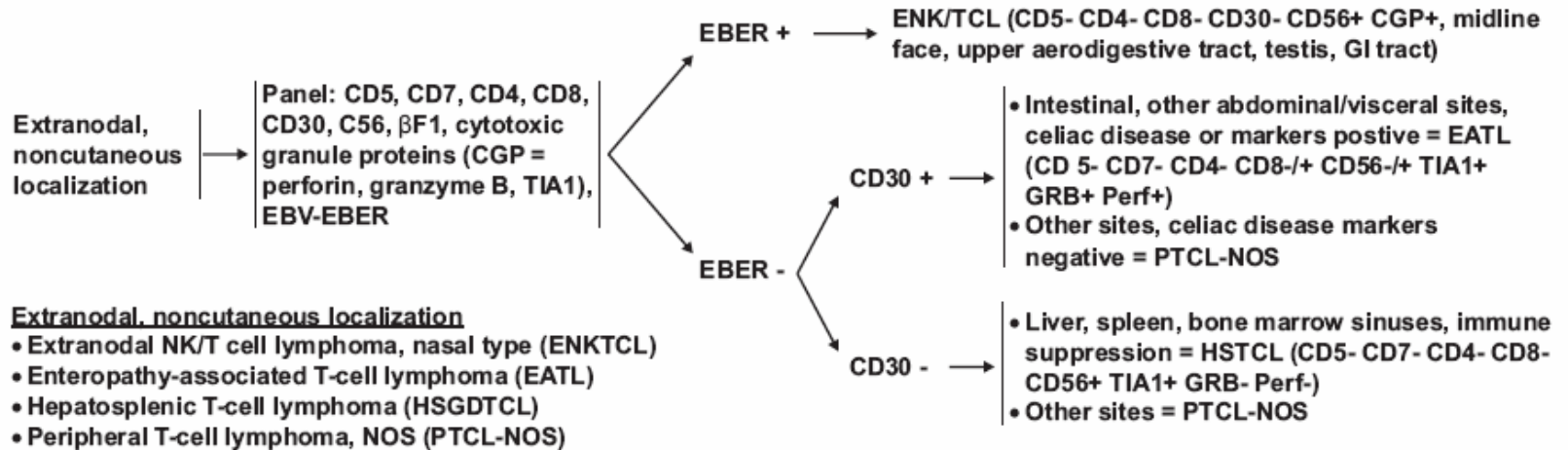
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Nodal localization

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- Peripheral