Immunohistochemical classification of haematolymphoid tumours

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Haematolymphoid Neoplasias: Leukaemia vs Lymphoma

Bone marrow
Lymph node
Extranodal site
Blood
Leukaemia
Lymphoma

Malignant lymphoproliferative diseases

- Malignant lymphoma
- Leukaemia
  - Acute lymphoblastic leukaemia
  - Chronic lymphocytic leukaemia (CLL)
- Ca. 1,600 per year in DK
- Ca. 800,000 per year in the world (?)

Classification!

Thomas Hodgkin 1798–1866


WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 2008

- 70s – 80s: Kiel classification
  - B vs T cells: BIC
- 90s: REAL classification
- WHO (2008…..2016/18)
  - “Real” disease entities
  - Clinical features
  - Morphology
  - Immunophenotype
  - Molecular genetics
Lymphoma

Hodgkin's lymphoma
Non-Hodgkin's lymphoma

B-cell
- precursor
- peripheral
- ~32 subtypes
T/NK-cell
- precursor
- peripheral
- ~20 subtypes

WHO Classification - 2008:
B-cell Lymphoma

<table>
<thead>
<tr>
<th>Type of Lymphoma</th>
<th>Distribution and Genes</th>
<th>Clinical Features</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>85%</td>
<td>Young adults</td>
<td>Genetic, environmental</td>
</tr>
<tr>
<td>NS</td>
<td>40%</td>
<td>Older adults</td>
<td>Genetic, environmental</td>
</tr>
<tr>
<td>MC</td>
<td>Rare</td>
<td>Any age</td>
<td>Genetic, environmental</td>
</tr>
<tr>
<td>LR</td>
<td>Rare</td>
<td>Any age</td>
<td>Genetic, environmental</td>
</tr>
</tbody>
</table>

WHO Classification - 2008:
T-cell & NK-cell neoplasms

<table>
<thead>
<tr>
<th>Type of Lymphoma</th>
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</tr>
</thead>
<tbody>
<tr>
<td>B-cell</td>
<td>85%</td>
<td>Young adults</td>
<td>Genetic, environmental</td>
</tr>
<tr>
<td>T-cell/Percell</td>
<td>40%</td>
<td>Older adults</td>
<td>Genetic, environmental</td>
</tr>
<tr>
<td>NK-cell/Percell</td>
<td>Rare</td>
<td>Any age</td>
<td>Genetic, environmental</td>
</tr>
</tbody>
</table>

WHO Classification - 2016 (2018?)

Updated WHO Classification – 2016 (2018?)

- It's not got any smaller!
- > 100 lymphoma entities

Why does it all have to be so complicated?
Disease classification is easy when there is no effective treatment!

Updated WHO Classification – 2016 (2018?)

Major phenotypic changes:

**Diffuse large B-cell lymphoma**

- COO – cell of origin analysis now required
  - to distinguish GCB vs ABC/non-GC types
    - either by gene expression profiling or immunohistochemistry
- IHC for MYC and BCL2 expression
  - to identify "double-expressors"

Lymphoma frequencies

What is lymphoma?

- Clonal malignancy
  - → mutational events cause cells to freeze at a single stage of normal lymphocyte differentiation
- Morphology, immunophenotype & molecular features:
  - mirror stages of normal lymphocyte development

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

Lymphoid neoplasms: Correlation with normal T or B-cell differentiation
What is lymphoma?

- Clonal malignancy
  - Mutational events cause cells to freeze at a single stage of normal lymphocyte differentiation
- Morphology, immunophenotype & molecular features:
  - Mirror stages of normal lymphocyte development
- Resemble normal haematopoietic cells in their:
  - Morphology, immunophenotype, molecular genetics

Lymphoma & Leukaemia diagnosis

- Clinical features
- Morphology
- Immunophenotype
- Molecular diagnosis

Lymphoma differential diagnosis

- Assess morphology:
  - Cell size
  - Architecture
- Select appropriate immune panel(s)

Enlarged lymph node

Is it malignant?

