IHC classification of haematolymphoid tumours

Workshop in Diagnostic Immunohistochemistry Oud St. Jan/ Old St. John – Brugge (Bruges), Belgium June 13th – 15nd 2018

Rasmus Røge, MD, NordiQC scheme organizer

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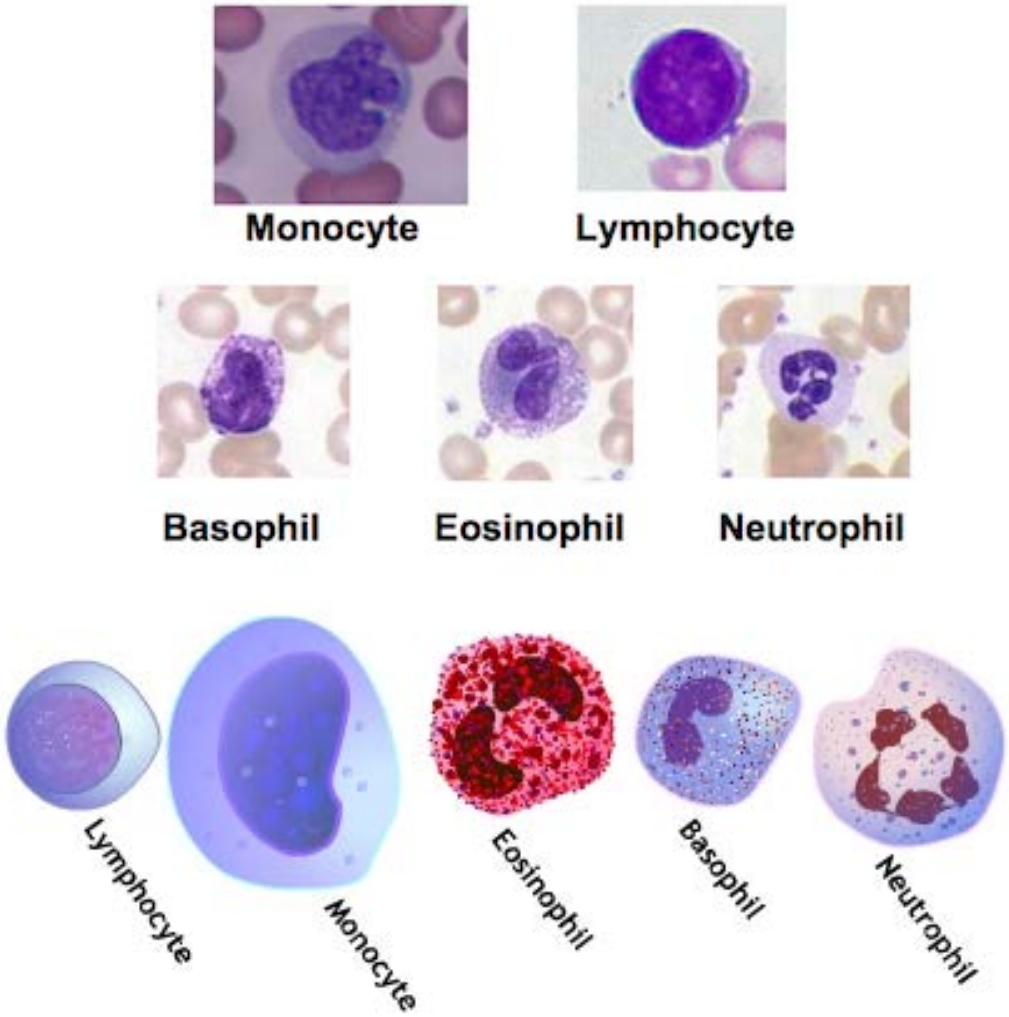
White blood cells - function



- Neutrophils: most abundant. First responders in inflammation. Target bacteria and fungi
- Eosinophils: Targets parasites. Abundant in mucous membranes. Elicits allergy reaction
- Basophils: Allergic and antigen reaction. Releases histamins that widens blood vessel

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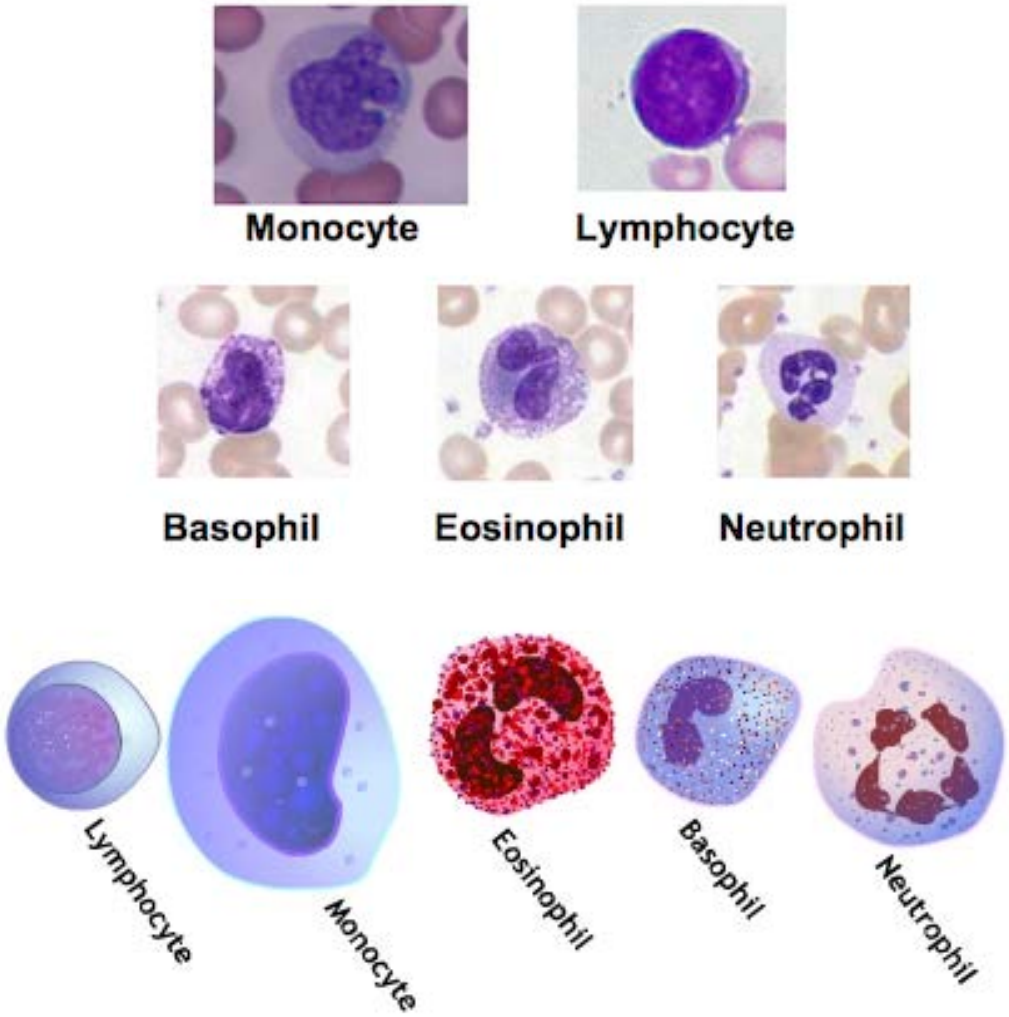
White blood cells - function



- Monocytes: Leaves blood stream to become tissue macrophages. They are phagocytic and functions as ”vacuum cleaners” and degrade cell debris in inflamed tissue
- Lymphocyte: One of main cell types involved in the immune system. In blood, most lymphocytes are naive (unstimulated) circulating before activation

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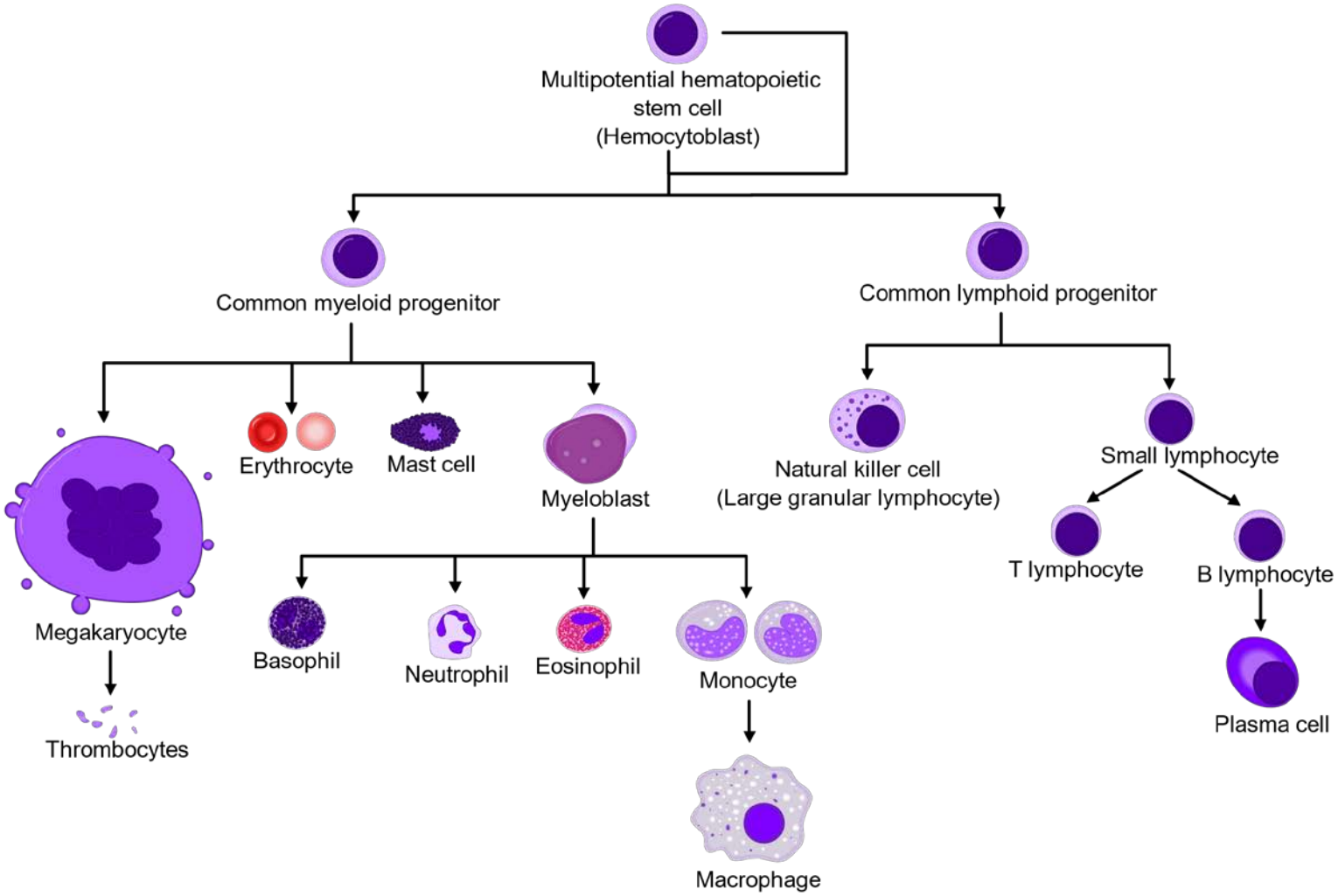
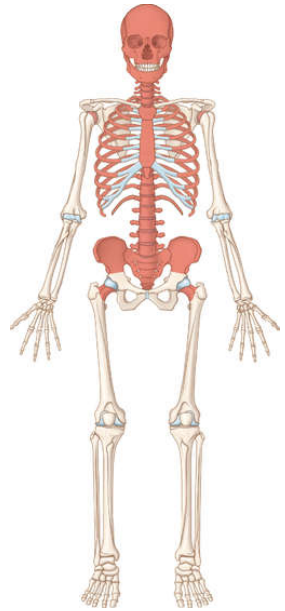
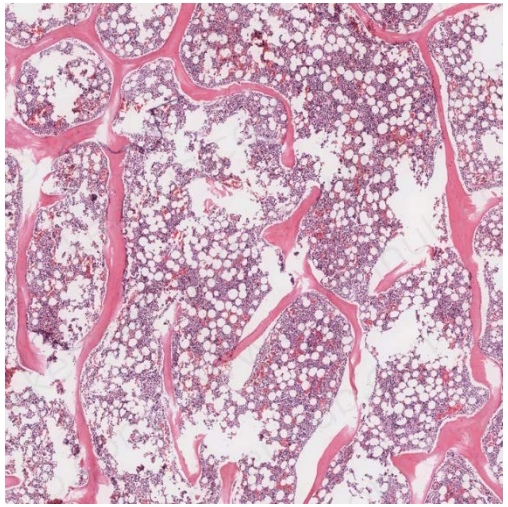
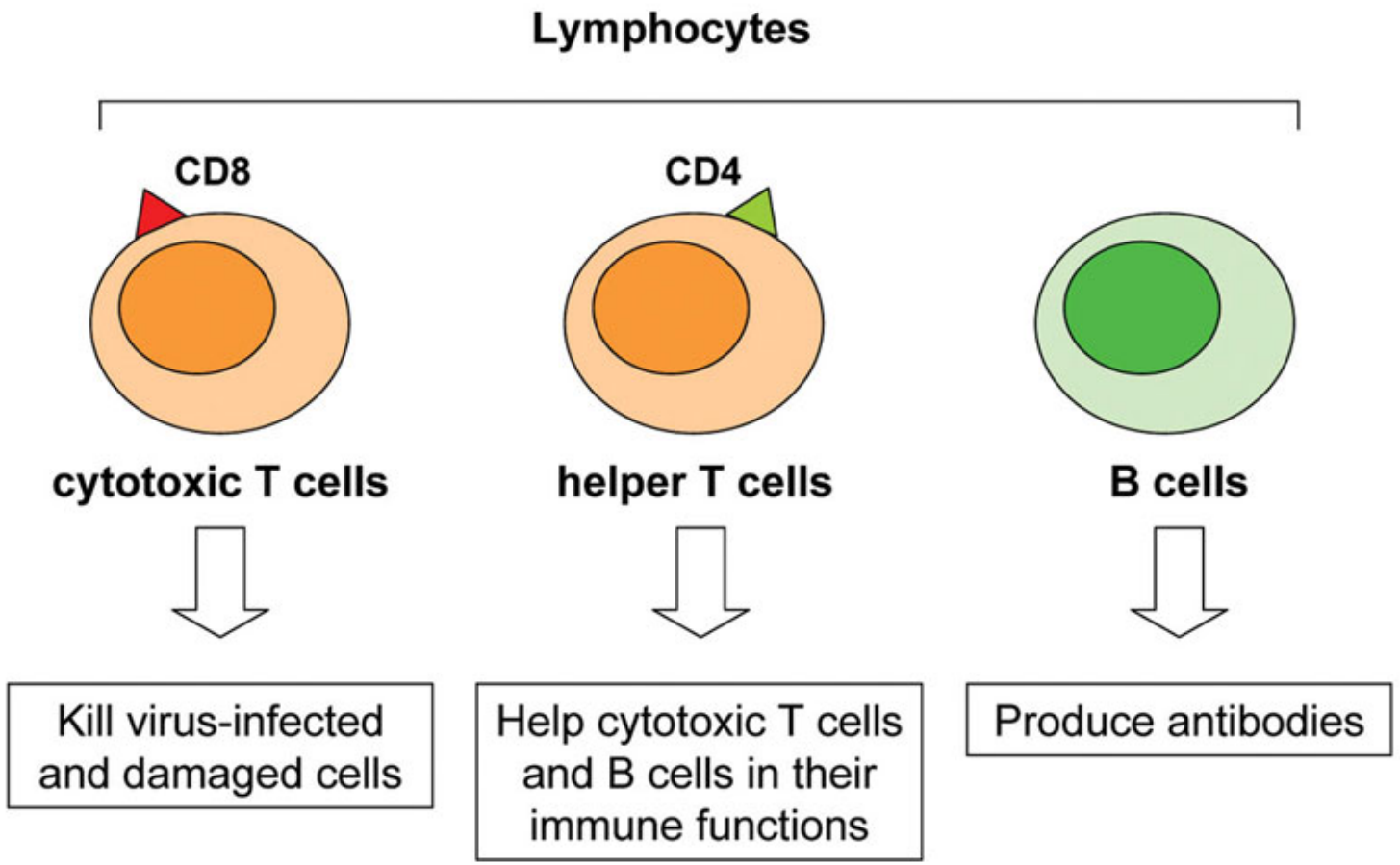
Haematopoiesis