T-cell lymphoma, NOS (PTCL-NOS)

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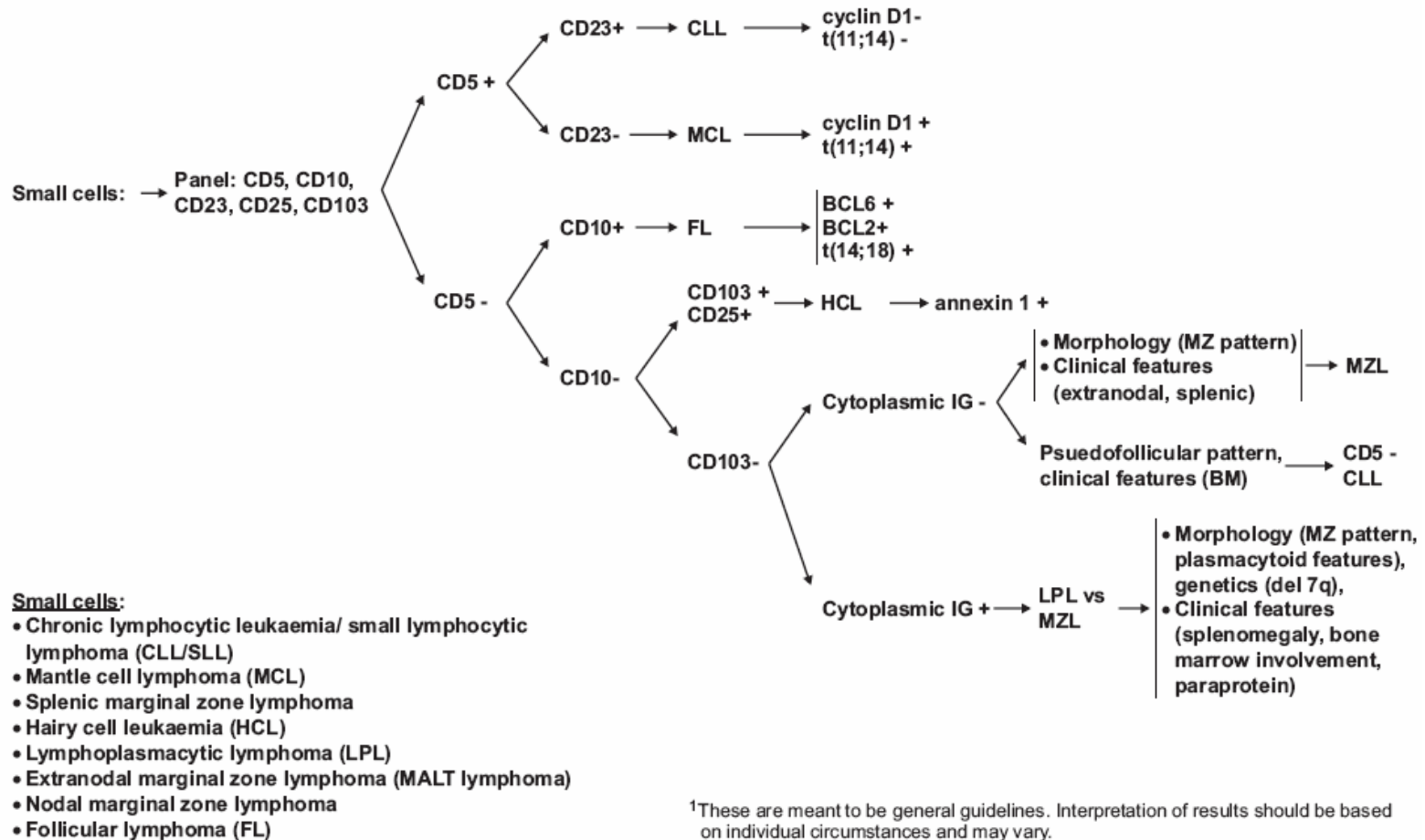
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