- Emphasis on lymphoma classification
- Reactive vs malignant
  - Often more challenging diagnosis
- Use IHC to evaluate lymphoid tissue cytology and architecture
- Correlate immunophenotype with disease entity

International recommendations for lymphoma diagnostics

http://www.lymphoma.dk/index.php?id=56,0,0,1,0,0
See “Lymphomdiagnostik”

What are CD numbers?

- CD: “clusters of differentiation”
- Classification system for antigens (and antibodies)
- Originally for surface antigens on leucocytes
- Now includes other cells and intracellular antigens (no CD no.)
- 10 workshops since 1982
- Currently > 350 CD antigens
IHC Dogma
(also applies in diagnostic haematopathology)

- IHC complements routine staining
- Helps characterise cells and architecture
- No single antibody is disease specific
- Antibodies should be used in panels
- Interpret findings in relation to the histology

Diagnostic Applications of IHC 1
Reactive vs malignant
- Polyclonal vs monoclonal Ig
- Follicular hyperplasia vs follicular lymphoma
- Diff. diagnosis of small cell B-cell lymphomas
  - CLL/SLL vs MALT vs FL vs Mantle cell
  - Aggressive B-cell lymphomas
    - DLBCL vs BL vs BL-like / grey-zone NHL
    - DLBCL – ‘cell of origin’ – GCB vs ABC

Diagnostic Applications of IHC 2
- T-cell lymphoma vs B-cell lymphoma
- T-cell lymphoma vs T-zone hyperplasia
- Hodgkin lymphoma vs NHL
  - NLPHL vs classical HL
  - Lymphoblastic vs. Myeloblastic vs. Burkitt
- Undifferentiated malignant tumor
- Lymphoma prognosis
  - e.g. Ki-67, ALK, c-myc
  - Targeted therapy
  - e.g. CD20: Rituximab, CD30: brentuximab, idelalisib (anti-CD20)

Useful antigens in haematopathology

Basic IHC panel for lymphoma diagnosis
- CD45
- CD20
- CD79a
  - (PAX-5)
- kappa/lambda
- CD3
- CD5
- CD30
- CD43
- Bcl-2
- Bcl-6
- CD23 (CD21)
- Cyclin-D1
- Ki-67

Basic stains: CD45
- Membrane glycoprotein family
- Positive in all (T) haemopoietic cells
- Not expressed on non-BM-derived cells
- CD45 isoforms are more lineage specific

In lymphomas:
- Most NHLs positive
  - Often/always negative in:
    - Plasma cell neoplasia
    - Anaplastic large cell lymphoma
    - Hodgkin lymphoma
    - LP: Popcorn cells positive
    - HRS cells in classical HL are negative

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    - HRS cells in classical HL are negative
Basic stain: Immunoglobulin

The demonstration of plasma cells and other immunoglobulin-containing cells in formalin-fixed, paraffin-embedded tissues using peroxidase-labelled antibody

C. R. TAYLOR AND J. BURNS
From the Department of Pathology, Churchill Laboratory, Radcliffe Infirmary, Oxford

- IHC-lg
  - first protocol for IHC in FFPE
  - still one of the hardest to perform & evaluate!

Basic stains: Immunoglobulin

- B-cell specific
- Normal κ/λ ratio ca. 3:4:1
- Monotypic Ig restriction
  - Suggests clonality
  - >10:1 or <2:2.1 = restriction
- Cytoplasmic Ig easily shown
- In lymphomas:
  - Cy Ig:
    - lymphoplasmacytic; myeloma; MCL, DLBCL, FL
  - Surface Ig

Basic stains: CD20

- Many B-cell neoplasms
- Negative in:
  - early precursor B-LB
  - plasma cell neoplasms
- Negative in T-cell lymphomas
  - rare cases positive
- Hodgkin lymphoma
  - HL-LP: 95% positive
  - Other types – variably positive (10% - 30% not all HRS cells)
- Predictive marker for Rituximab therapy