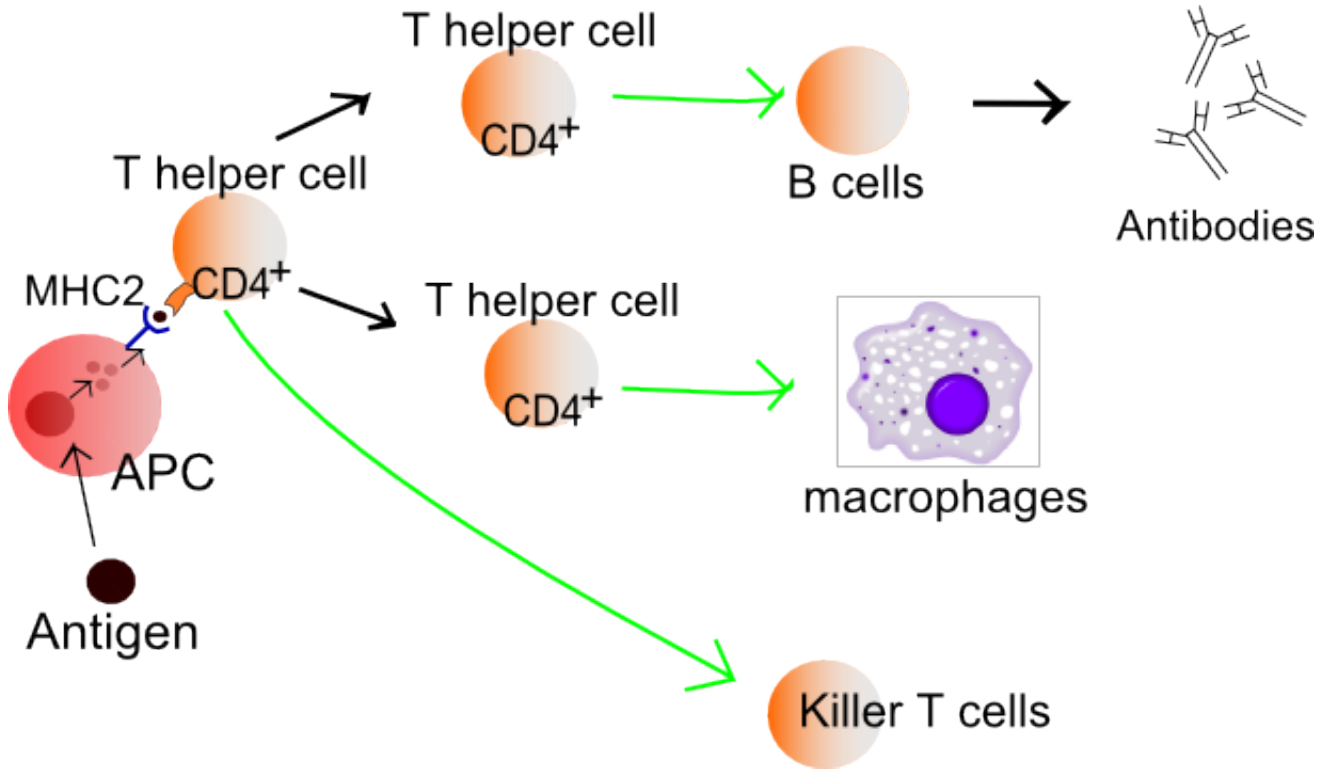




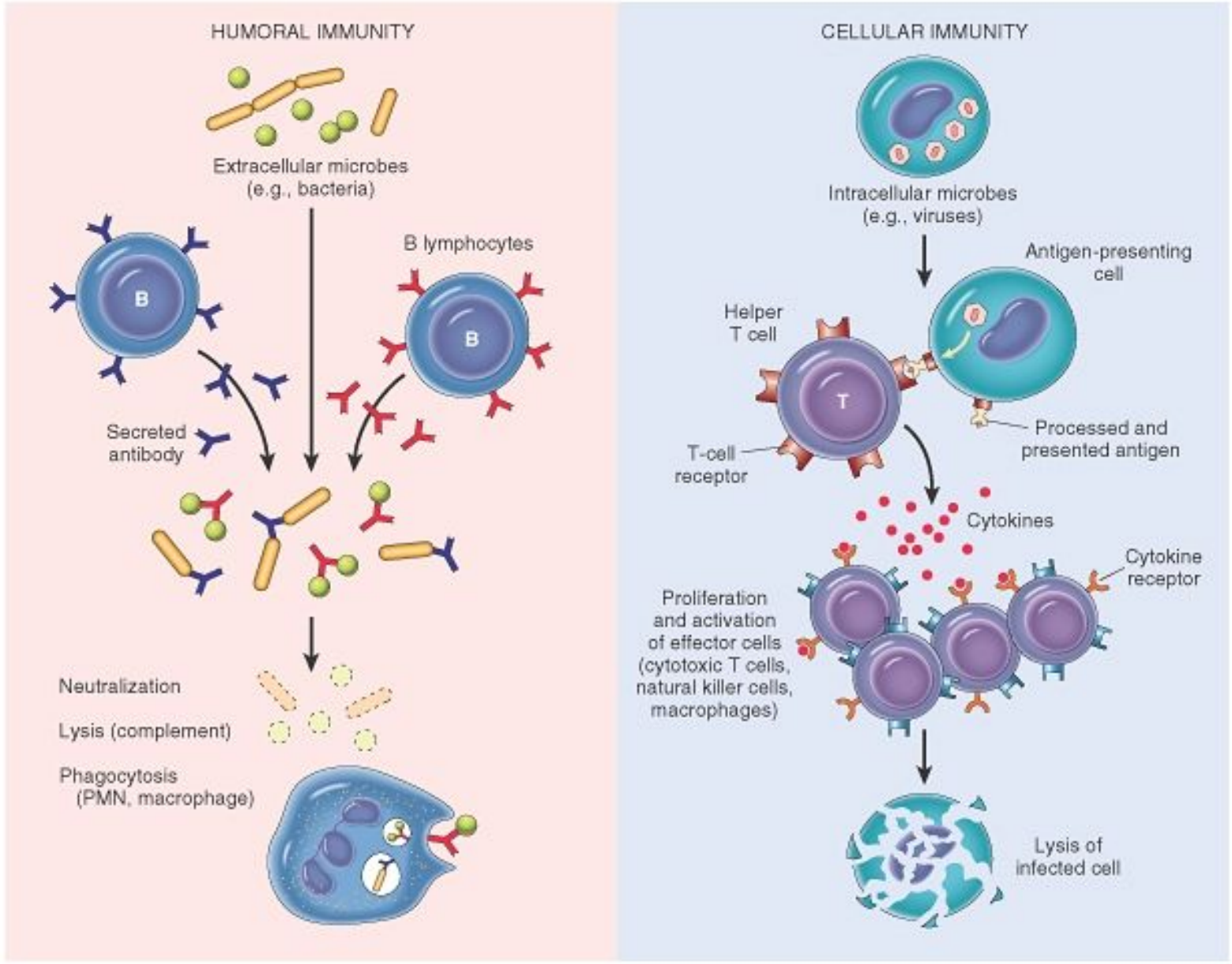
Lymphocyte subtypes



Immune system



Immune system



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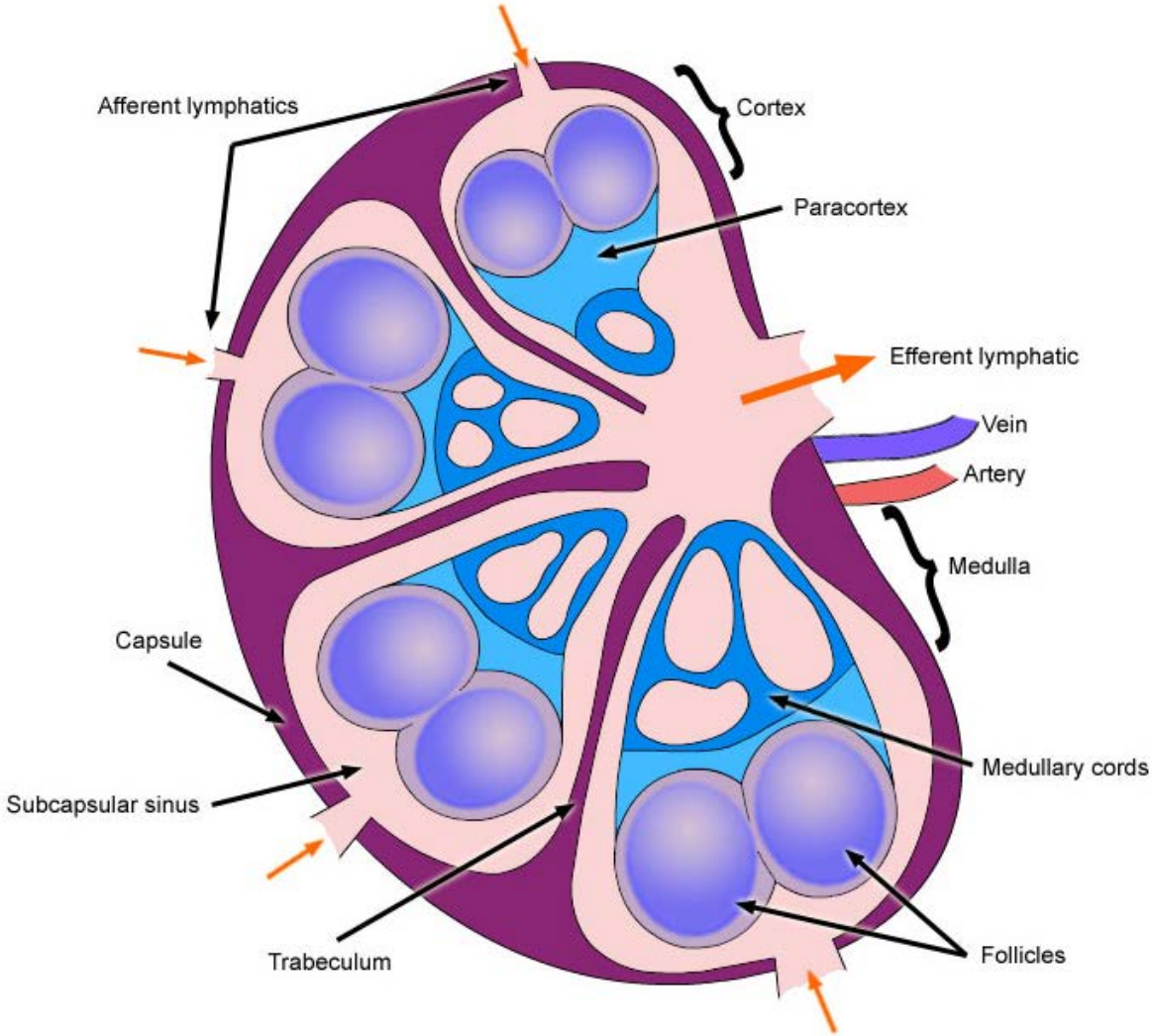
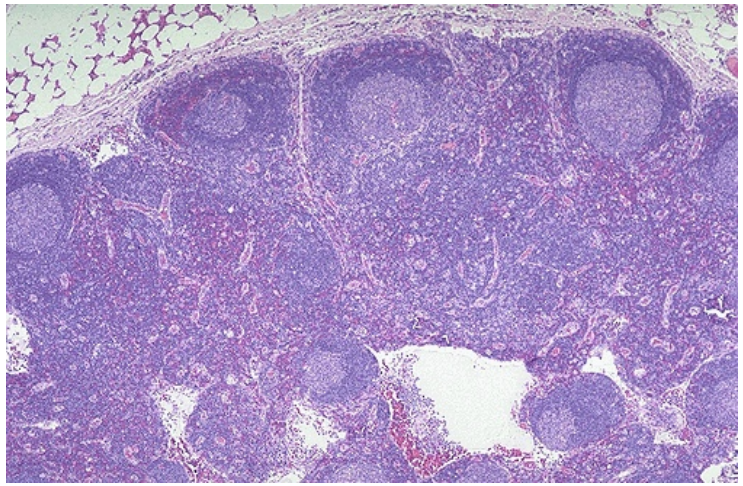
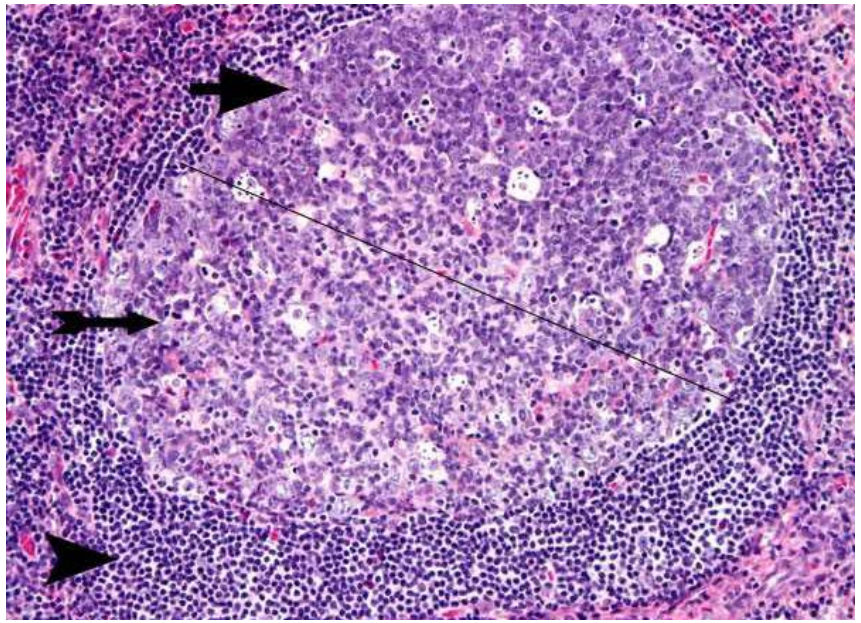
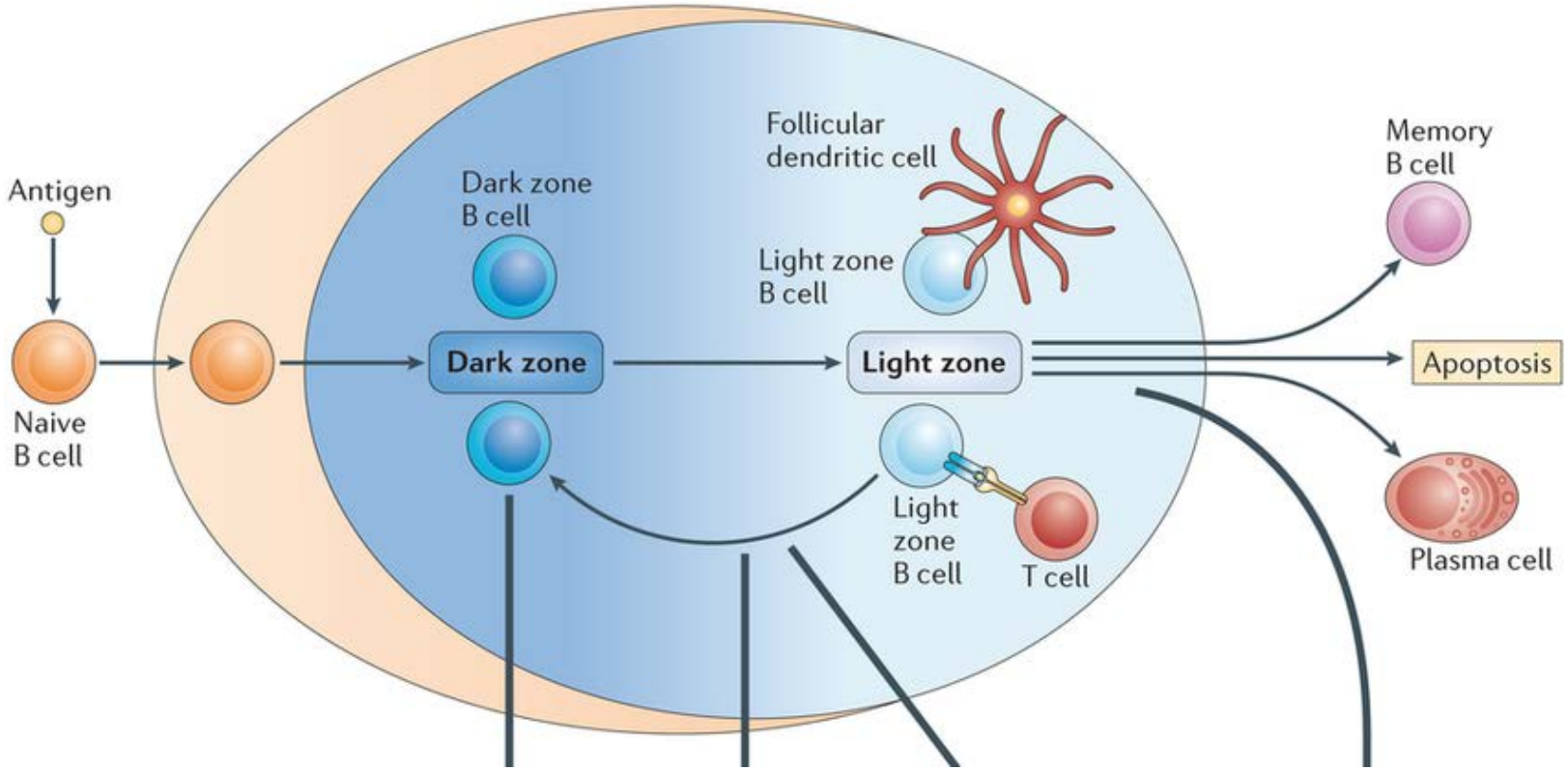
Lymph node


Afferent lymphatics
Cortex
Paracortex
Efferent lymphatic
Vein
Artery
Medulla
Capsule
Medullary cords
Subcapsular sinus
Trabeculum
Follicles



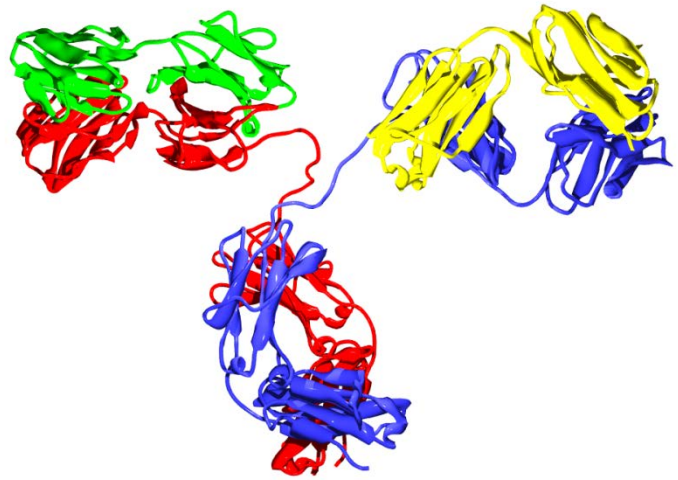


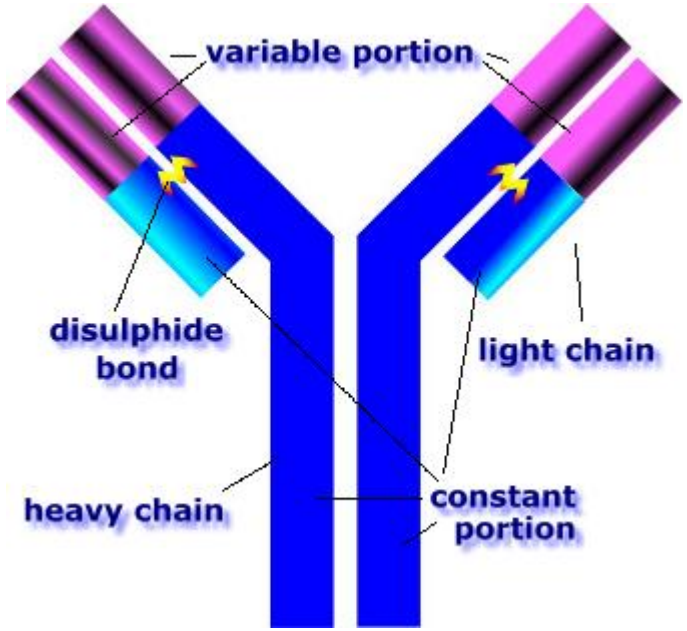
B-cell development



Antibodies – structure

- Antibody (Ab) or Immunoglobulin (Ig)
- Produced by mature plasma cells
- Can exist as membrane-bound (BCR) or secreted form
- Structured by two heavy chains and two light chains





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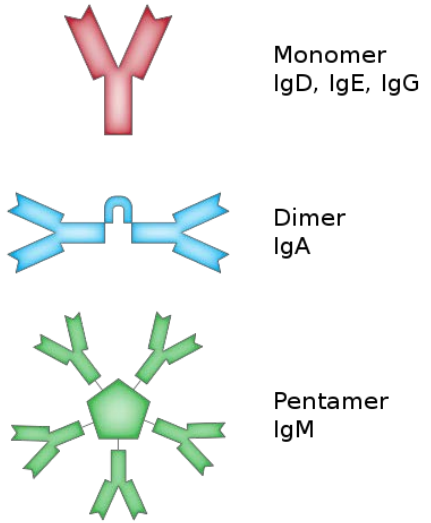
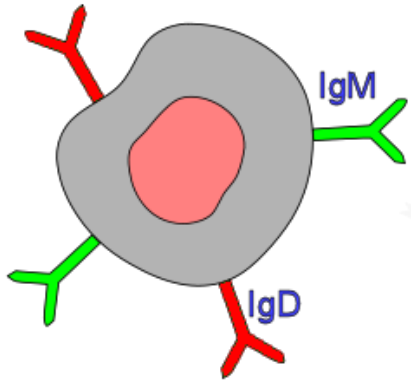
Antibodies – structure

- Light chains (211-217 amino acids) – either type κ or λ
- Heavy chains (450-550 amino acids) – either type α, δ, γ, μ or ε
- Heavy chains determines isoform / isotype
- IgA, IgD, IgG, IgM or IgE





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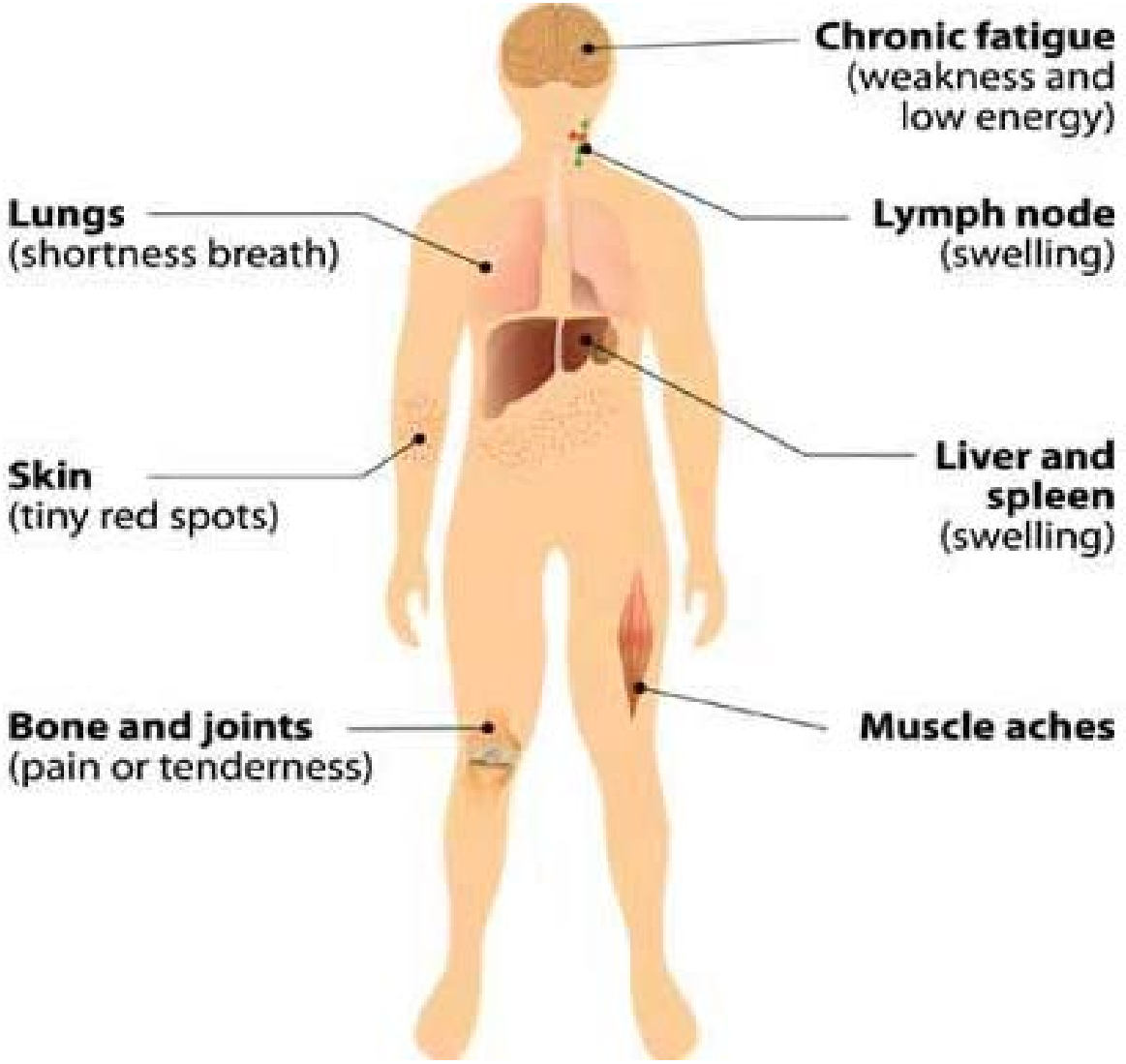
Signs and symptoms of lymphoma

- Enlarged lymph nodes
- Fever
- Drenching sweats (particulary at night)
- Unintended weight loss
- Itching
- Feeling tired



What is a lymphoma?