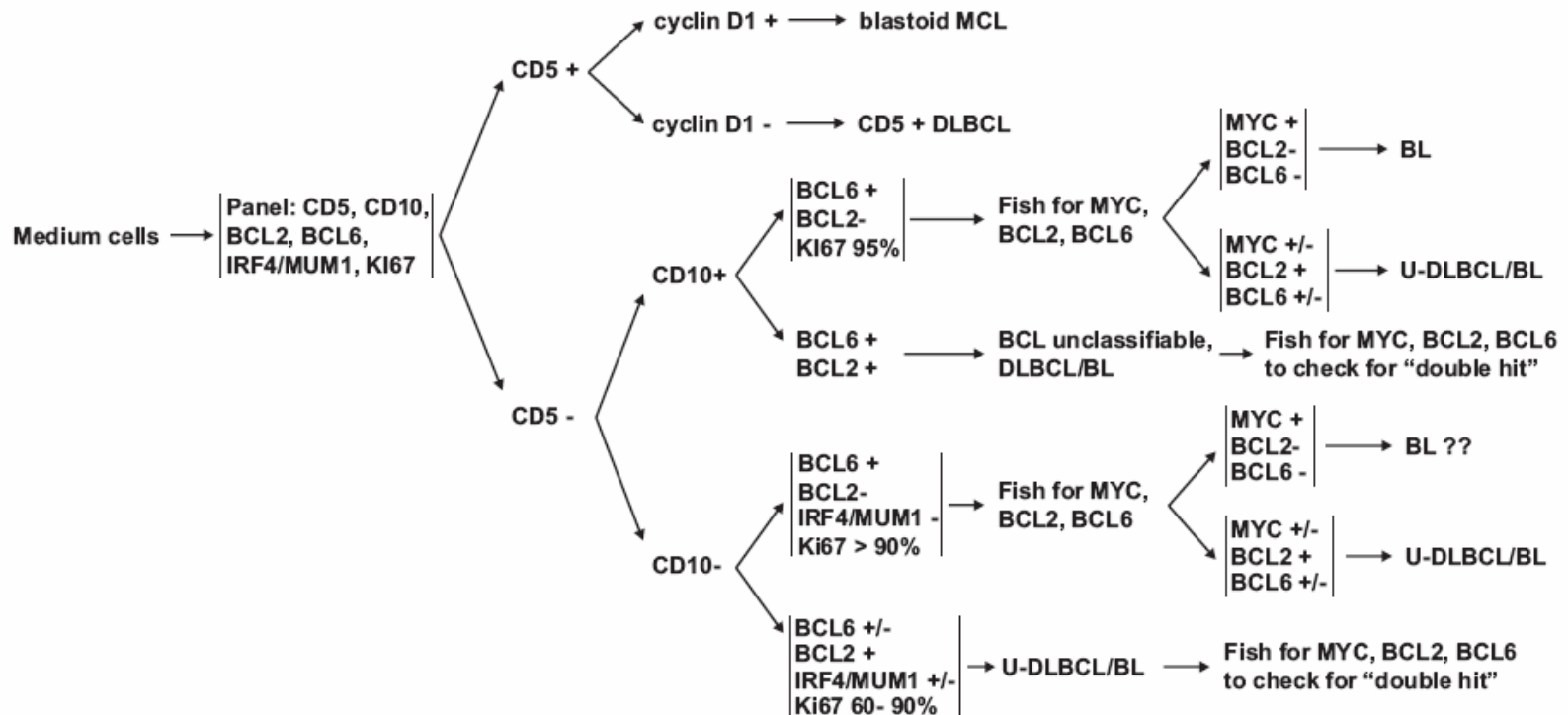
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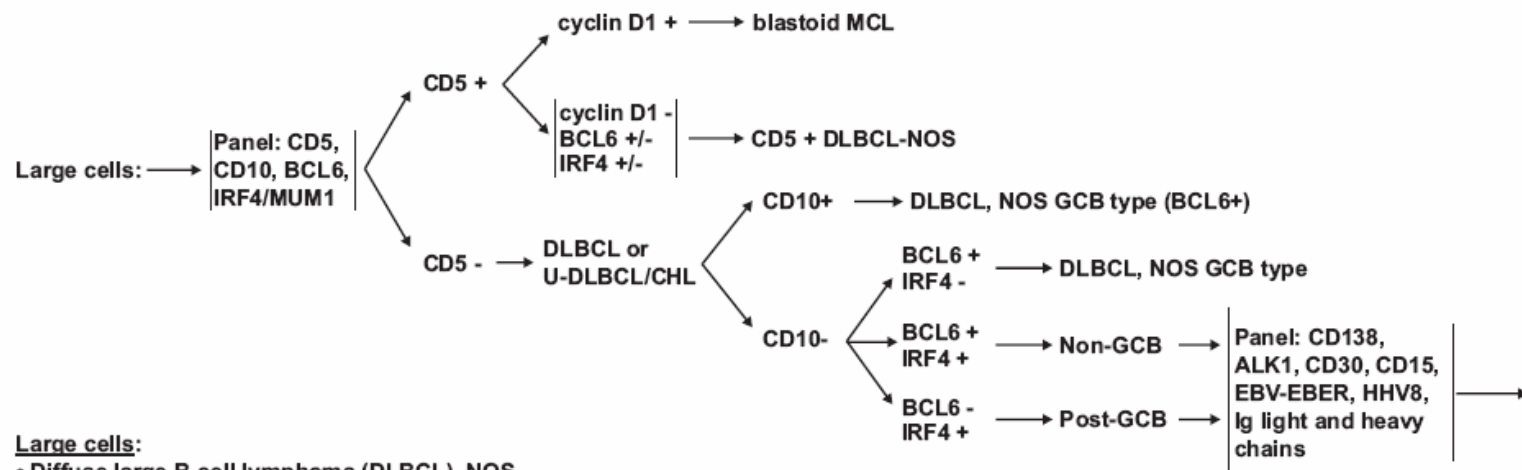
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