Basic stains: CD79α

- Fairly specific, sensitive B-cell marker
- Normal (wide B-cell expression):
  - pre-B cell to plasma cell
- Lymphomas:
  - majority B-cell leukaemias and lymphomas
  - 50% myelomas
  - 10% T-LBs positive
  - rare in mature T-cell NHL
- Hodgkin lymphoma:
  - L&H/popcorn cells positive

Basic stains: Pax-5 (BSAP)

- Most specific B-cell marker available
- B-cell nuclear transcription factor
- Normal – many B cells
- Lymphomas:
  - nearly all B-cell NHLs
  - Hodgkin: HRS cells and variants positive in most cases
  - plasma cell neoplasms negative
  - peripheral TCLs negative
  - some pre-TLB positive
  - some ALL positive
Usual staining pattern of B-cell neoplasms

<table>
<thead>
<tr>
<th>Phenomenon</th>
<th>DLBCL</th>
<th>MCL</th>
<th>B-CLL/SLL</th>
<th>Mantle cell NHL</th>
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- **CD5**:
  - Modulates T & B cell signalling
  - Pan-T cell marker
  - 95% thymocytes
  - 100% post-thymic T-cells
  - ↑↑ ↑↑ expression with maturity

- **Cyclin D1**
  - Small cell B-Cell lymphomas: Overall Survival
  - Normal:
    - activated germinal centre cells
    - basophilic follicular reticulum cells
    - mature B cells
  - In lymphomas:
    - some small cell B-cell NHL
    - SLL/CLL
    - negative in MCL, pre-LB, TCLs

- **Basic stains: CD23**
  - Normal:
    - activated germinal centre cells
    - some mantle zone lymphocytes
    - some mature B cells
  - In lymphomas:
    - some small cell B-cell NHL
    - SLL/CLL
    - negative in MCL, pre-LB, TCLs

- **Basic stains: CD5**
  - Modulates T & B cell signalling
  - Pan-T cell marker
  - 95% thymocytes
  - 100% post-thymic T-cells
  - ↑↑ ↑↑ expression with maturity

- **Basic stains: Cyclin D1**
  - Normal:
    - control cell cycle
    - normal proliferating cells, e.g. basal epithelial cells positive
    - variable clone sensitivity
    - Bcl-1 gene product at 11q13
    - upregulated in cells with t(11;14)
    - >90% MCLs positive (nuclear)
    - 15% myelomas positive (nuclear)
**B-cell Small Lymphocytic Lymphoma (CLL)**

**Morphology**
- small lymphocytes
- proliferation centres

**Immunology**
- surface IgMD weak
- CD19, 20, 79a +
- CD5 +
- CD23 +
- CD10, CyclD1 -

**Mantle Cell Lymphoma**

**Morphology**
- small--medium lymphocytes
- cleaved / irregular
- blastoid variant
- nodular / mantle / diffuse

**Immunology**
- surface Ig +
- CD19, 20, 22, 79a +
- CD5 +
- CD23 -
- Cyclin D1 +
- CD10 -

**Immunophenotype: Small B-Cell Lymphomas**

<table>
<thead>
<tr>
<th></th>
<th>CD20</th>
<th>CD79A</th>
<th>CD10</th>
<th>CD23</th>
<th>CD43</th>
<th>bcl-2</th>
<th>CyclinD1</th>
<th>TdT</th>
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<tbody>
<tr>
<td>CLL</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<td>+</td>
<td>-</td>
</tr>
<tr>
<td>FL</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<tr>
<td>MALT</td>
<td>+</td>
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<td>+</td>
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</tr>
<tr>
<td>HCL</td>
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<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>BLB</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

**Follicular Lymphoma**

**Morphology**
- germinal centre cells
- CBs & CCs
- follicular

**Immunology**
- surface Ig +
- CD19, 20, 22, 79a +
- BCL-2 +
- CD10 +/-
- Bcl-6 +
- CD5 -

**Basic stain: bcl-2**

- Apoptosis inhibitor
- Nuclear and cytoplasmic stain

**Normal:**
- Mature B- and T-cells
- Negative in cortical thymocytes and germinal centre cells

**In lymphoma:**
- Positive in most peripheral B-NHL and T-NHL
- Negative in BL
- Associated with, but not specific for t(14;18)
- Positive in neoplastic germinal centres
- Often negative in skin lymphomas
- Ca 10% of follicular lymphomas bcl-2 negative