Clonal proliferation of mutated lymphoid cells

Mutations cause cells to freeze at a single stage of normal lymphocyte differentiation

Morphology, immunophenotype and molecular features mirror stages of normal lymphocyte development

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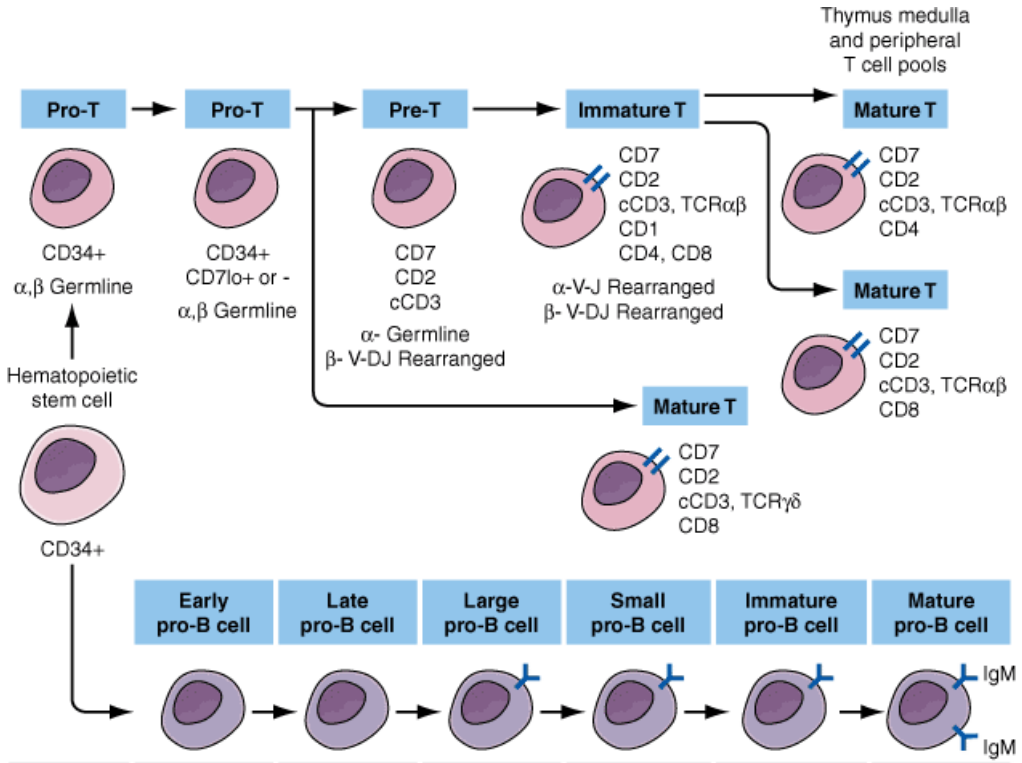
T- and B-cell differentiation: Stage specific surface antigen expression



High-chain genes	DJ rearranged	VDJ rearranged	VDJ rearranged	VDJ rearranged	VDJ rearranged	VDJ rearranged
Low-chain genes	Germ line	Germ line	Germ line	VDJ rearranged	VDJ rearranged	VDJ rearranged
Surface Ig	Absent	Absent	μ H-chain at surface as part of pre-β receptor	μ H-chain in cytoplasm and at surface	IgM expressed on cell surface	IgD and IgM made from alternatively spliced H-chain transcripts
Surface marker proteins	CD34 CD10 CD19 CD38	CD10 CD19 CD20 CD38 CD40	CD19 CD20 CD38 CD40	CD19 CD20 CD38 CD40	CD19 CD20 CD40	CD19 CD20 CD21 CD40

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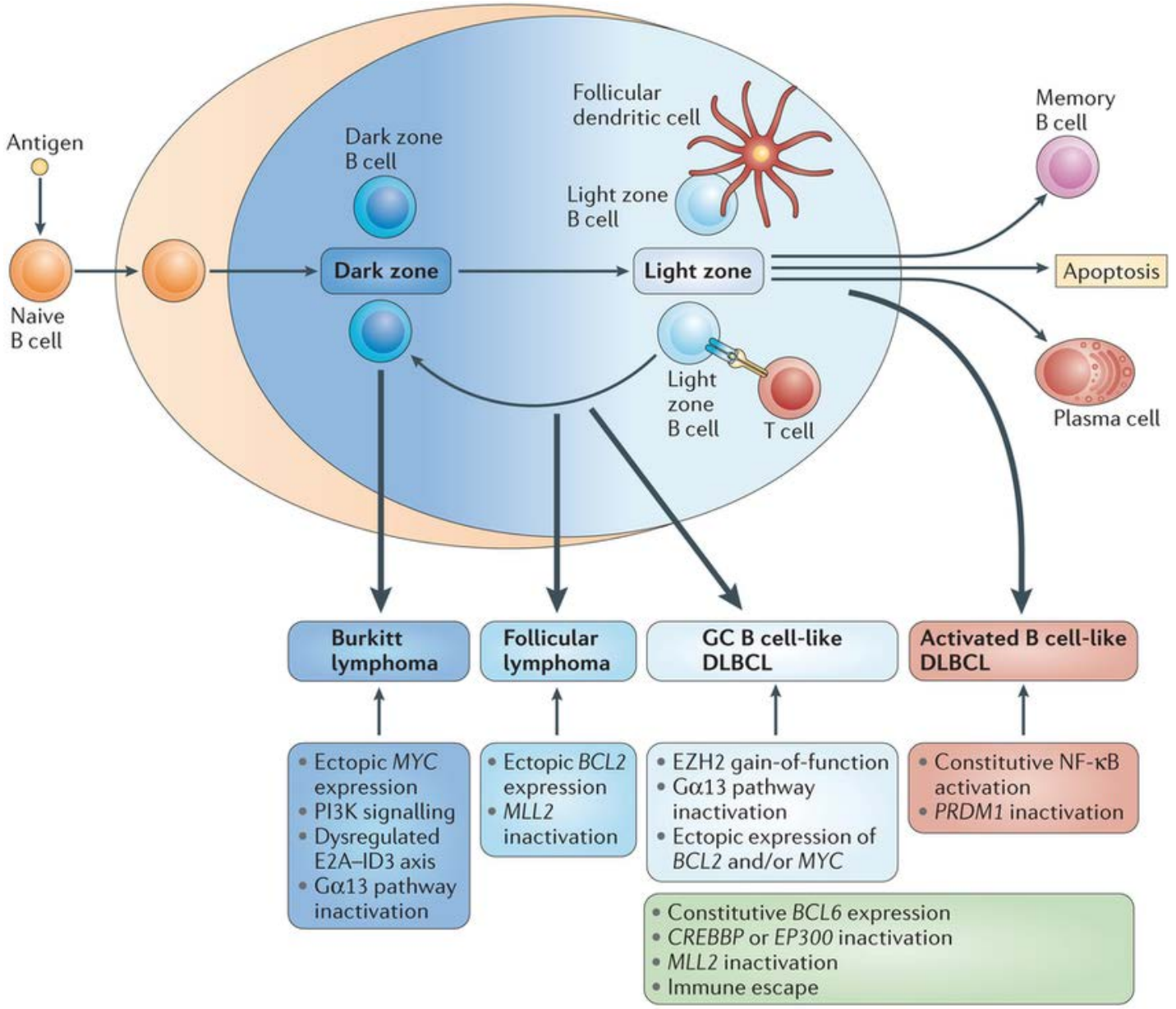
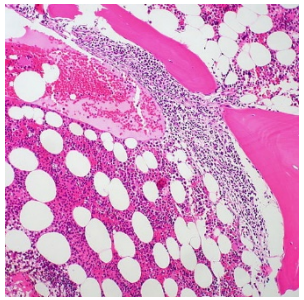
Lymphoid neoplasms: Correlation with normal B-cell development



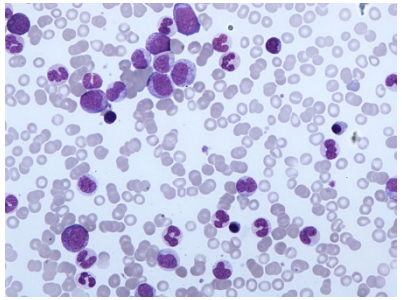
Haematopoietic and lymphoid neoplasias

Anatomical location

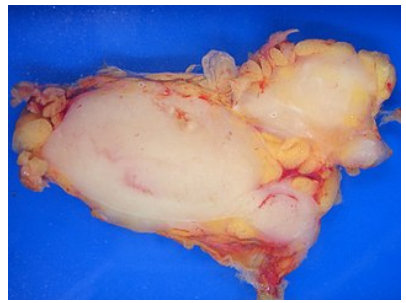
Bone marrow



Blood



Lymph node(s)
Extranodal



Lymphoma

Leukaemia

Adapted from S. Hamilton

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What is the cause of lymphoma?

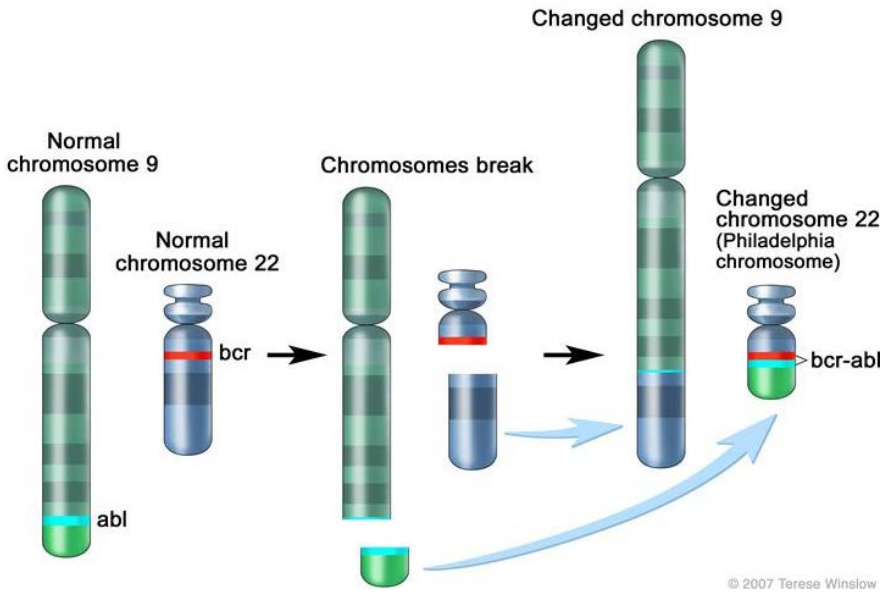
- DNA mutations
- DNA translocations

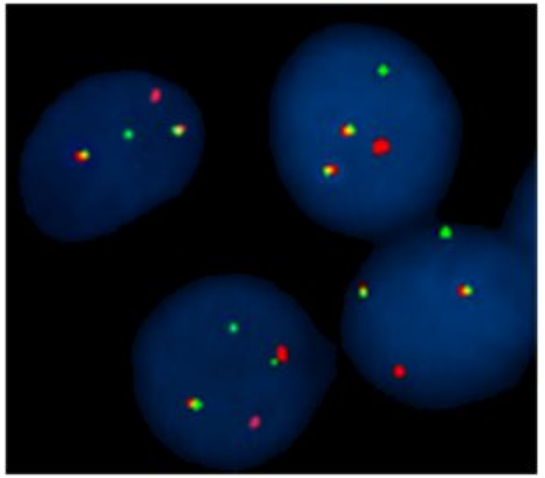
Risk factors

- M>F
- Chemical (benzene, herbicides, insecticides)
- Drugs (methotrexate, TNF-inhibitors, chemotherapy)
- Radiation
- Immune deficiency
- Autoimmune diseases
- Chronic infections

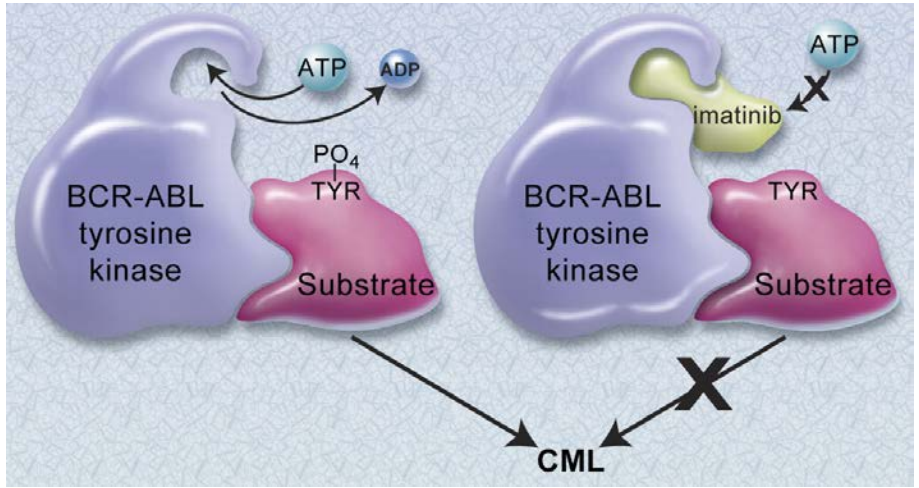
Translocations – examples

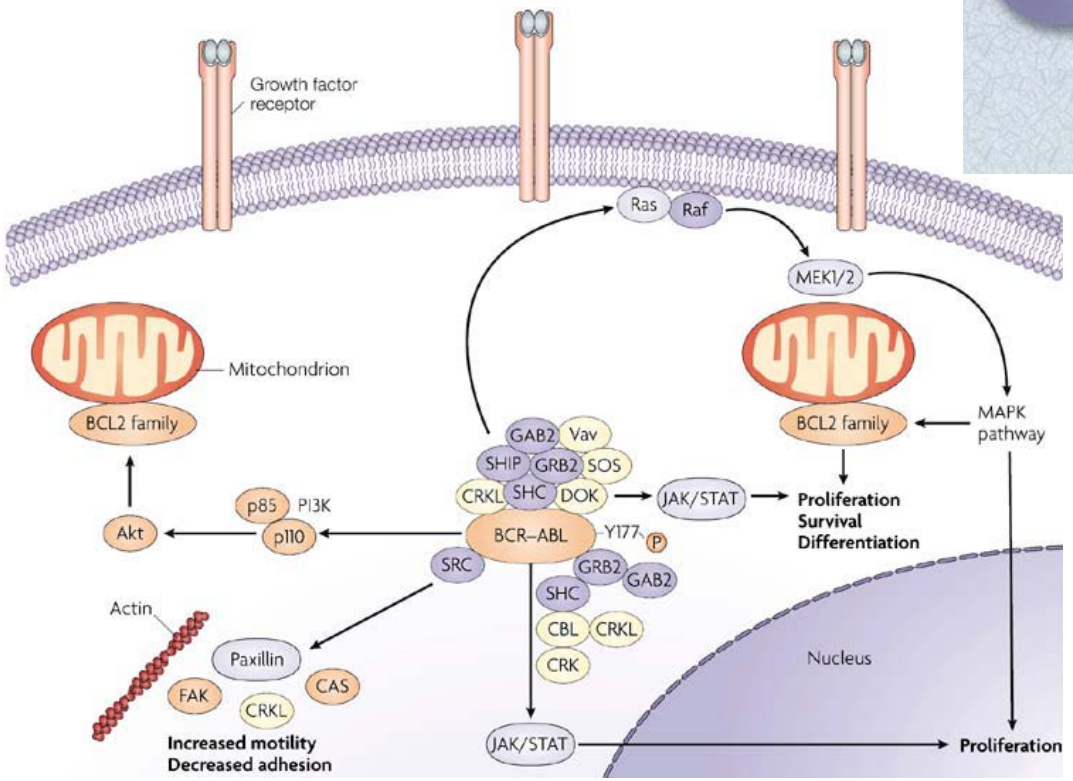
- Philadelphia chromosome: Translocation of (9;22) (q34;11.2). Seen in CML. Creates a fusion gene BCR-ABL1 coding for an ”always-on” tyrokin kinase that induces cell to uncontrolled proliferation.
- Follicular lymphoma: Translocation of (14;18). Results in overexpression of BCL-2 and unopposed proliferation.
- Can be visualized using FISH





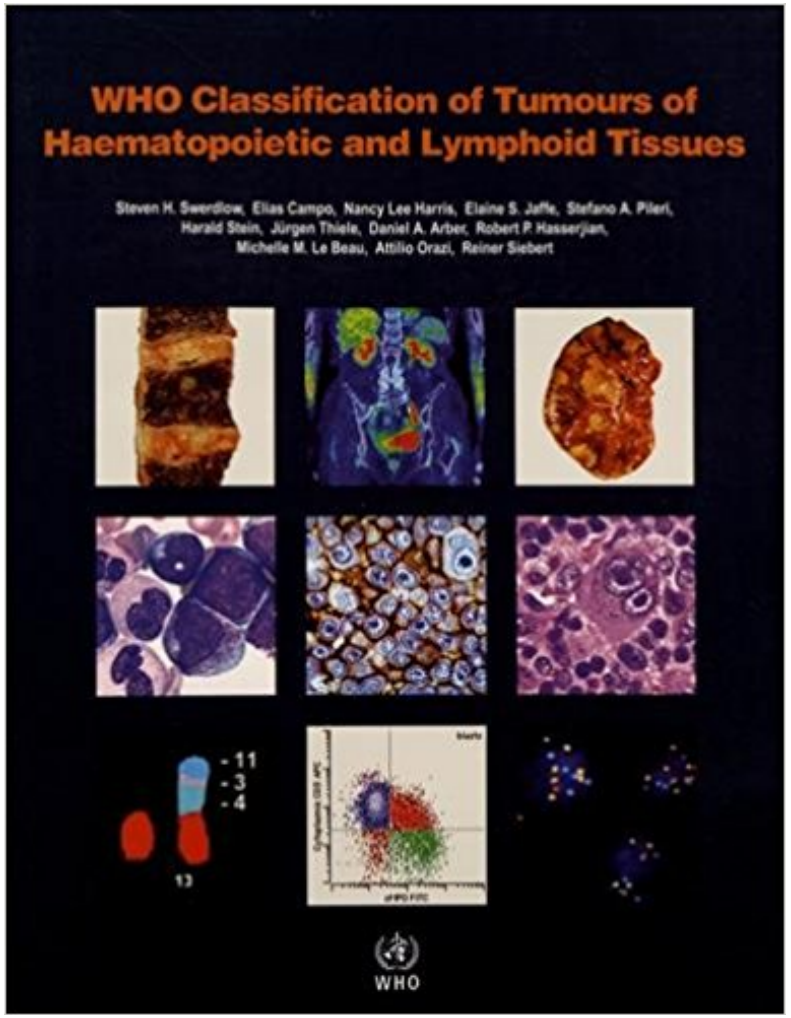
CML


ATP
ADP
PO4
TYR
BCR-ABL
tyrosine
kinase
Substrate
ATP
imatinib
X
TYR
BCR-ABL
tyrosine
kinase
Substrate
X
CML