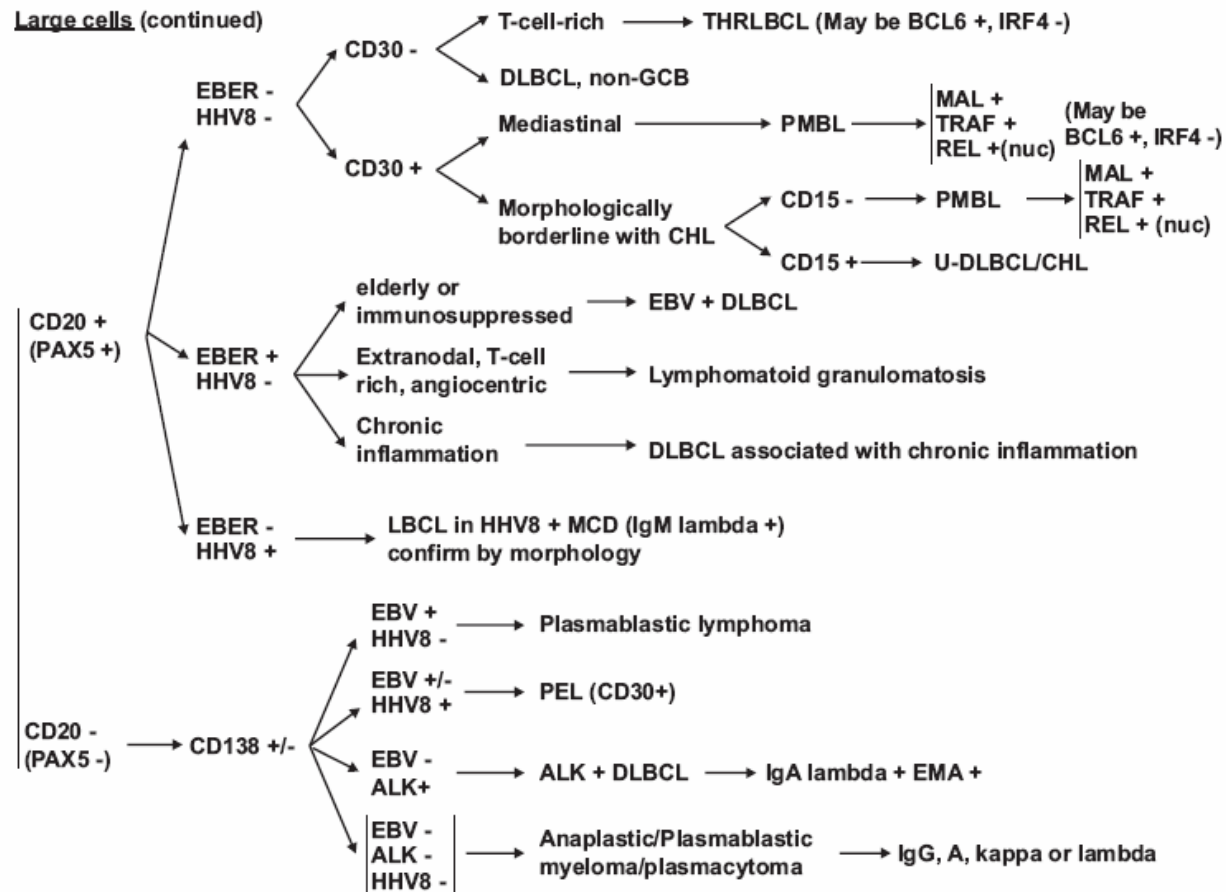
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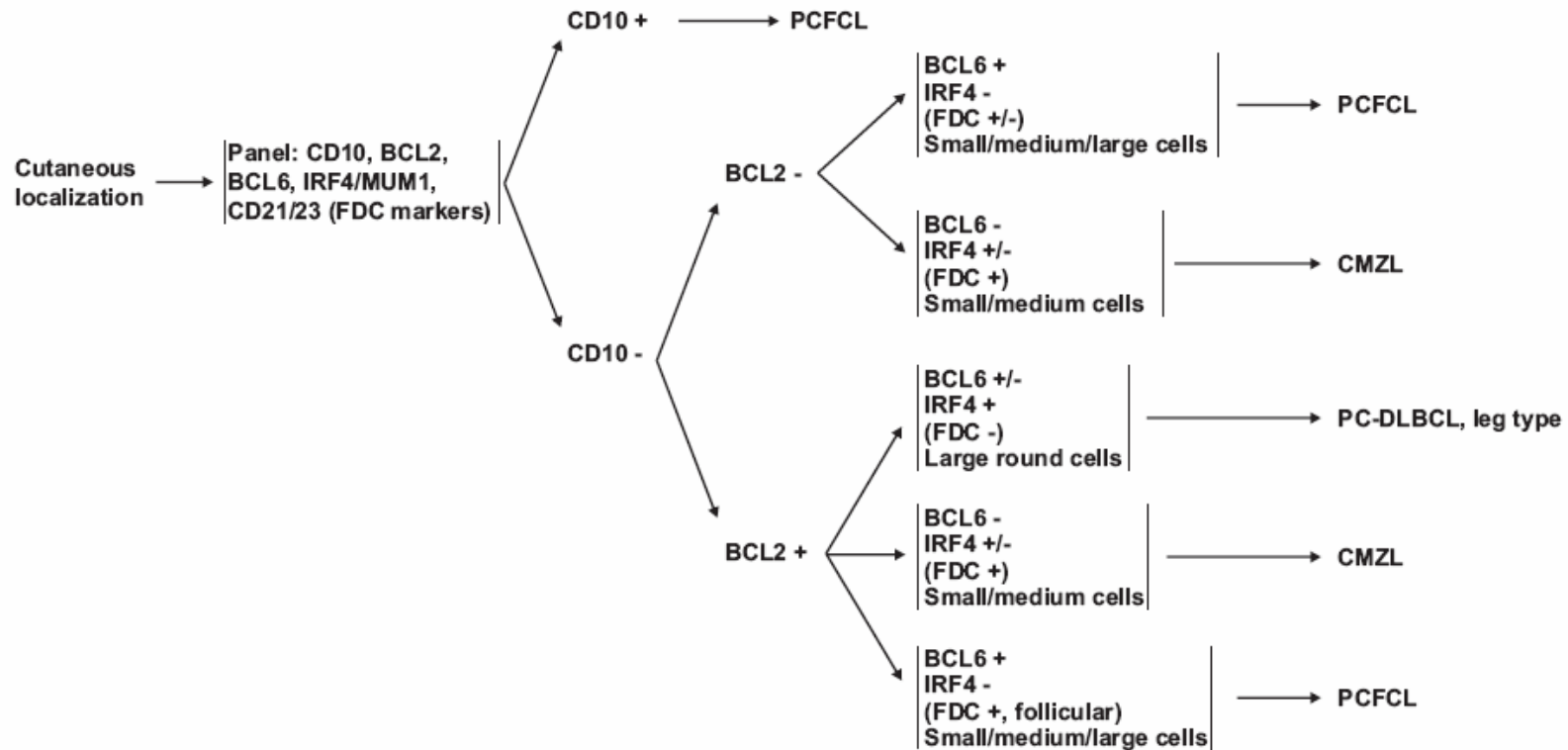
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