**Lack of Bcl-2 expression in follicular lymphoma may be caused by mutations in the BCL2 gene or by absence of the t(14;18) translocation**
**Diffuse Large B-cell Lymphoma**

**Morphology**
- Large cells
- Diffuse

**Immunology**
- CD79a
- CD20

**Basic stain: Ki-67**
- Nuclear protein
- Expressed in all cell cycle stages except G0
- In lymphomas:
  - Roughly
  - Indolent: aggressive: highly aggressive NHL
  - Prognostics?
  - Characteristic pattern in HRS cells in HL

**Basic stain: Bcl-6**
- Nuclear protooncogene product
- Normal:
  - Germinal centre cells
- In lymphomas:
  - Follicular lymphoma
  - Most BL
  - Variable DLBCL
    - "Cell of origin" staining in DLBCL
    - HL-LP (not classical)
  - SLL, MCL, MZL, HCL: negative

**IHC for DLBCL**
- Add to basic panel:
  - CD10
  - CD138
  - MUM1

**Secondary stain: CD10**
- >90% precursor B-LB (membrane & paranuclear stain)
- Ca. 25% precursor T-LB
- Burkitt lymphoma
- Follicular lymphoma
  - Interfollicular CD10 with marginal lymphoma
- Some DLBCL
  - "Cell of origin" algorithm in DLBCL
  - GCB vs ABC

**Large B-cell Lymphomas Molecular Variants**
- Gene profiling identified 2 types of DLBCL (Cell Of Origin – COO):
  - GCB
  - ABC
- Molecular profiling not applicable in routine setting
- IHC
  - Surrogate molecular profiling
  - Hans "cell of origin" classifier
DLBCL - the HANS Classifier:
Germinal centre (GC) & Activated B cell (ABC) types

DLBCL

CD10+
GC subtype

CD10–

Bcl6+
Non-GC (ABC) subtype

MUM1–
GC subtype

MUM1–
Non-GC (ABC) subtype

DLBCL - 'cell of origin':
Competing IHC classifiers

Immunophenotyping in Gray zone B-NHL

IHC for c-myc and bcl-2 identifies
double-hit & double-expressor B-NHL

Updated WHO Classification – 2016 (2018?)

Major phenotypic changes:
Diffuse large B-cell lymphoma

- COO – cell of origin analysis now required
  - to distinguish GCB vs ABC/non-GC types
  - either by gene expression profiling or Immunohistochemistry

- IHC for MYC and BCL2 expression
  - to identify double-expressors

Gray zone (bordeline) B-cell lymphomas
Hodgkin's Lymphoma: Differential Diagnosis

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>CD30+</th>
<th>CD30-</th>
<th>T-cell</th>
<th>B-cell</th>
<th>EMA</th>
<th>ALK</th>
<th>CD15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical Hodgkin lymphoma</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Falciform HL</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Anaplastic large cell lymphoma</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lymphocyte-rich B-cell lymphoma</td>
<td>+</td>
<td>-</td>
<td>0%</td>
<td>0%</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Key:
- The lymphoma cells are consistently but not always positive.
- The lymphoma cells are rarely but not always negative.