Growth factor
receptor
Ras
Raf
MEK1/2
Mitochondrion
BCL2 family
BCL2 family
MAPK
pathway
GAB2
Vav
SHIP
GRB2
SOS
CRKL
SHC
DOK
JAK/STAT
Proliferation
Survival
Differentiation
p85
PI3K
p110
Akt
BCR–ABL
Y177
P
SRC
GRB2
GAB2
SHC
CBL
CRKL
CRK
Actin
Paxillin
FAK
CRKL
CAS
Increased motility
Decreased adhesion
Nucleus
JAK/STAT
Proliferation

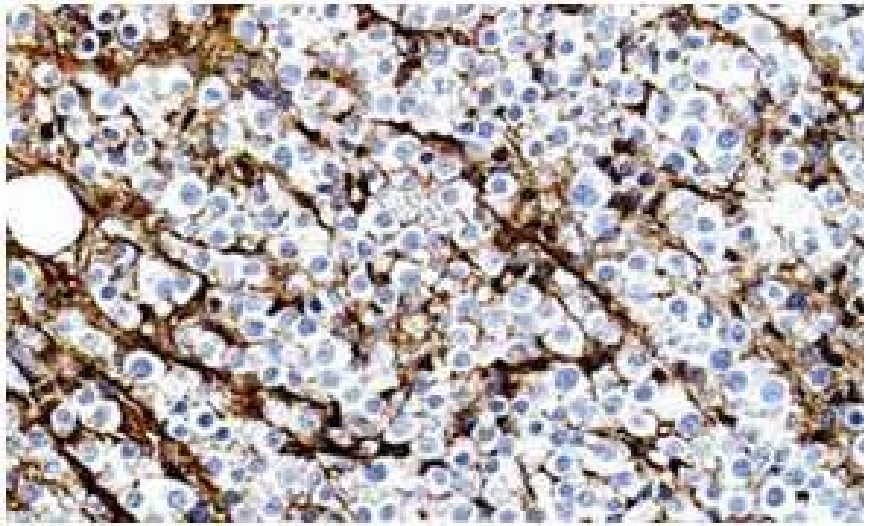
WHO Classification – update 2016

- "WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues - revised 4th edition"
- More than 100 lymphoma entities!
- Contains
  - Clinical features
  - Morphology
  - **Immunophenotypes**
  - Molecular genetics



Clonality

- Normal immunoglobulin producing lymphoid tissue make both kappa and lambda light chain
- B-cell lymphomas producing immunoglobulins all make the same light chain (kappa or lambda) (light chain restriction)
- Expression of one type of immunoglobulin in a lymphoid tissue is indicative of clonality (neoplasia)



DLBCL: kappa

DLBCL: lambda

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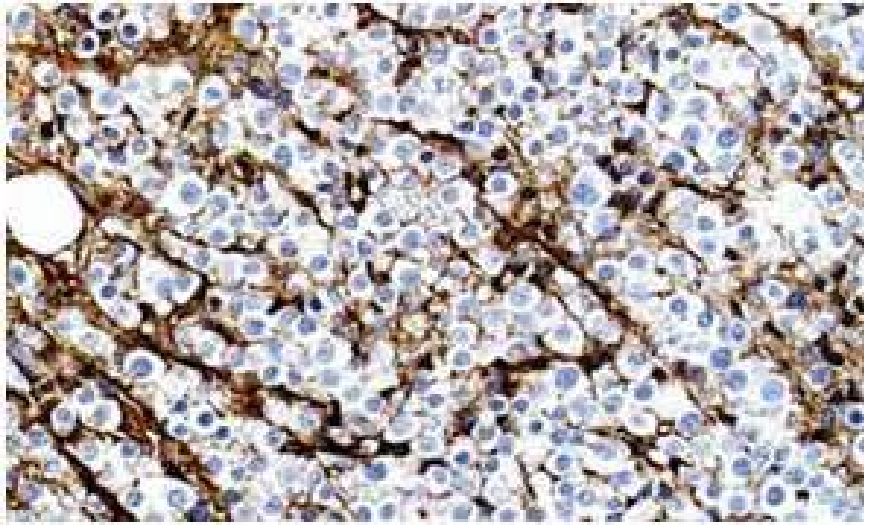
Basic IHC stains – Ig kappa/lambda

- B-cell specific
- Monotypic immunoglobulin light chain suggests clonality
- Assay is relatively easy to optimize and interpret in high-level expressing lymphomas (as myeoloma)
- Assay is challenging in low-level expressing lymphomas, where sensitive protocols must be optimized. Interpretation is difficult due to serum immunoglobulins



DLBCL: kappa

DLBCL: lambda

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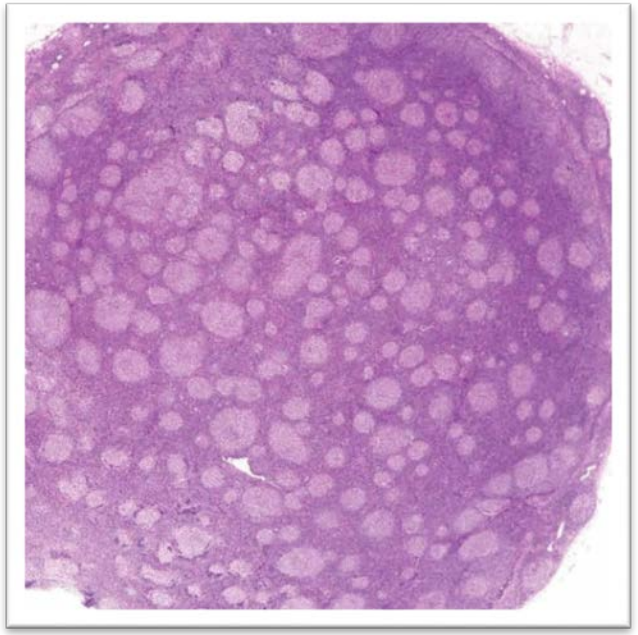
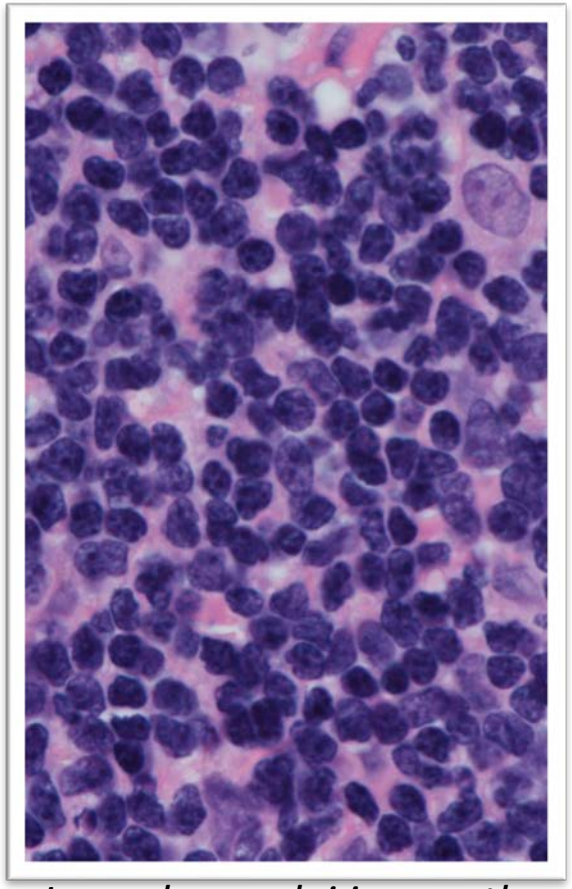
How are lymphomas diagnosed

- Morphology
  - Cell size
  - Cell types (uniform or different)
  - Mitosis
- Architecture
  - Normal architecture?
  - Growth through capsule?
  - Sclerosis?
- Immunophenotype
  - IHC
  - Flow cytometry
- Material
  - Biopsy (excision of lymph node preferred)
  - No fine needle aspiration



Abnormal architecture in follicular lymphoma



Irregular nuclei in mantle cell lymphoma

Basic IHC stains for lymphoma diagnosis

Marker	
CD45	
CD20	
CD79a	
PAX5	
Kappa/lambda	
CD3	
CD5	
CD30	
Bcl-2	
Bcl-6	
CD23	
Cyclin D1	
Ki67	

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What CD numbers?

- CD = ”Cluster of differentiation” or ”Cluster of designation”
- Classification system for antigens
- Antigens are located on cell surfaces (but also in other compartments) on leucocytes (but also other cell types)
- More than 370 CD antigens has been identified
- The antigens can function as receptors or ligands important to cell signaling or adhesion. However, in many cases function is unknown.
- Important in haematopathology for immunophenotyping of morphologically similar cells

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Cluster of differentiation

Cell type	CD Markers
stem cells	CD34+, CD31-, CD117
all leukocyte groups	CD45+
Granulocyte	CD45+, CD11b, CD15+, CD24+, CD114+, CD182+
Monocyte	CD45+, CD14+, CD114+, CD11a, CD11b, CD91+, CD16+
T lymphocyte	CD45+, CD3+
T helper cell	CD45+, CD3+, CD4+
T regulatory cell	CD4, CD25, and Foxp3
Cytotoxic T cell	CD45+, CD3+, CD8+
B lymphocyte	CD45+, CD19+ or CD45+, CD20+, CD24+, CD38, CD22
Thrombocyte	CD45+, CD61+
Natural killer cell	CD16+, CD56+, CD3-, CD31, CD30, CD38

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Primary panel

Primary panel for the unknown primary tumour

"Real"	CD45	CK	S-100	VIM
Haemato-lymphoid neoplasms	+/(-)	-/(+)	-/(+)	+/(-)
Epithelial neoplasms	-	+/(-)	-/+	-/+
Mesothelial neoplasms	-	+	-	+
Mesenchymal and neuronal neoplasms	-	-/(+)	-/+	+
Non-neuronal neuroepithelial neoplasms	-	-/(+)	+	+
Germ cell neoplasms	-	-/+	-/+	+

Courtesy of M. Vyberg

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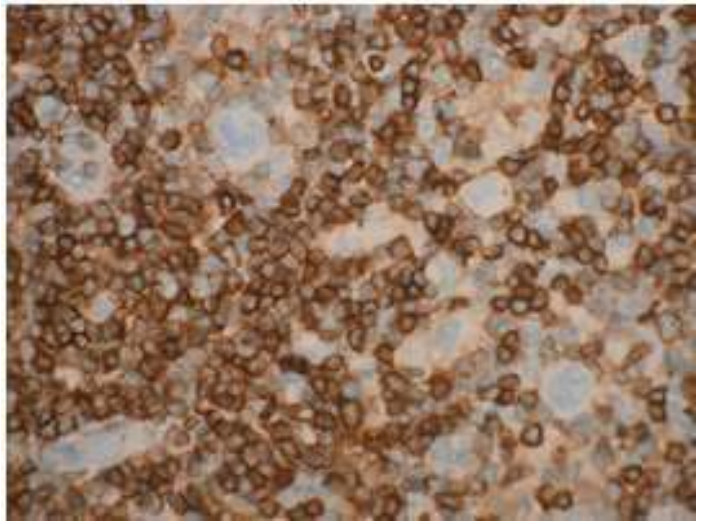
Basic IHC stains: CD45

- Membrane bound tyrosine phosphatase regulating B- and T-cell antigen receptor signaling
- Positive in most haematopoitic cells
- Several isoforms exist (more lineage specific)
- Not expressed on non-bone marrow derived cells
- Lymphomas
  - Most non-HL are positive
  - Can be negative in Precursor LB, plasma cell neoplasia and ALCL
  - HL: Reed Sternberg cells in classical HL are negative



HL: CD45- in Reed Sternberg
Courtesy of S. Hamilton

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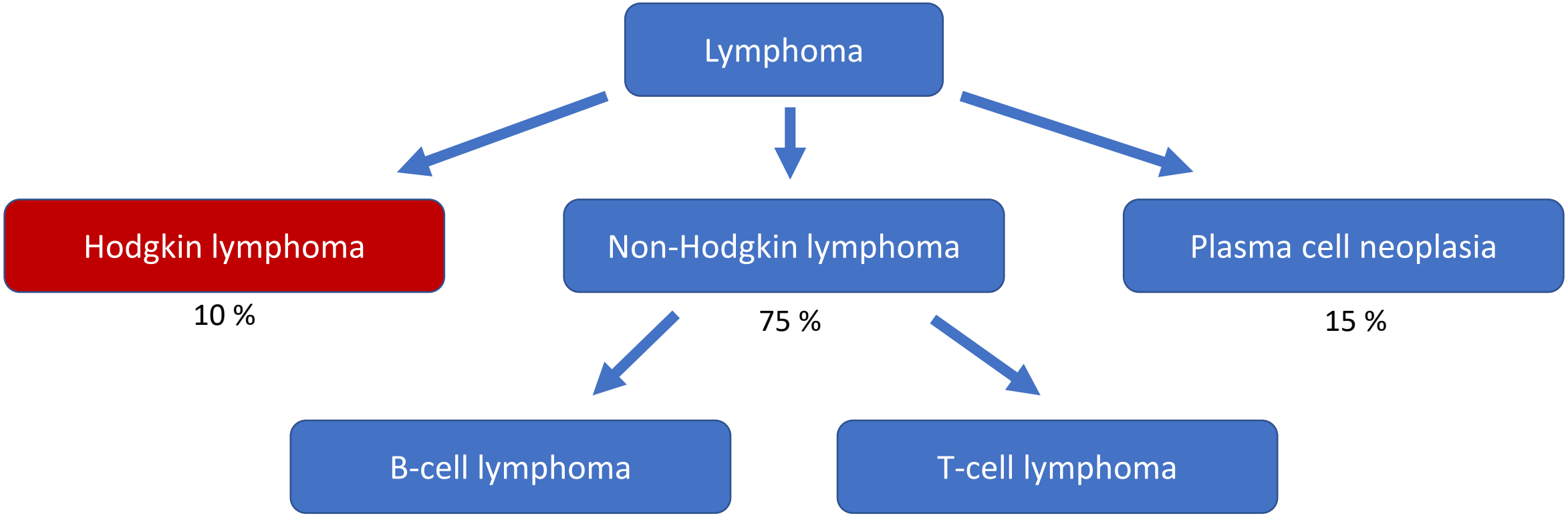
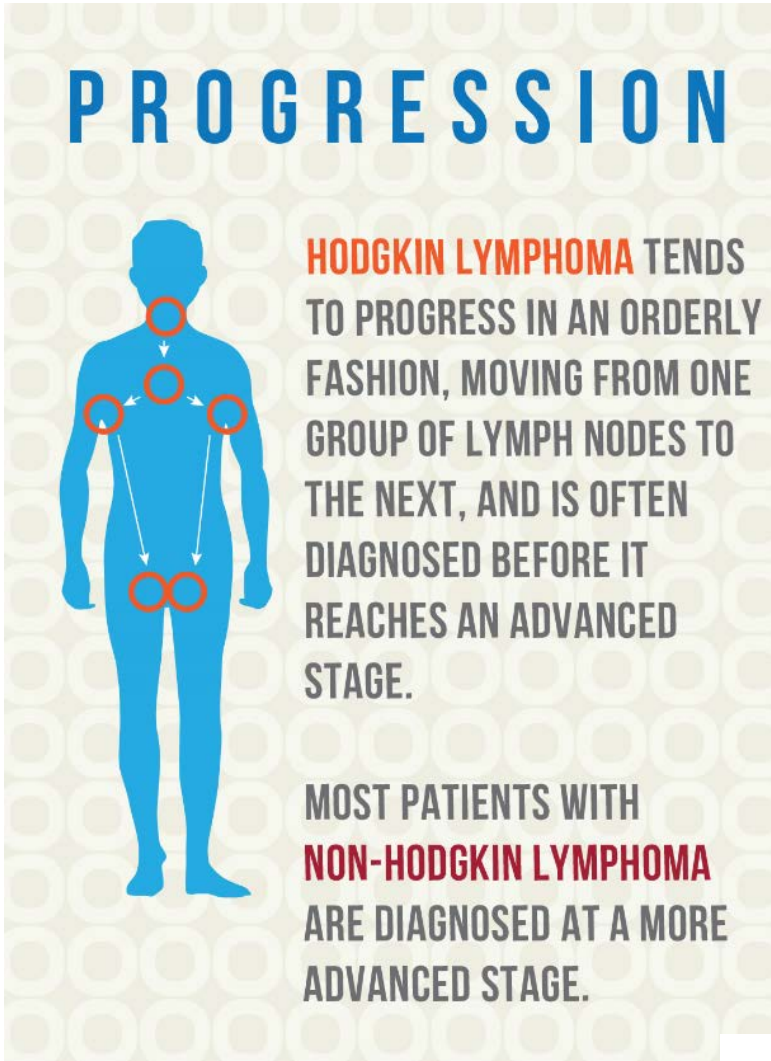
Classification of lymphomas



Hodgkin versus non-Hodgkin lymphoma

- Generally both types of lymphoma are developed from lymphocytes
- Age of onset is different
- HL tend to develop on neck or chest, while non-HL can arise throughout the body
- Non-HL tend to be diagnosed at at a more advanced stage than HL
- HL have better survival (5-year: 90%) than non-HL (overall)