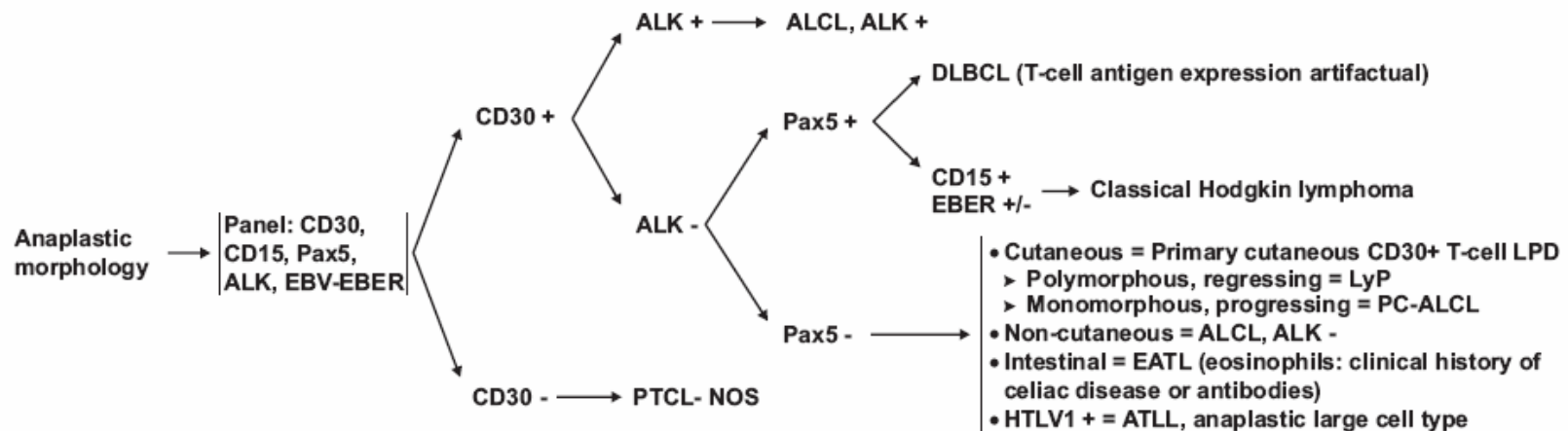
FDC = Follicular dendritic cells

- Cutaneous marginal zone lymphoma (CMZL)
- Primary cutaneous follicle center lymphoma (PCFCL)