CD30 in lymphoma

- "CD30+ lymphoproliferations":
  - Primary cutaneous anaplastic large cell lymphoma (ALCL)
  - Systemic ALCL
  - Lymphomatoid papulosis
  - Mycosis fungoides transformation
  - Hodgkin lymphoma
    - Reed-Sternberg cells in classical types
    - Popcorn cells in HL-LP: 0% - 10%
  - Ca. 30% of other T-cell NHL
  - Ca. 20% DLBCL
  - Target for Brentuximab

IHC for Hodgkin's Lymphoma

Add to basic panel:
- PAX-5 (ALCL?)
- BCL-6, CD57, BOB-1, OCT-2 (HL, LP?)
- ALK (ALCL?)
- EBV
- (CD15)

HL vs ALCL: Immunophenotype

<table>
<thead>
<tr>
<th></th>
<th>HL</th>
<th>ALK pos T/null - ALC</th>
<th>ALK neg T/null - ALC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALK</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>EBV</td>
<td>&gt; 40 %</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CD30</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CD15</td>
<td>ca. 90 %</td>
<td>&lt; 5 %</td>
<td>+/-</td>
</tr>
<tr>
<td>EMA</td>
<td>-</td>
<td>ca. 50 %</td>
<td>ca. 50 %</td>
</tr>
<tr>
<td>PAX5</td>
<td>-</td>
<td>&gt; 80 %</td>
<td>-</td>
</tr>
<tr>
<td>CD20</td>
<td>ca. 25 %</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CD3</td>
<td>ca. 2 %</td>
<td>+ +/-</td>
<td>+ +/-</td>
</tr>
<tr>
<td>CD45</td>
<td>-</td>
<td>ca. 50 %</td>
<td>ca. 50 %</td>
</tr>
<tr>
<td>CD43</td>
<td>-</td>
<td>most +</td>
<td>most +</td>
</tr>
<tr>
<td>Granyme/ perforin</td>
<td>10 – 20%</td>
<td>ca. 90 %</td>
<td>ca. 70 %</td>
</tr>
<tr>
<td>TCR genes</td>
<td>G</td>
<td>R (single cell)</td>
<td>G</td>
</tr>
<tr>
<td>Ig genes</td>
<td>R</td>
<td>R</td>
<td>R</td>
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Expression of transcription factors Pax-5, Oct-1, Oct-2 and BOB.1 in Hodgkin's Lymphoma
Most viral antigens not relevant
- Latent membrane protein 1
  - Normal primary infection (IM)
  - Latency patterns II and III
  - HRS-cell-like morphology
- EBNA2
  - Nuclear reaction
  - Normal primary infection (IM)

In lymphomas:
- Hodgkin lymphomas:
  - Classical types: 25% - 50% positive in HRS cells: LMP1+/EBNA2- DLCL, L&H: permea infraparaploidal
  - EBV+ in mononuclear infiltrate
  - LMP1 gene rearranged with latency pattern I
- Sporadic INHL:
  - Co-ex: EBV, L&H, DLCL
- T cell lymphomas:
  - Variably positive (25% - 100% depending on type)
  - ALCL are negative

EBV+ immunodeficiency associated lymphomas

- Variable (diagnostically useful) latency patterns
- Sporadic B-NHL
- Ca. 5% (EBV+ DLBCL, NOS)

T cell lymphomas
- Variably positive (5% - 100% depending on type)
- ALCL are negative

**Secondary stain: EBV**

- Most viral antigens not relevant
- Latent membrane protein 1
  - Normal primary infection (IM)
  - Latency patterns II and III
  - HRS-cell-like morphology
- EBNA2
  - Nuclear reaction
  - Normal primary infection (IM)

**Basic stain: CD3**

- transmembrane molecule
- Ig superfamily
- part of T-cell receptor
- most specific T-cell marker
- thymocytes: cytoplasmic
- most post-thymic T-cells
- activated NK-cells

**CD3 in lymphoma**

- >90% peripheral TCLs
- Primitive precursor T-LB in cytoplasm
- B-cell lymphomas negative
- Hodgkin lymphoma negative
- (NK-lymphoma: cytoplasmic)

**IHC for PTL**

Add to basic panel:

- CD1a
- CD2
- CD4
- CD7
- CD8
- CD3epsilon, TdT, CD43
- T-LB?
- CD10, CD21, CD23, PD-1
- AILD?
- CD56, CD57, perforin, granzyme B, TIA-1
- NK/NK-like?
- EBV