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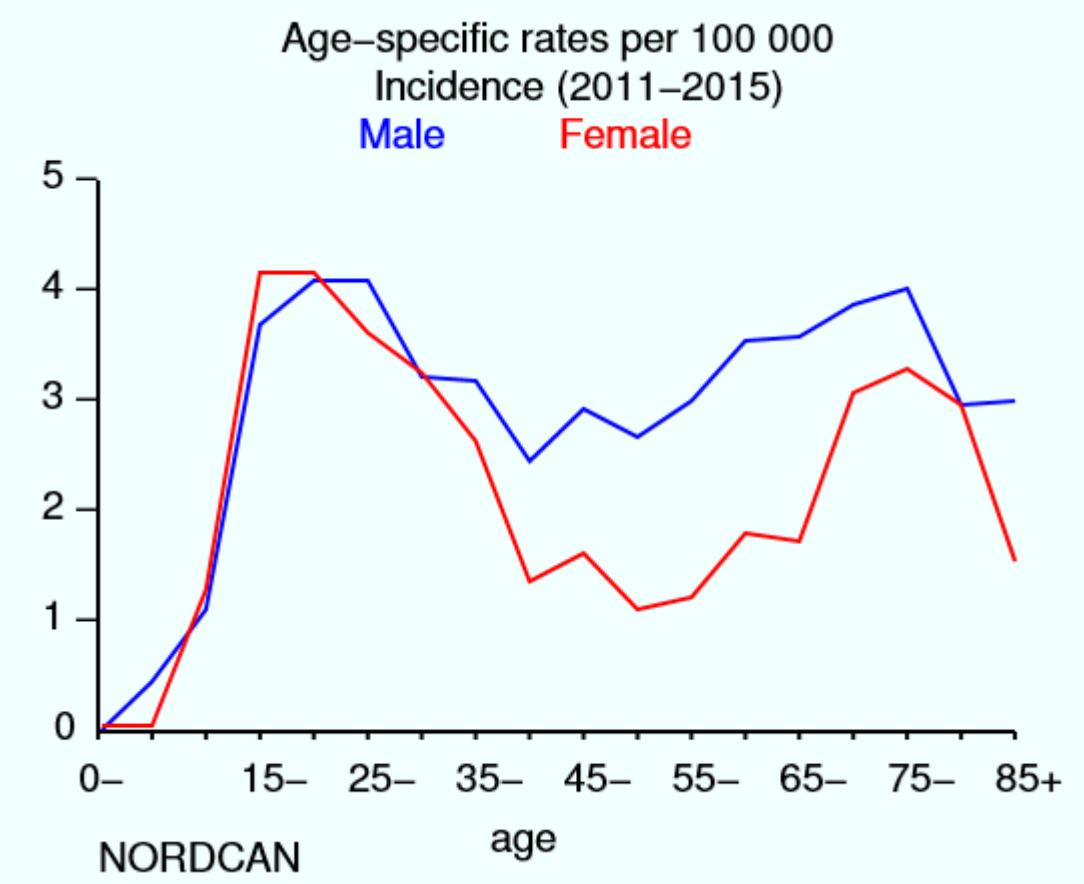
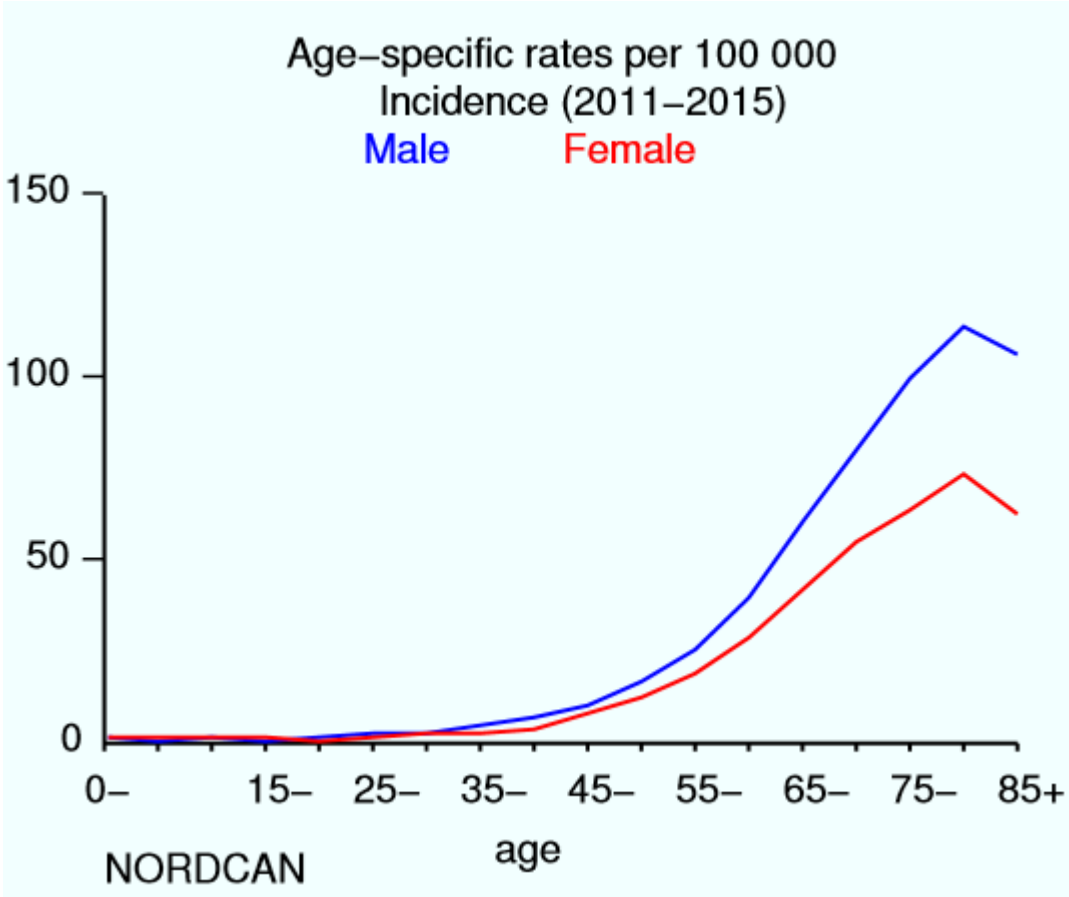
Hodgkin vs. non-Hodgkin lymphoma (age)

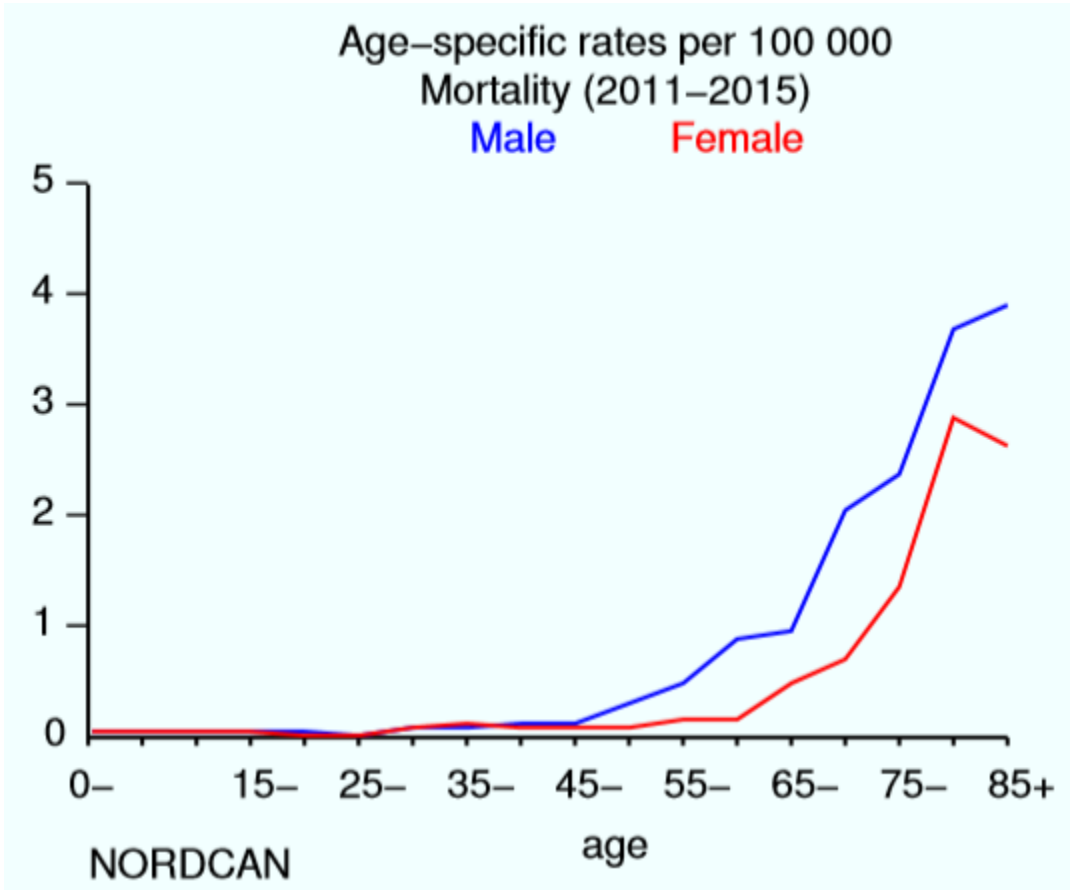


Hodgkin lymphoma

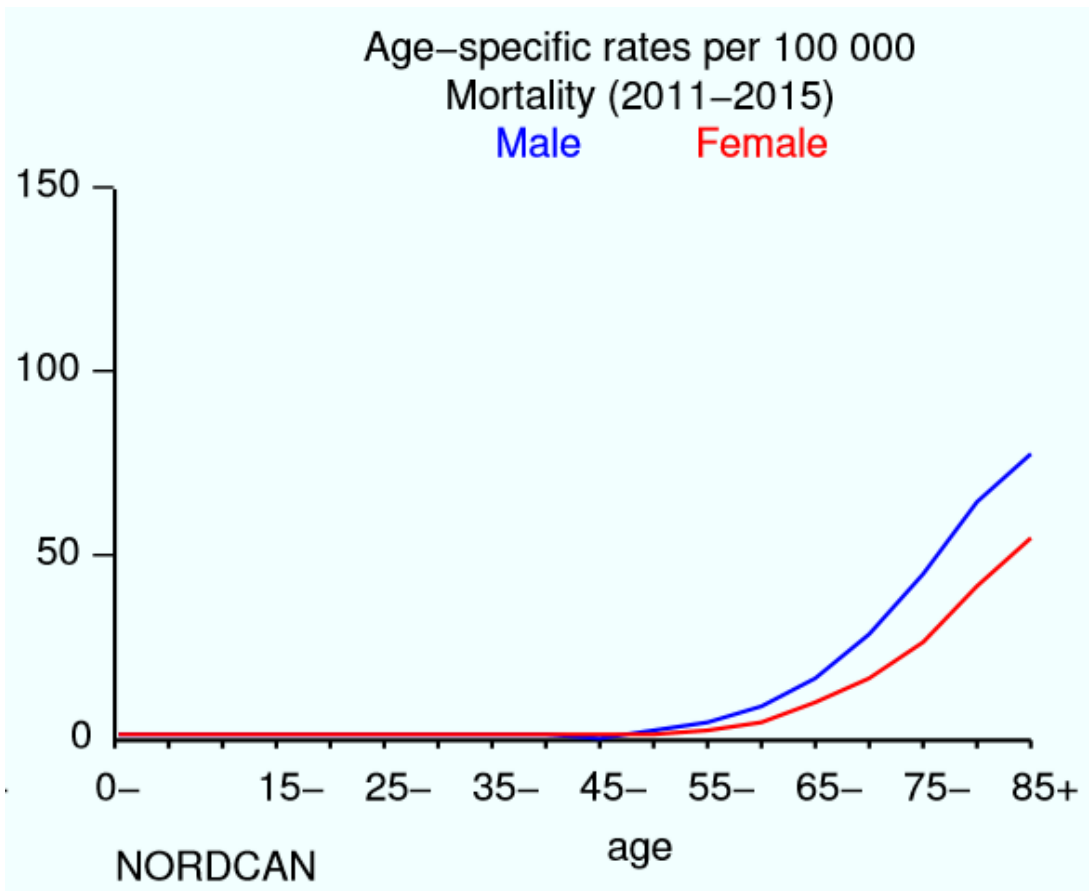


Non-Hodgkin lymphoma

Hodgkin vs. non-Hodgkin lymphoma (mortality)



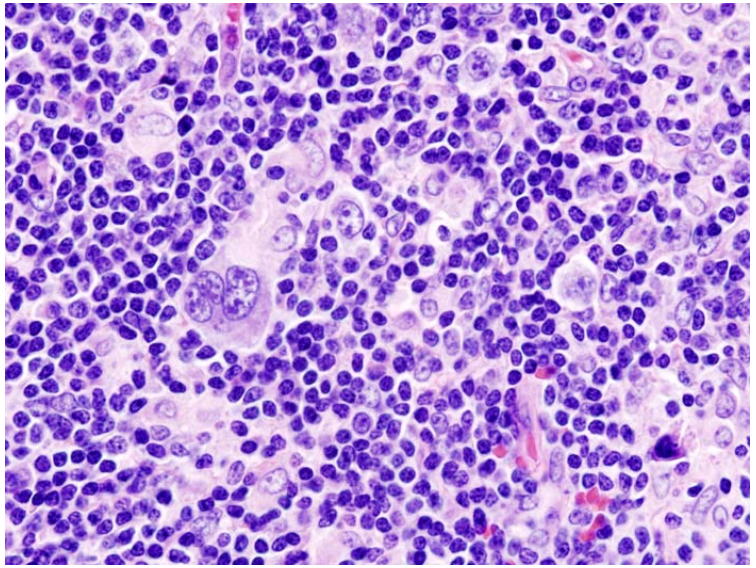
Hodgkin lymphoma



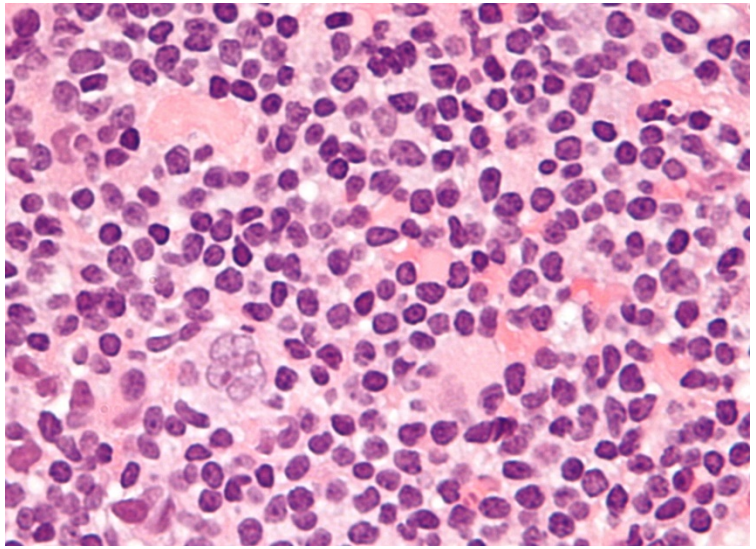
Non-Hodgkin lymphoma

Hodgkin lymphoma (HL)

- Reed-Sternberg cells: large multinucleated cells with abundant cytoplasm
- Mononuclear RS = Hodgkin cells
- Eosinophils
- Divided in
  - Classical HL
    - Nodular sclerosis CHL
    - Lymphocyte rich CHL
    - Mixed cellularity CHL
    - Lymphocyte depleted CHL
  - Nodular lymphocyte predominant HL
    - Popcorn cells



Reed-Sternberg and Hodgkin cells in classical HL



Popcorn cells in NLPHL

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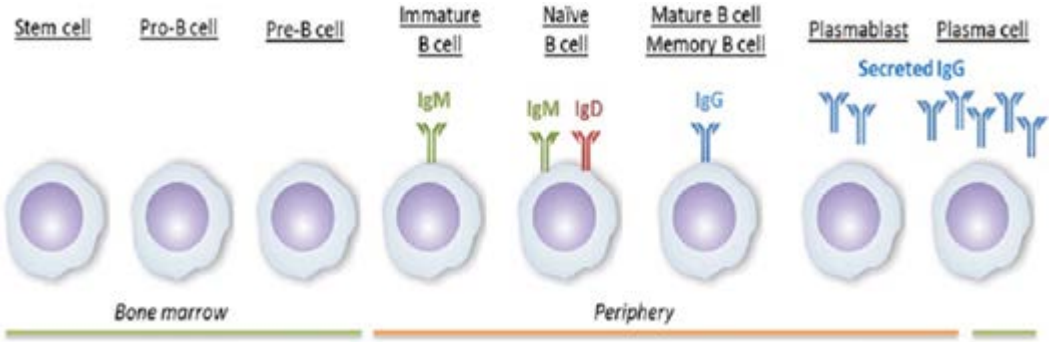
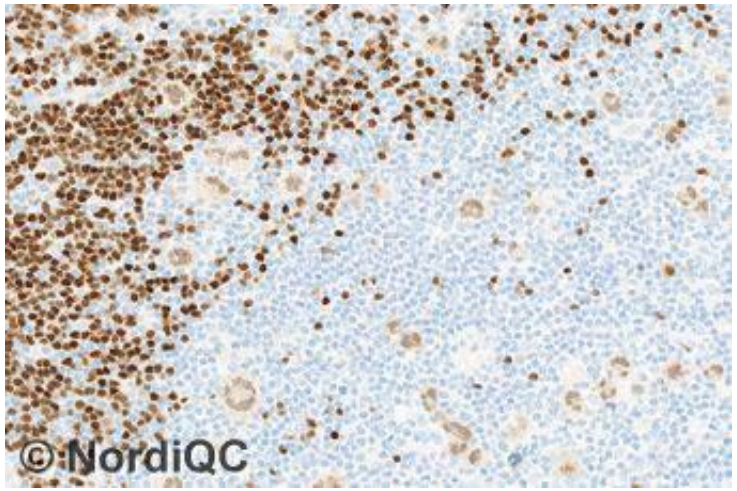
Basic IHC stains: PAX5 / BSAP

- Transcription factor involved in B-cell development
- Nuclear staining reaction
- Specific B-cell marker
- Positive in nearly all B-cell non-HL and HL (RS-cells)
- Negative in plasma cell neoplasms, T-cell lymphomas



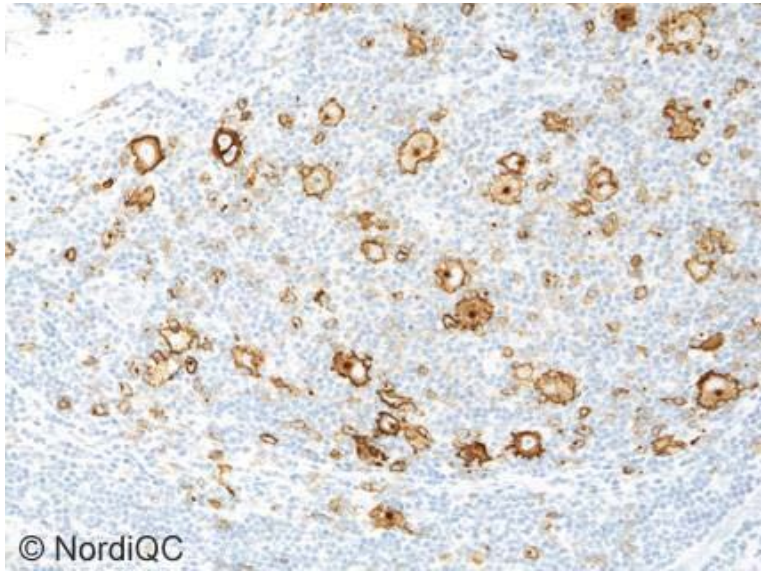
PAX5



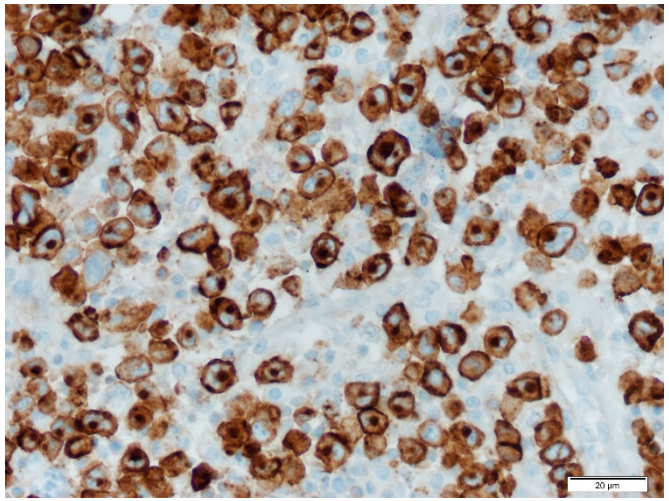
Weak PAX5 staining reaction of Hodgkin and Reed Sternberg cells. Strong staining of B lymphocytes.