- Primary cutaneous DLBCL, leg type (PC-DLBCL, leg type)

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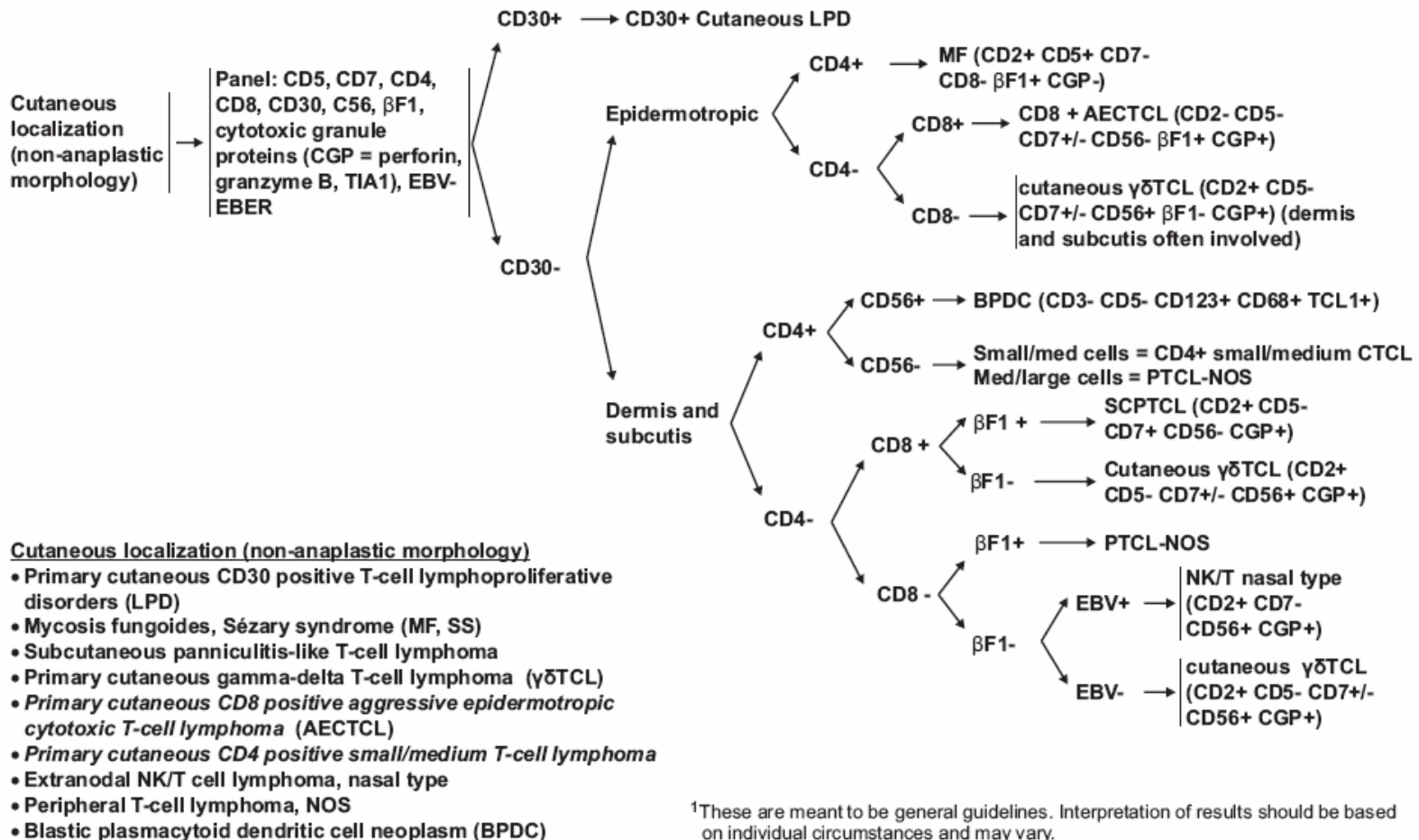