**Secondary stain: Anaplastic lymphoma kinase (ALK, CD246)**

- Normal tissues only in CNS
- In neoplasia:
  - ALCL, with t(2;5) or other translocation
    - positive prognostic factor
    - cellular localization varies with partner gene
  - ALK+ B-cell NHL (rare)
  - Negative in primary cutaneous ALCL
**Secondary stain: Terminal deoxynucleotidyl transferase (TdT)**

- **Nuclear protein involved in DNA synthesis**
- **Normal expression:**
  - early thymocytes
  - pre-B and pre-pre-B cells
- **In lymphomas:**
  - stem cell leukaemias
  - most (>90%) precursor LBs
  - negative in most peripheral TCLs
  - some AMLs (up to 20%)

**Secondary stain: CD1a**

- **T-cell marker**
  - 70% cortical thymocytes
  - Peripheral T-cells negative
  - Langerhans cells / Interdigitating reticulum
- **In lymphomas:**
  - 50% precursor T-LB
  - Langerhans cell histiocytosis
  - Peripheral TCLs are negative in paraffin
- **NB! May be positive in mediastinal biopsies from normal thymus or lymphocyte-rich thymoma**

**Secondary stain: CD7**

- **Early pan-T cell marker**
  - 90% thymocytes
  - B-cells negative
  - ↑↑↑ NK cells negative
- **In lymphoma:**
  - nearly all T-LB +
  - many peripheral TCLs +
  - often lost in TCL
  - negative in B-NHL

**Secondary stains: CD4 & CD8**

- **CD4**
  - Thymocytes
  - T-helper cells
  - Monocytes
  - Macrophages
  - Granulocytes
- **CD8**
  - T-cytotoxic/suppressor cells
  - NK cells
  - Intraepithelial lymphocytes CD8+
  - Most lymphomas CD4+
  - γδTCL usually CD4- CD8-
  - ALC: CD4 > CD8
  - Double negs & double pos:
  - aberrant, neoplastic?

**Basic stain: CD21**

- **Membrane glycoprotein**
- **Normal:**
  - Mature B cells
  - mantle zone & marginal zone B cells
  - Lost on B-cell activation
  - Follicular dendritic reticulum cells – in GCs
- **C3d/EBV receptor**
- **In lymphomas:**
  - most follicular lymphomas
  - some other B-cell NHL
  - FDC network in GC-derived tumours
  - MCL, HL, AILD
T-cell lymphoma: immunophenotype

**Complex!**

Oncogenes/ Tumor Suppressor Genes Evaluation by Immunohistochemistry

- **Bcl-2**: Follicular lymphoma, t(14;18)
  - antigen expression not specific for translocation
- **Cyclin D1**: Mantle cell lymphoma, t(11;14); myelomas (15%)
- **p53**: Progression in lymphomas, high grade lymphomas
- **Bcl-6**: Germinal center origin
  - 'cell of origin' staining in DLBCL
- **c-myc**
- **ALK-1**: ALCL; NPM/ALK (t2;5)
- **CD99**: Lymphoblastic, myeloblastic

IHC for lymphoma vs other

**Add to basic panel:**

- **panCK**
- **S-100**
- **Melan-A**

IHC for lymphoid vs myeloid

**Add to basic panel**

- **Myeloperoxidase**
- **CD43**
- **CD68**
- **CD163**
- **CD33**
- **(CD14, CD15, CD34, CD61, glycoporphin C)**

Acute myeloid leukaemia:

**CD33 (paraffin section):**
Myeloid sarcoma: testis

- CD33
- Myeloperoxidase
- Lysozyme

Targeted therapy

- Rituximab (anti-CD20)
  - B-cell NHL
- Brentuximab (anti-CD30)
  - HL
  - ALCL
  - CD30+ DLBCL
- Alemtuzumab (anti-CD52)
  - B-CLL
  - T-cell lymphoma

Immune checkpoint inhibitory therapy?

- Angioimmunoblastic T-cell lymphoma
  - PD-1 positive tumour cells

Immune checkpoint inhibitory therapy?

- Hodgkin lymphoma
  - PD-L1 positivity in the tumour microenvironment

Thanks!