Basic IHC stains: CD30

- Tumor necrosis factor (cytokin) receptor. Regulator of cell apoptosis
- Expressed in activated cells
- Expressed on activated B- and T-cells, macrophages and immunoblasts and in some macrophages
- Membranous staining with a dot in Golgi-zone
- Target for brentuximab
- <u>Positive</u>
  - Hodgkin (Reed Sternberg and Hodgkin cells), minor proportion of Pop corn cells in HL-LP)
  - Anaplastic large cell lymphoma
  - Some T-cell lymphomas
  - Some DLBCL

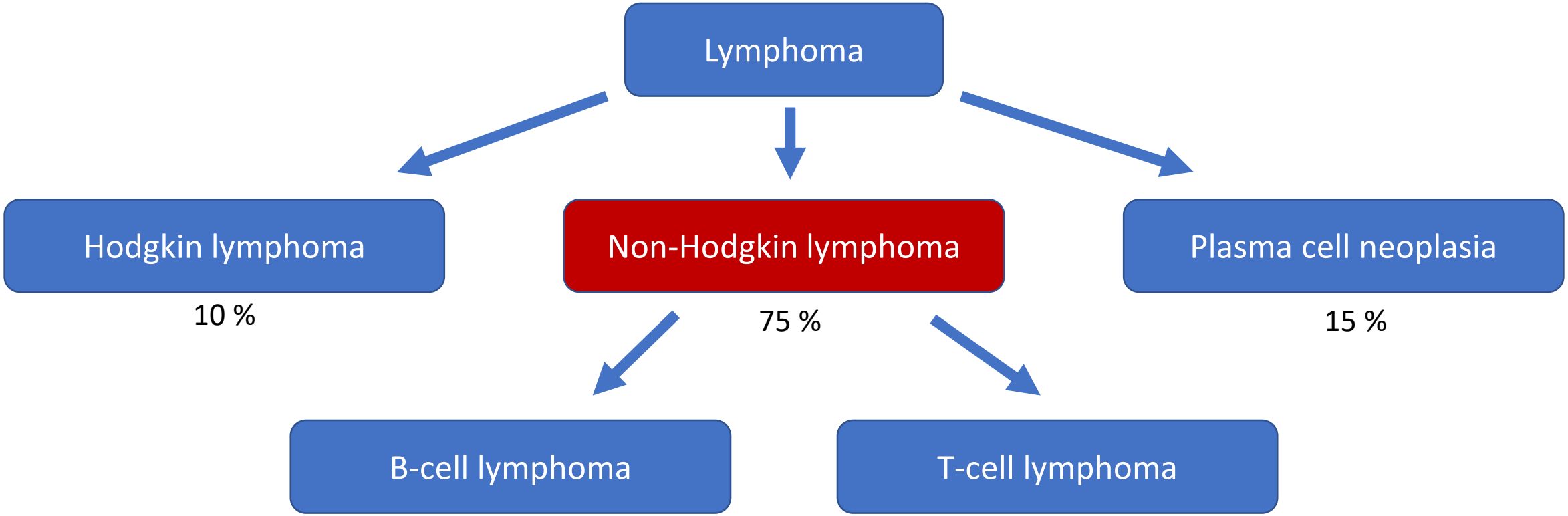


CD30 staining in lymph node with HL. Reed-Sterberg and Hodgkin cells display moderate membranous and Golgi-zone staining



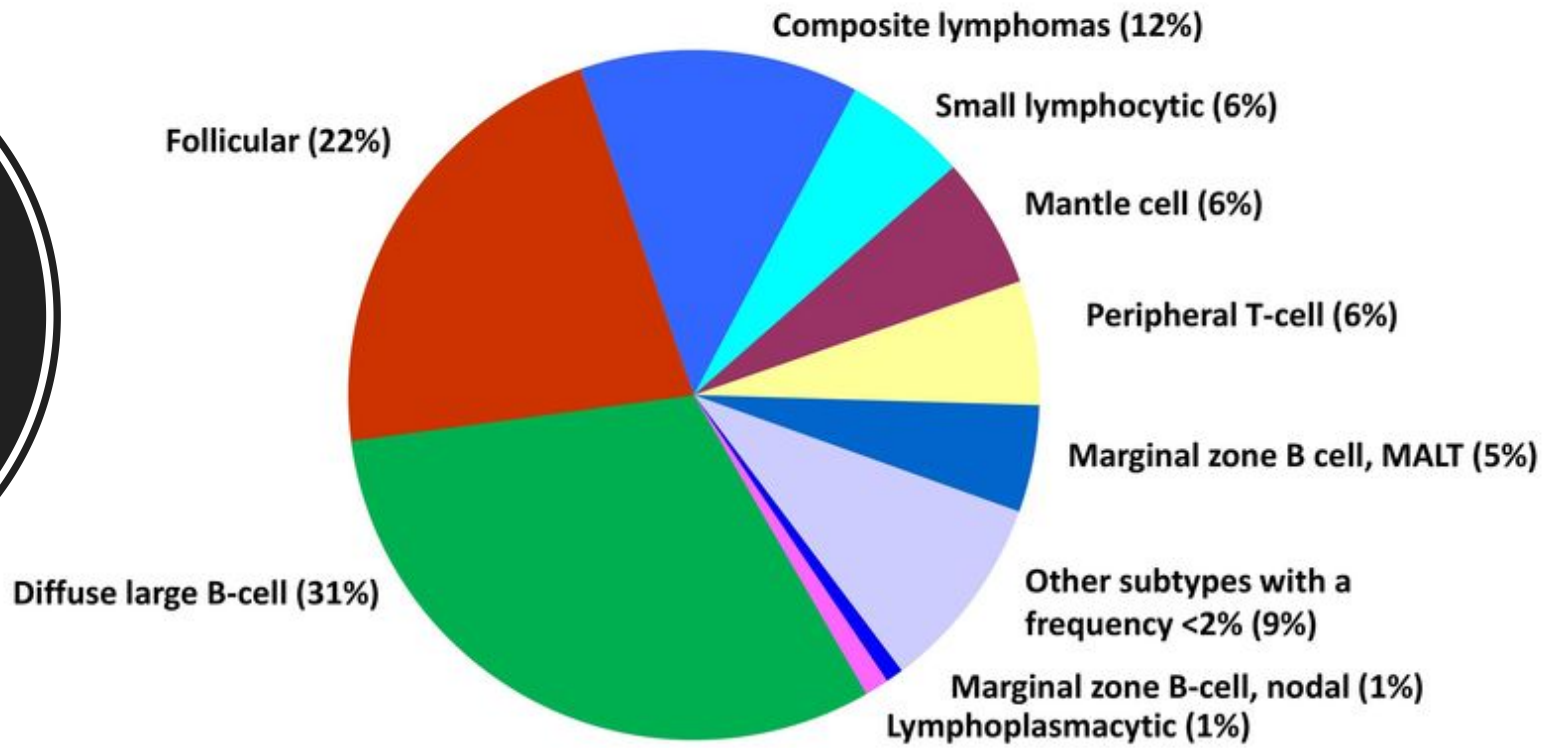
CD30 staining in lymph node with ALCL. Neoplastic cell all display moderate to strong membranous and Golgi-zone staining

Classification of lymphomas



Frequency of Non-Hodgkin lymphomas

Frequency of NHL subtypes in adults

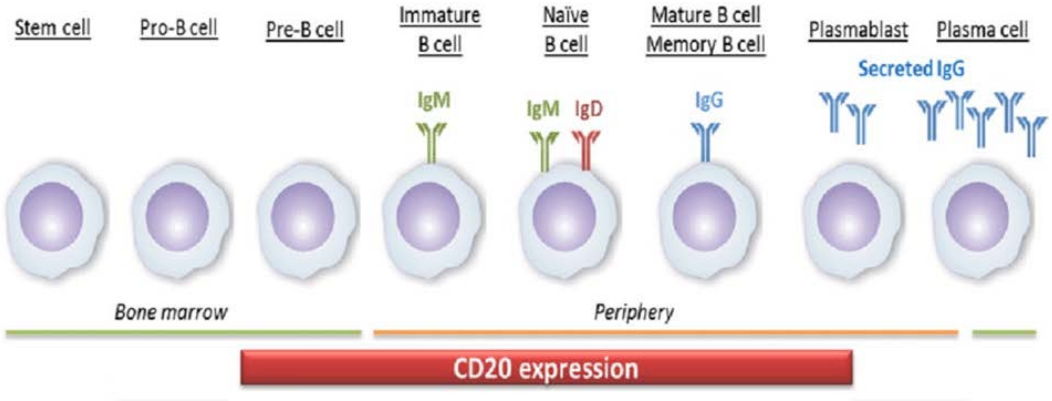


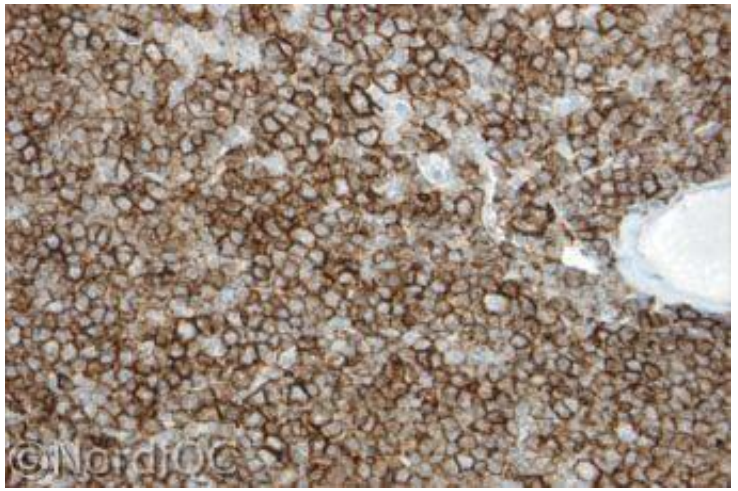
MALT: mucosa associated lymphoid tissue; NHL: non-Hodgkin lymphoma
Armitage JO, Weisenburger DD. *J Clin Oncol* 1998; **16**: 2780–2795.

NordiQC

Basic IHC stains: CD20

- Surface protein involved into differentiation of B-cells to plasma cells
- Common B-cell marker
- Expressed from Pro-B cells untill maturity
- Target for treatment (i.e. rituximab)
- Positive in the majority of B-cell neoplasms (except precursor B-LB and myeloma)
- Negative in T-cell lymphomas



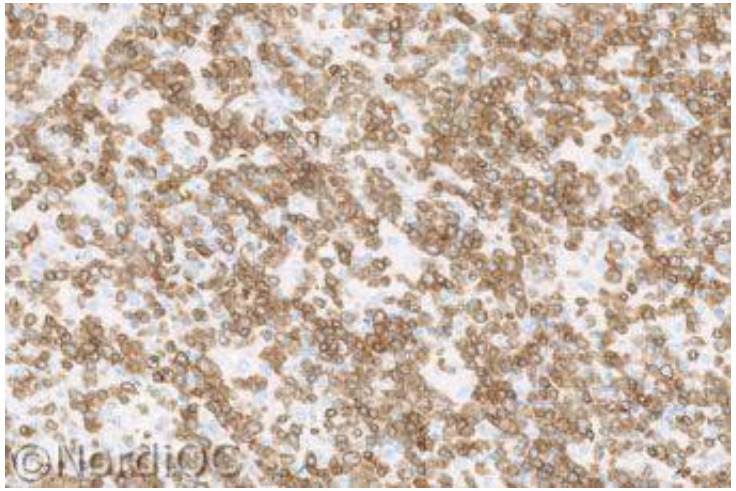


B-CLL/SLL: Strong membranous CD20 staining reaction

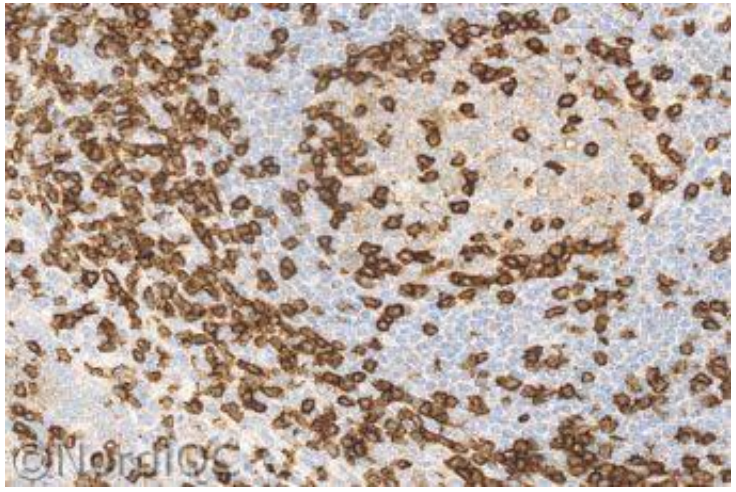
NordiQC

Basic IHC stains: CD3

- Part of the T-celle (co)receptor consisting of several subunits. Transmits signals through the cell membrane.
- Expressed on T-lymphocytes (CD4 and CD8)
- Positive
  - T-cell lymphomas
- Negative
  - B-cell lymphomas
  - Hodgkin lymphoma



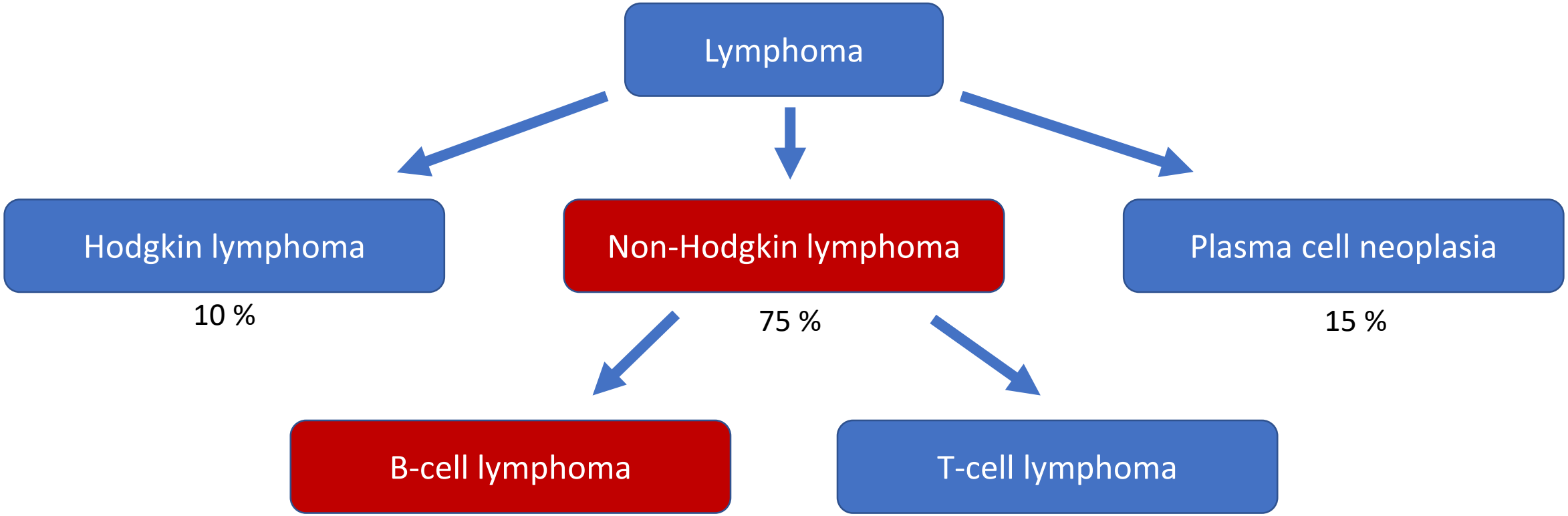
CD3 staining in peripheral T-cell lymphomas. All neoplastic cells display a moderate to strong membranous staining



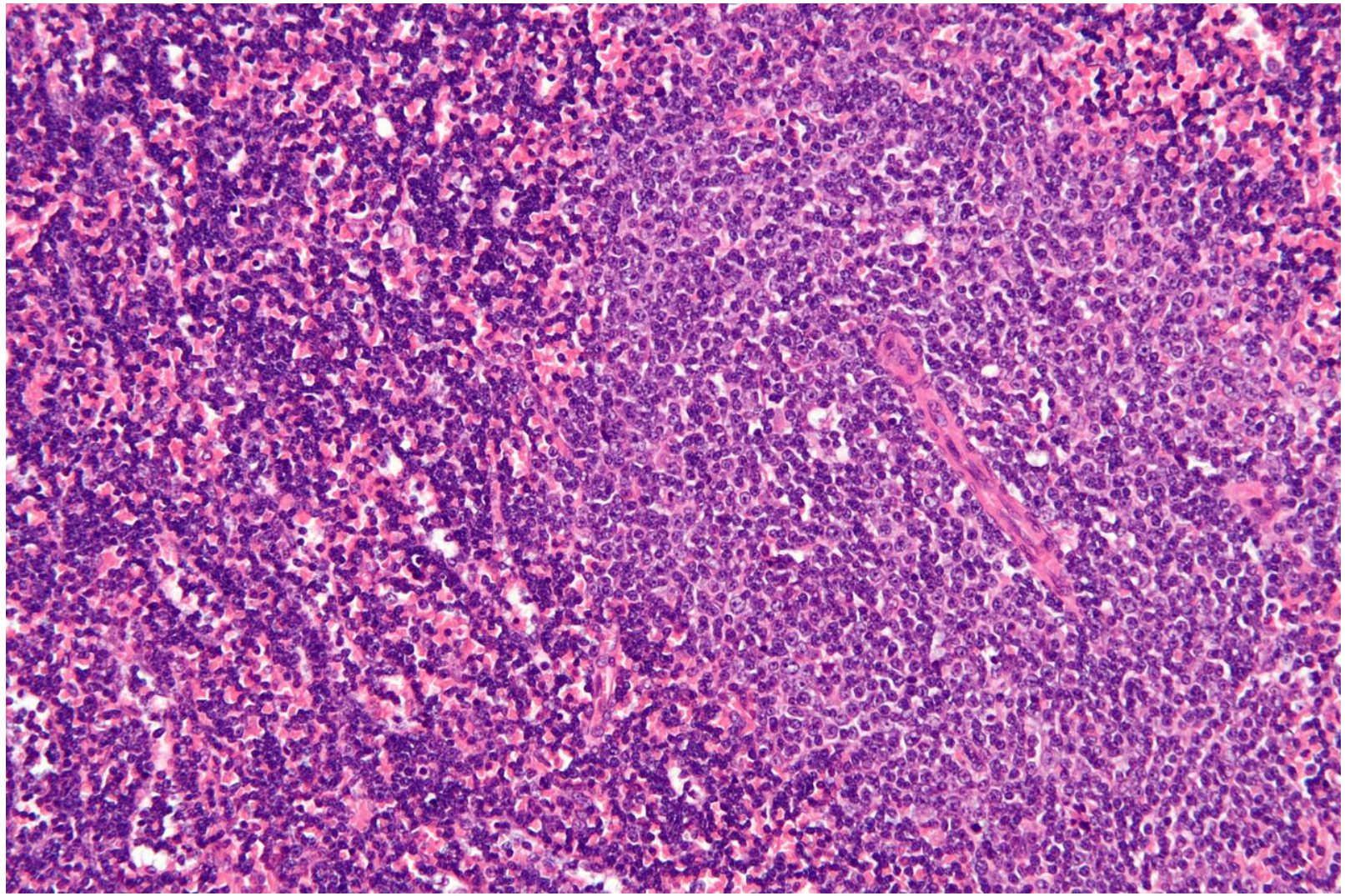
CD3 staining in tonsil, strong membranous staining in T cells

NordiQC

Classification of lymphomas



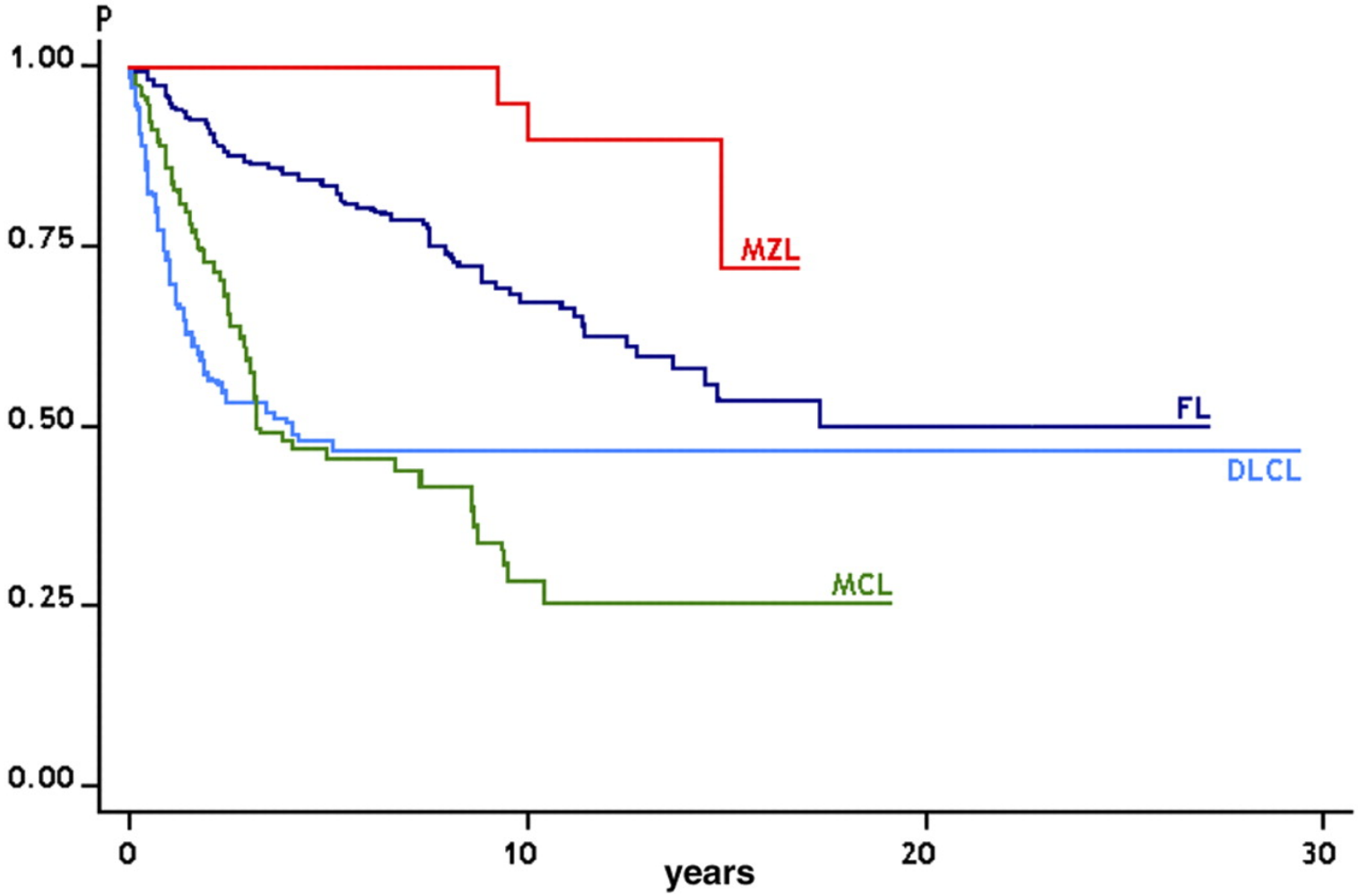
Small B-cell lymphomas



Survival B-cell lymphomas

Michele Ghielmini and Emanuele Zucca

Blood 2009 114:1469-1476; doi: https://doi.org/10.1182/blood-2009-02-179739



Cause-specific survival of the main B-cell lymphoma subtypes in the series of the Oncology Institute of Southern Switzerland, 1980-2006.