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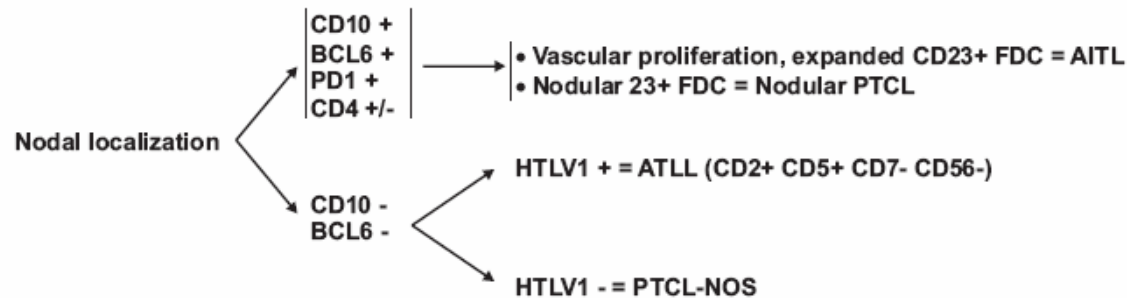
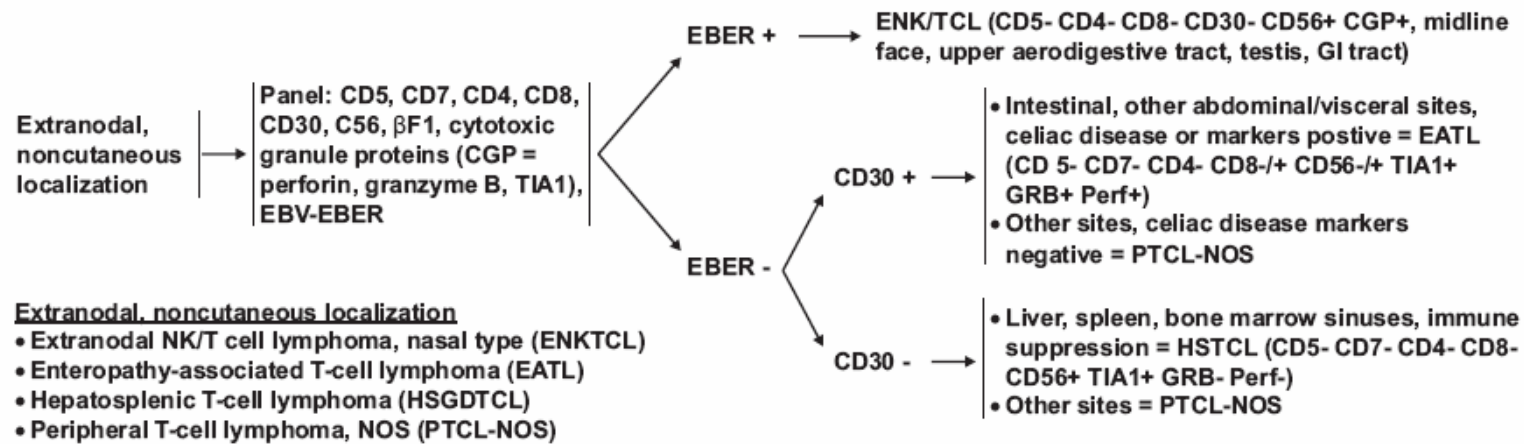
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