NordiQC

IHC: Small B-cell lymphomas

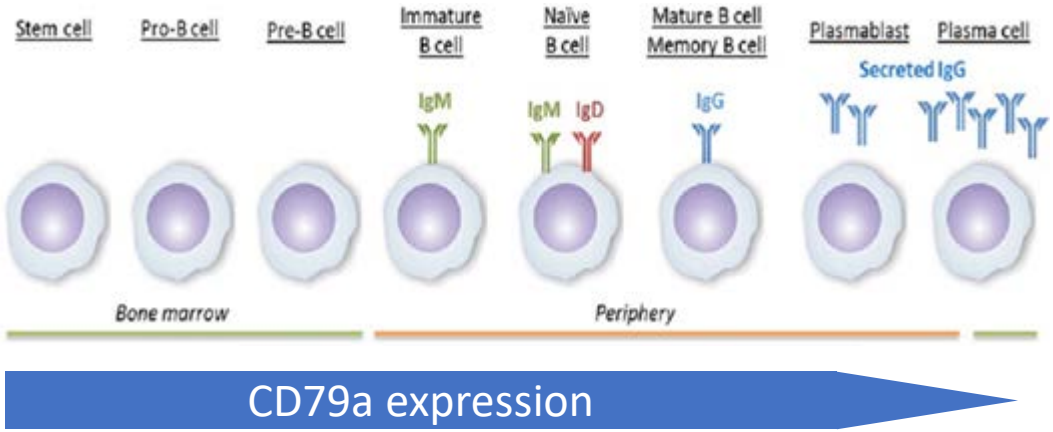
Immunophenotype: Small B-Cell Lymphomas

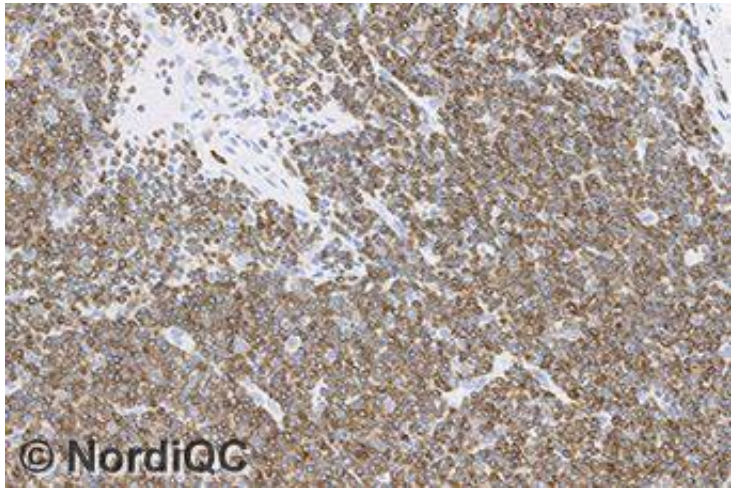
	CD20	CD79A	CD10	CD23	CD5	CD43	bcl-2	CyclinD1	TdT
CLL	+	+	-	+	+	+	+	-	-
FL	+	+	+	-	-	-	+	-	-
MCL	+	+	-	-	+	+	+	+	-
LPL	+	+	-	-	-	-/+	+	-	-
MZL	+	+	-	-	-	-/+	+	-	-
SMZ	+	+	-	-	-	-/+	+	-	-
MALT	+	+	-	-	-	-/+	+	-	-
HCL	+	+	-	-	-	-	+	-	-
BLB	-/+	+	+/-	+/-	-	-	+	-	+

NordiQC

Basic IHC stains: CD79a

- Transmembrane protein involved in signal transduction following antigen recognition. Forms heterodimer complex with CD79b
- Specific and sensitive marker expressed in all steps of B-cell maturation
- Positive in most B-cell lymphomas, myeoloma (50%), HRS (20%)
- Negative in T-cell lymphomas

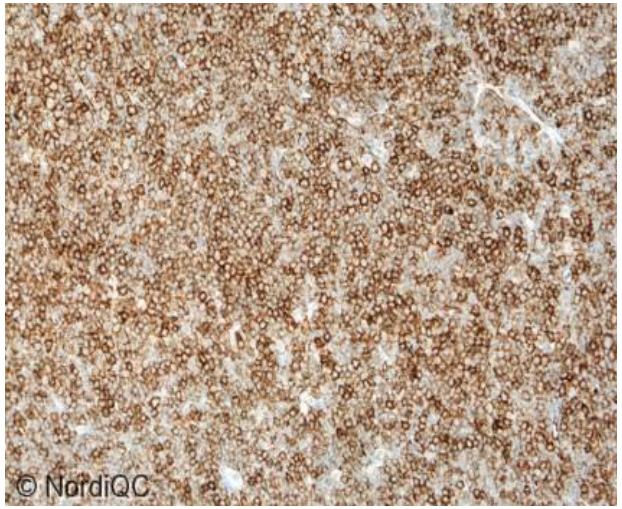




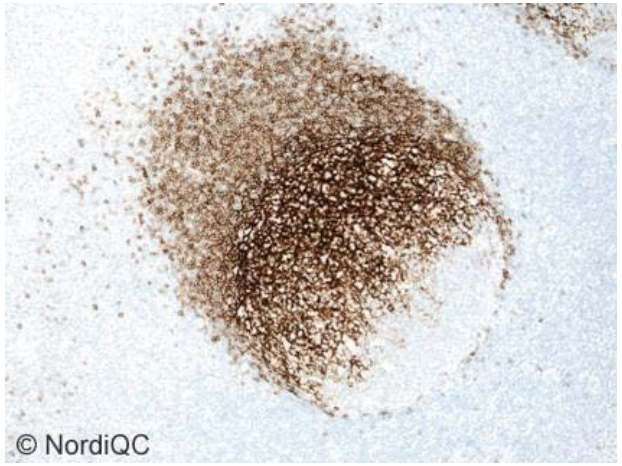
B-CLL/SLL: Moderate membrane CD79a staining reaction

Basic IHC stains: CD23

- Low affinity receptor for IgE and via this involved in allergic response and defence against parasites
- In normal cells, expressed in eosinophils, mature B-cells (mantle and marginal zone), activated macrophages and platelets
- Can be used as a marker of follicular dentric cells (CD21 alt.)
- <u>Positive</u>
  - B-SLL/CLL
- <u>Negative</u>
  - Mantle cell lymphomas
  - T-lymphomas



CD23 staining reaction of B-CLL, all neoplastic cells display a strong membranous staining

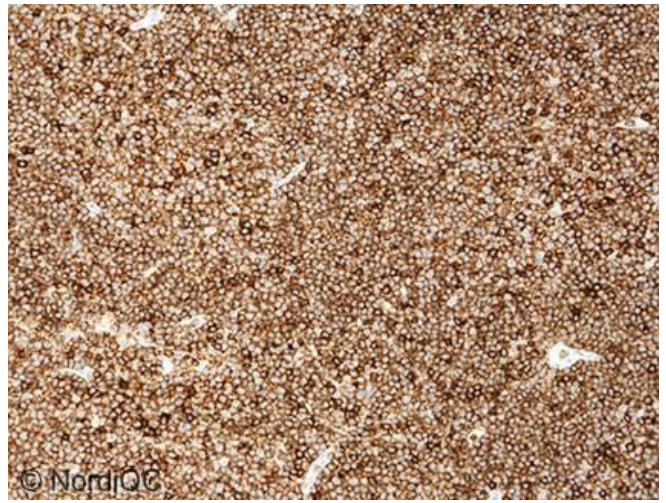


CD23 staining reaction in tonsil, moderate staining of B-cells in mantle zone, strong staining of dendritic cells

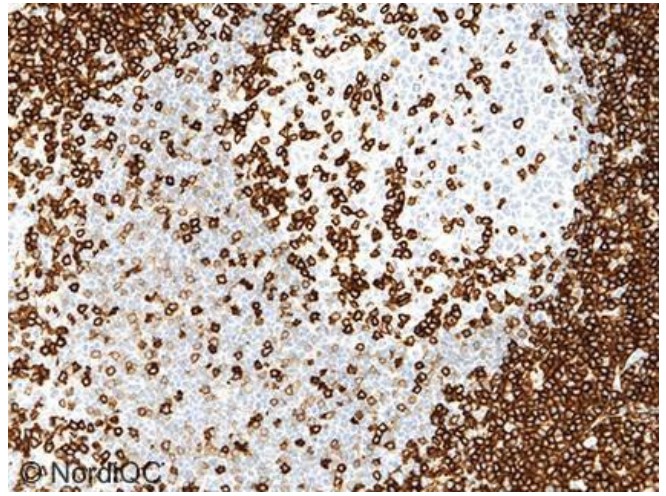
NordiQC

Basic IHC stains: CD5

- Unknown function, may be involved in signal mediation of proliferation and apoptosis
- Relative specific T-cell marker, although a subset of B-lymphocytes may express CD5
- <u>Positive</u>
  - Most T-cell lymphomas
  - Some non-HL B-cell lymphomas
    - B-CLL
    - Mantle cell
    - DLBCL (minority)
- <u>Negative</u>
  - Most other non-HL B-cell lymphomas
  - Hodgkin lymphoma



Strong membranous staining for CD5 in all neoplastic cells of B-CLL

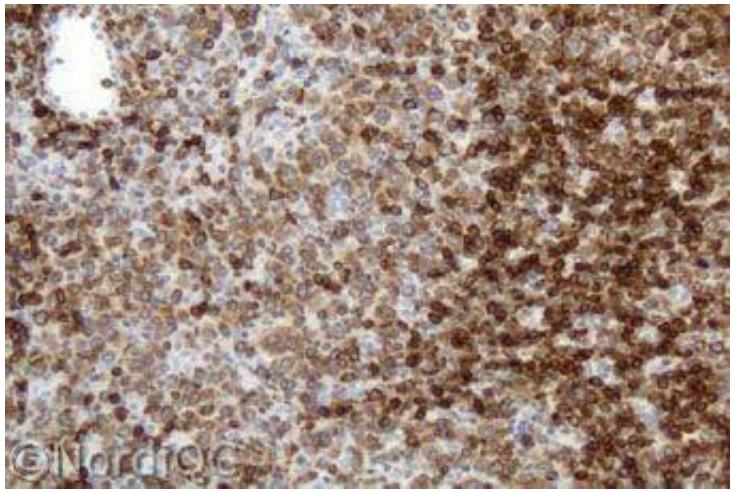


Staining pattern in tonsil

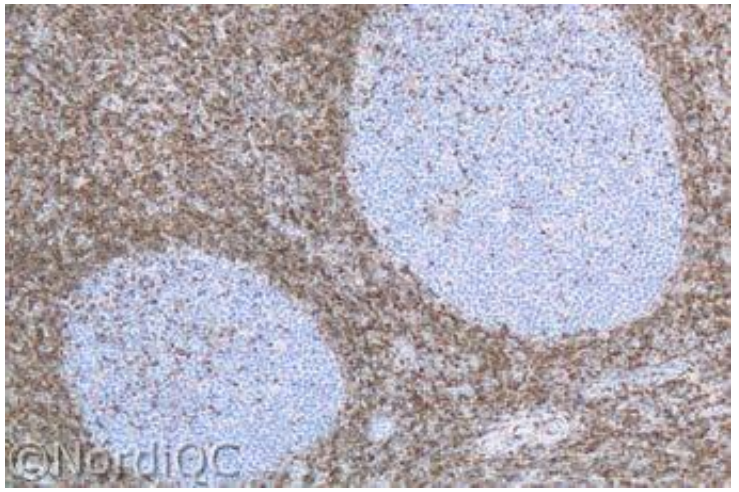
NordiQC

Basic IHC stains: Bcl-2

- Protein that regulate cell cycle by inhibiting apoptosis
- Cytoplasmic and nuclear staining reaction
- Expressed in mature T- and B-cells, but negative in germinal centers
- Associated with t(14;18)
- Positive
  - Most B- and T-non-HL
  - Distinguish reactive (-) versus neoplastic germinal centers (+)
- Negative
  - Burkitt lymphoma



Bcl-2 staining in lymph node with follicular lymphoma, where neoplastic cells show moderate staining reaction

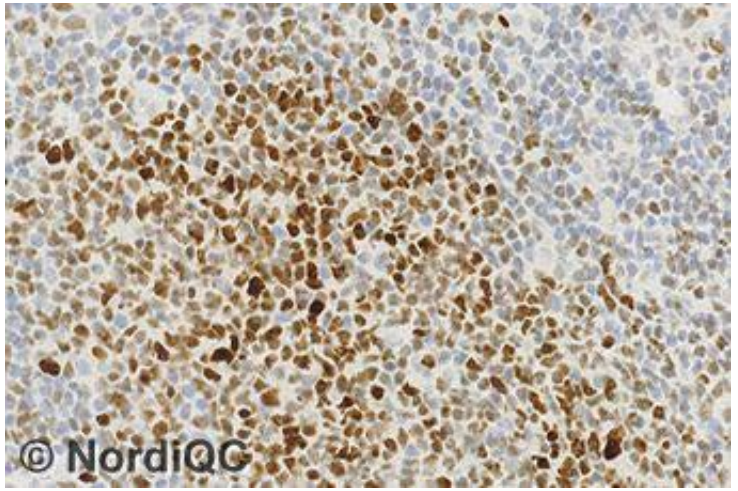


Bcl-2 staining in lymph node. Germinal center cells are negative

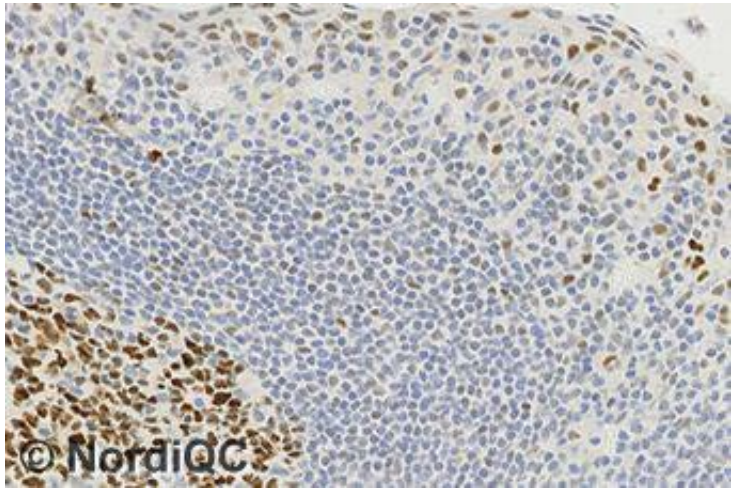
NordiQC

Basic IHC stains: Bcl-6

- Transcription factor involved in regulation of germinal centers
- Nuclear staining
- Positive in normal germinal center cells
- Positive
  - Follicular lymphomas
  - Burkitt lymphoma
  - DLBCL
- Negative
  - Mantle cell lymphoma



Bcl-6 staining in lymph node with follicular lymphoma, where neoplastic cells show moderate nuclear staining reaction

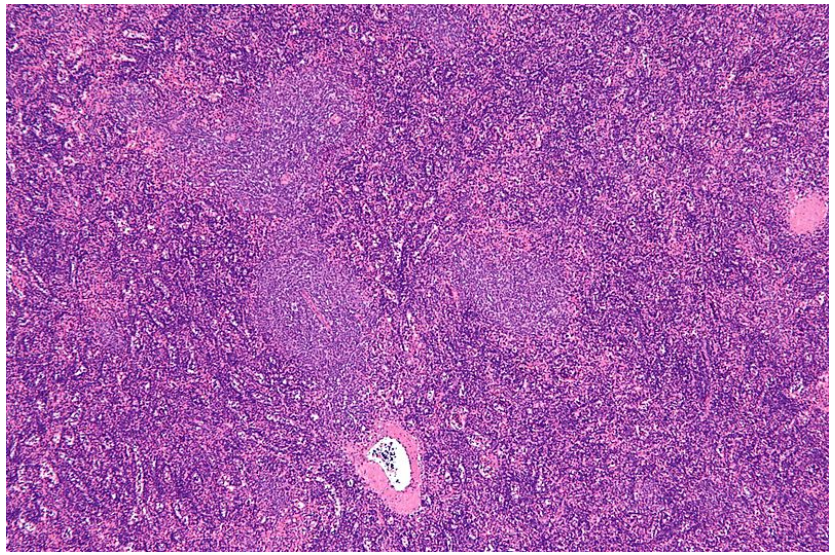


Bcl-6 staining in lymph node. Germinal center cells are positive, while mantle zone is negative

NordiQC

Chronic lymphocytic leukemia (B-CLL) / Small-cell lymphocytic lymphoma (B-SLL)

- B-cell derived neoplasia
- Presentation: If present in blood (alone >$5*10^9$ in 3 months), BM and spleen = B-CLL. If <$5*10^9$, but lymph node involvement = B-SLL
- Morphology: small lymfocytes, small amount of cytoplasm, dense chromatin
- Symptoms: very few
- Good prognosis, but no cure. May transform to DLBCL (Richer transformation).

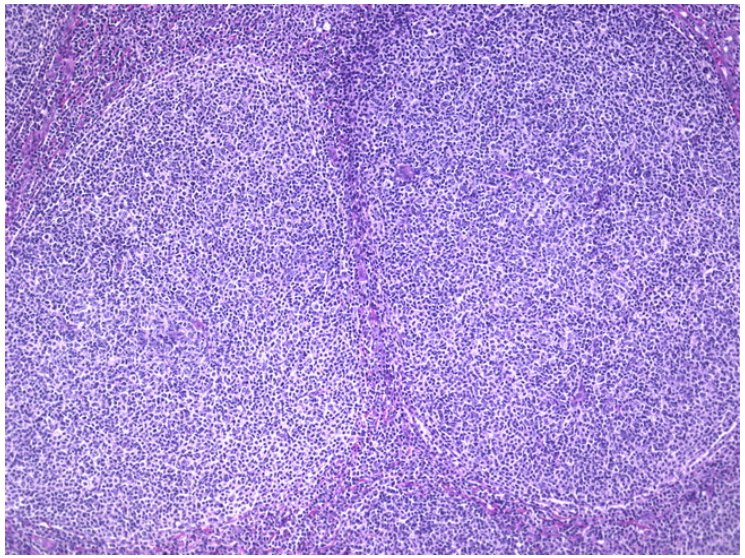


IHC	
CD19, CD20, CD79a	+
Bcl-2	+
CD5	+
CD10	-
Ki67	low

NordiQC

Follicular lymphoma

- B-cell lymphoma
- Morphology: similar to germ center cells (both centrocytes and centroblasts). Growth pattern with abnormal follicles
- Cytogenetics: 90% with translocation t(14;18), (q32;q21), which creates overexpression of Bcl-2.
- Peak presentation at 60 years.
- Prognosis: 5 year between 90% and 50% depending on stage

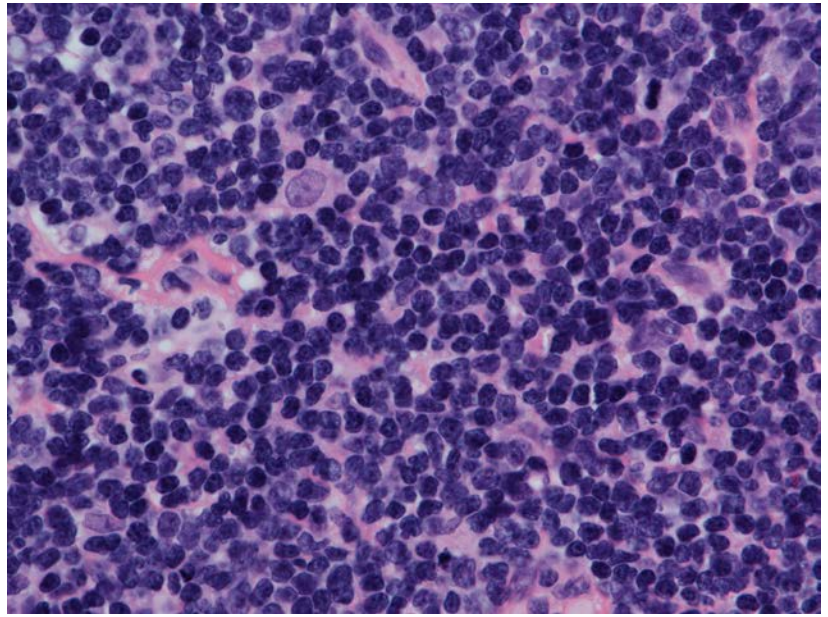


IHC	
CD19, CD20, CD79a	+
Bcl-2	+
CD10	+/-
Bcl-6	+
CD5	-
Ki67	low

NordiQC

Mantle cell lymphoma

- B-cell neoplasia, monomorphe cells with irregular nuclei.
- IHC: CD15, CD20, Cyclin D1, SOX11
- Cytogenetics: translocation t(11,14) (q13;q32) induces Cyclin D1 ekspression that, in turn, stimulates cell proliferation
- Epidemiology: Rare
- Prognosis: 5 year: 50-70%

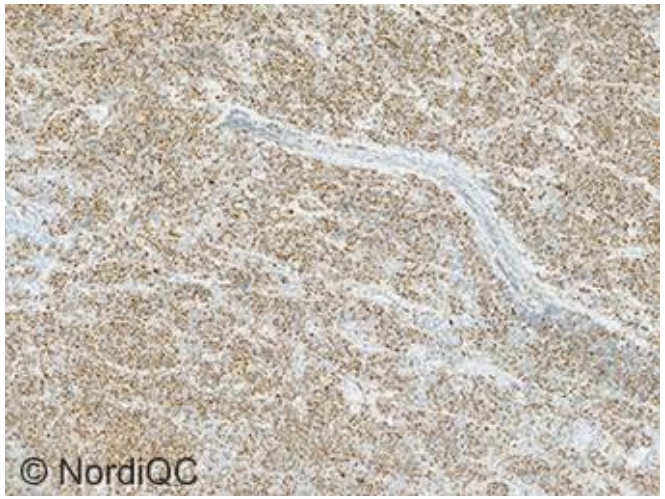


IHC	
CD19, CD20, CD79a	+
CD5	+
CD23	-
CD10	-
Cyclin D1, SOX11	+

NordiQC

Basic IHC stains: Cyclin D1

- Part of the cyclin family – highly conserved protein family involved in cell mitosis. Expressed in G1 phase
- Nuclear staining reaction
- Normal expression in proliferating cells
- Upregulated in cells with translocation 11;14
- <u>Positive</u>
  - Mantle cell lymphomas (most)
  - Myeloma (minority)
- <u>Negative</u>
  - Other lymphomas



Cyclin D1 staining in mantle cell lymphoma, moderate nuclear staining in all neoplastic cells

NordiQC

SOX11 expression is highly specific for mantle cell lymphoma and identifies the cyclin D1-negative subtype

Ana Mozos,[1] Cristina Royo,[1] Elena Hartmann,[2] Daphne De Jong,[3] Cristina Baró,[4] Alexandra Valera,[1] Kai Fu,[5] Dennis D. Weisenburger,[5] Jan Delabie,[6] Shih-Sung Chuang,[7] Elaine S. Jaffe,[8] Carmen Ruiz-Marcellan,[9] Sandeep Dave,[10] Lisa Rimsza,[11] Rita Braziel,[12] Randy D. Gascoyne,[13] Francisco Solé,[4] Armando López-Guillermo,[1] Dolors Colomer,[1] Louis M. Staudt,[8] Andreas Rosenwald,[14] German Ott,[14] Pedro Jares,[1] and Elias Campo[1]

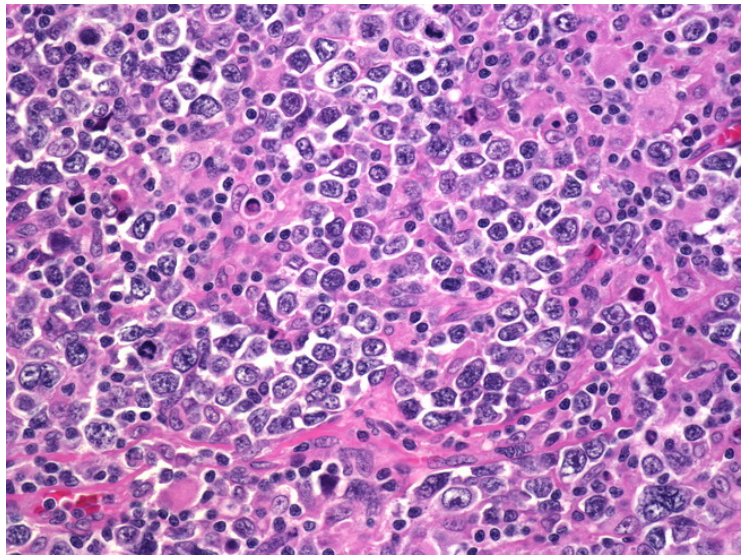
Conclusions
SOX11 mRNA and nuclear protein expression is a highly specific marker for both cyclin D1-positive and negative mantle cell lymphoma.

SOX11

NordiQC

Diffuse Large B-cell Lymphoma (DLBCL)

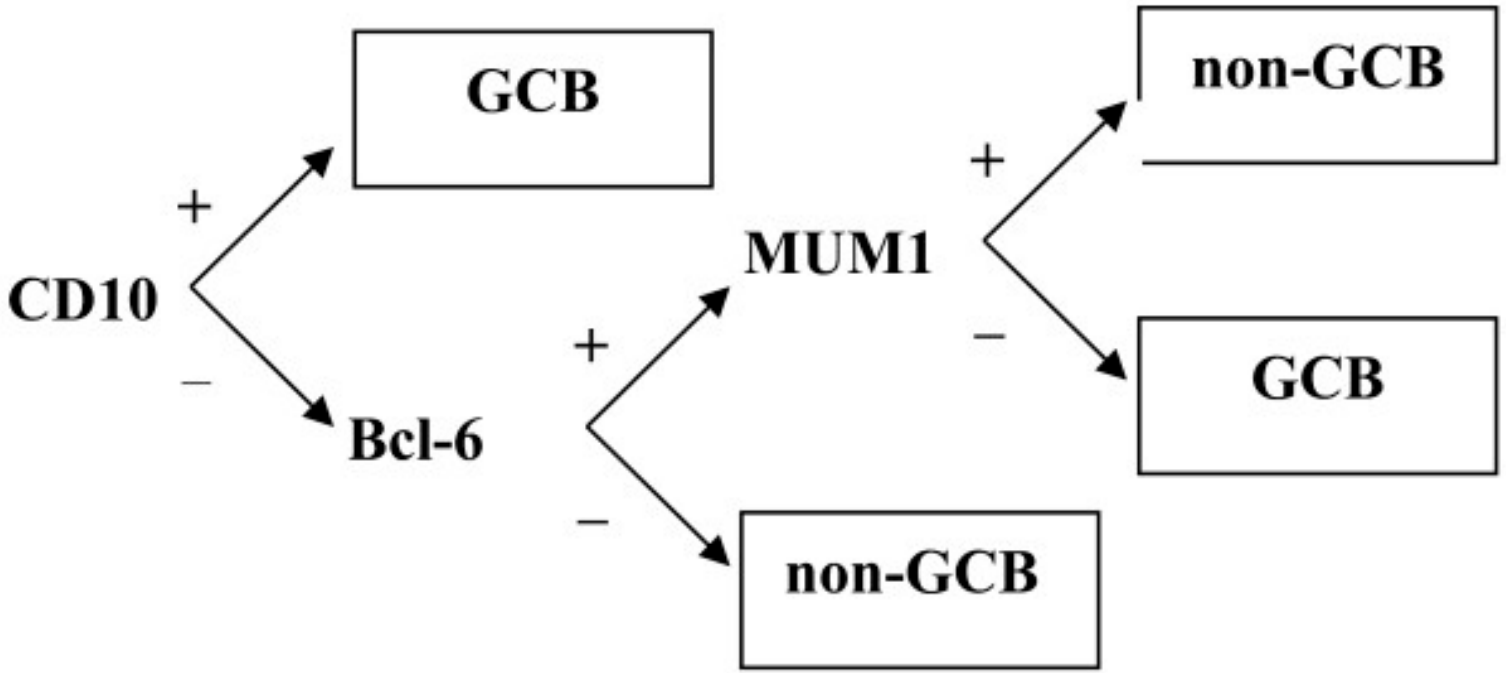
- Highly malign B-cell neoplasia. May be primary or transformation of other B-cell lymphomas
- Morphology: Large lymphoid cells with diffuse growth . Subtypes:
  - Centroblastic (marginalized nucleoli)
  - Immunoblastic (centra nucleoli)
  - Anaplastic (may resemble Hodgkin)
- Both nodal and extra nodal. 25% have involvement of BM
- Epidemiology: Elderly patients
- Prognosis: Dependent of stage



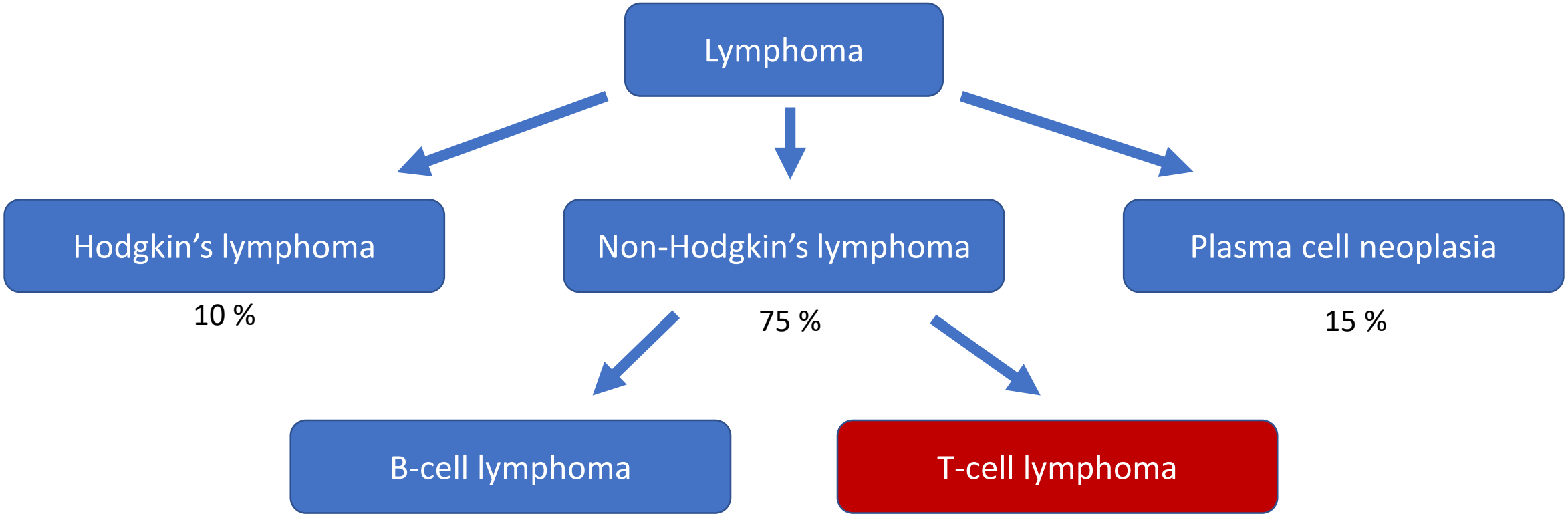
IHC	
CD19, CD20, CD79a	+
CD5	10%
CD10	40%
Bcl-6	80%

NordiQC

DLBCL – Hans' classification



Classification of lymphomas



Classification of T-cell lymphomas

TABLE 3: Immunophenotypic and histochemical markers of T-cell lymphomas/leukemias

Histology	CD3	CD5	CD7	CD4	CD8	CD30	NK16/56	Cytotoxic granules	TCR
T-PLL	+	–	+	+(–)	–(+)	–	–	–	α/β
T-LGL disease*	+	–	+	–	+	–	+/–	+	α/β >> γ/δ
Mycosis fungoides	+	+	+	+	–(+)	–(+)	–	–	α/β
Cutaneous ALCL	+	+(–)	+(–)	+(–)	(–)	++	–(+)/–(+)	+/–	α/β
Primary systemic ALCL^	+(–)	+(–)	+(–)	–(+)	–(+)	++	–	–	α/β
Peripheral T-cell lymphoma, unspecified	+(–)	+(–)	–(+)	+(–)	–(+)	–(+)	–(+)/–(+)	–(+)	α/β > γ/δ
Subcutaneous panniculitis-like T-cell	+	+	+	–(+)	+(–)	–(+)	–/–(+)	+	γ/δ >> α/β
Hepatosplenic T-cell lymphoma	+	–	+	–	–	–	+/+(–)	+	γ/δ >> α/β
Angioimmunoblastic T-cell lymphoma#	+	+	–	+(–)	–(+)	–	–	–	α/β'
Extranodal NK/T-cell lymphoma	S –, C +	–	–(+)	–(+)	–	–	–/+	+	–
Enteropathy-associated T-cell lymphoma	+	+	+	–(+)	+(–)	+(–)	–	+	α/β >> γ/δ
Adult T-cell leukemia/lymphoma§	+	+	–	+(–)	–(+)	+(–)	–	–	α/β

+ = > 90% positive; +(–) = > 50% positive; –(+) = < 50% positive; – = < 10% positive; ALCL = anaplastic large cell lymphoma; C = cytoplasmic; LGL = large granular lymphoproliferative; NK = natural killer; PLL = prolymphocytic leukemia; S = surface; TCR = T-cell–rearranged (molecular)

* Approximately 15% to 20% of LGL cases arise from a NK lineage; they are typically CD56+ and CD16-negative.

^ The anaplastic lymphoma kinase (ALK) protein is expressed in 50% to 60% of cases.

Expanded follicular dendritic cell clusters (CD21+) are present around proliferated venules; Epstein-Barr virus (EBV) genomes are detected in most cases (eg, EBER) and may be present in either T or B cells; in addition, TCR may be negative or oligoclonal in 20% to 25% of cases, whereas B-cell immunoglobulin may be rearranged in 10% of cases.

§ Adult T-cell leukemia/lymphoma cases are always associated with the presence of HTLV-I; further, CD25 is expressed in the majority of cases.

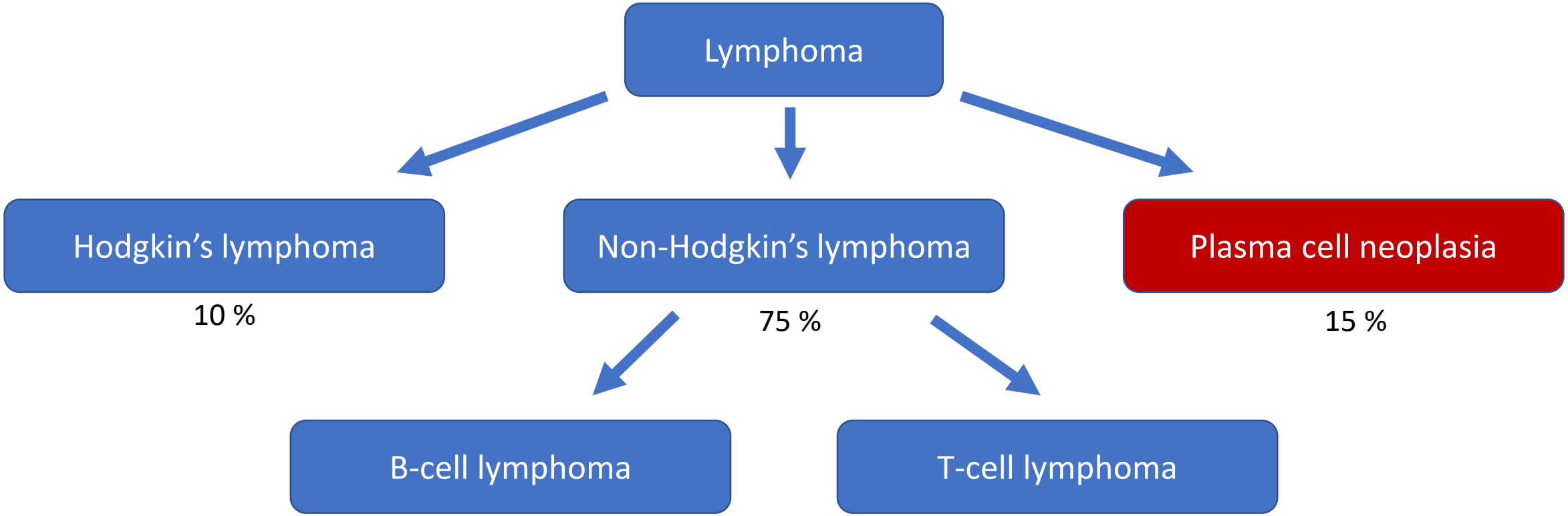
COMPLEX!

NordiQC

Additional IHC for T-cell lymphomas

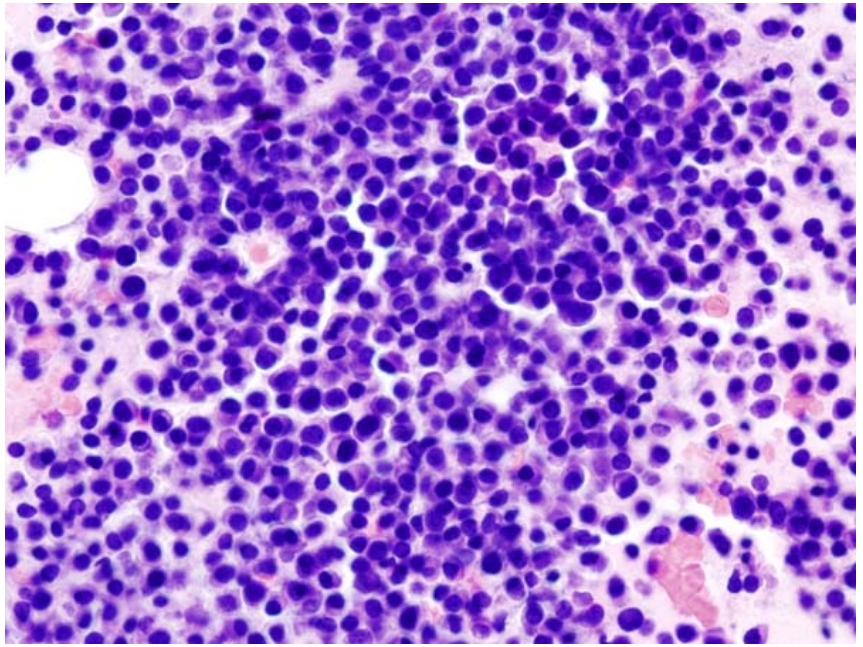
- CD1a: Langerhans cells Positive in precursor lymfoblastomas.
- CD4 / CD8: T-helper cells vs. Cytotoxic. Most T-lymphomas are CD4+
- CD7: Early pan-T marker. Positive in precursor lymfoblastomas.
- TdT: Thymocytes. Positive in precursor lymfoblastomas.
- CD56: NK-cells. Positive in NK-lymphoma.
- Cytotoxic granules (perforin, granzyme)

Classification of lymphomas



Multiple myeloma

- Neoplastic proliferation plasma cells.
- Cells synthesize monoclonal immunoglobulin chains
- Morphology: Small or large groups of plasma cells in BM. Increased number of osteoklasts
- Median age of onset: 70 years
- Prognosis: Overall 5 year: 35%



IHC	
CD79a	+
CD138, MUM1	+
CD19	-
Cyclin D1	(+)