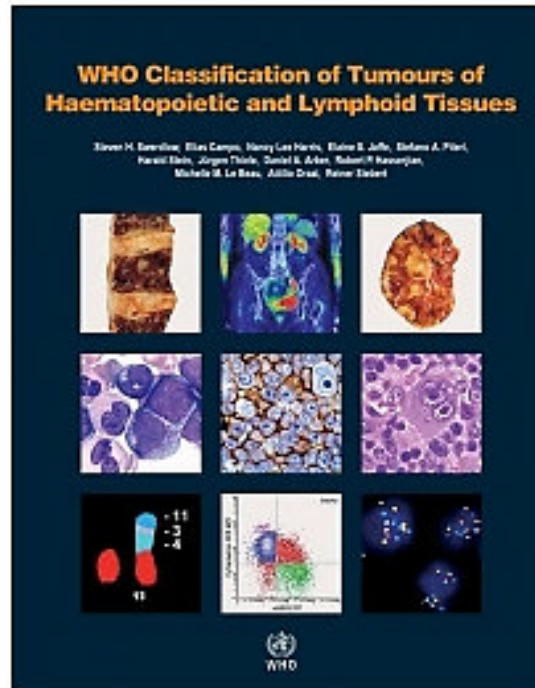


Neue WHO-Klassifikation – neue Lymphomtypen



**WLAD – Patientensymposium
Bern, 15. September 2018**

Stephan Dirnhofer
Institut für Pathologie







JEAN-LOUIS

KLAUS

**KINSKI
TRINTIGNANT**

EIN SERGIO CORBUCCI FILM

**Leichen pflastern
seinen Weg**



CSI:

CRIME SCENE INVESTIGATION™

Interactive Crime-Solving Adventure

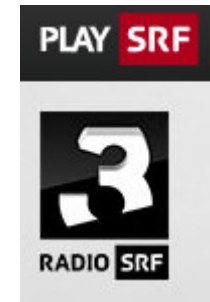


www.csi.ubi.com

Was verstehen Sie unter dem Wort „Pathologie“?

Was verstehen Sie unter dem Wort „Pathologie“?

- ✓ Fremdwort
- Hat mit Politik zu tun
- Hat mit Geisteskrankheiten zu tun
- ✓ Hat mit Toten zu tun
- Hat mit der Steinzeit zu tun
- ✓ Anderes



Kreuzen Sie Zutreffendes an!

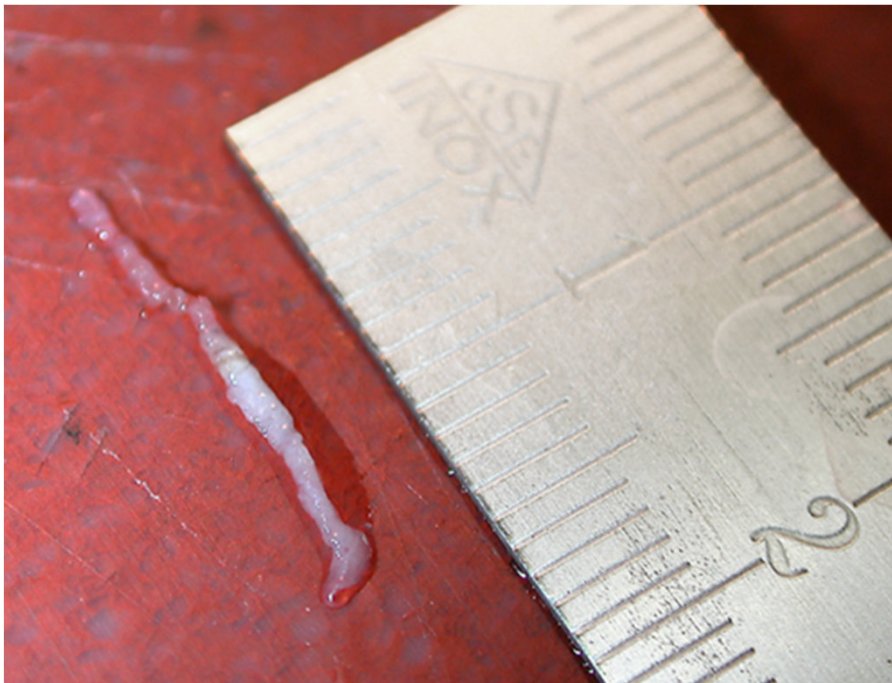
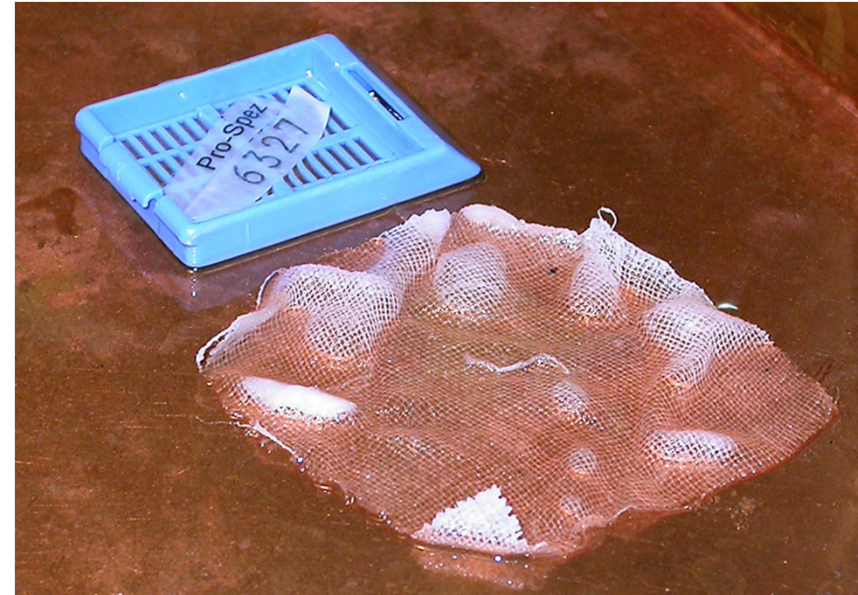
Was machen PathologInnen?

- Untersuchung von Zellen & Gewebe ***lebender*** Patienten (ca. 95%)
- Behandlungsentscheidende Diagnosen
- Prognose
- Prädiktion

Was machen PathologInnen?

- Sie schauen sich **Bilder** an
- Mit welchen Techniken?
 - Makroskopisch (grob)
 - Mikroskopisch (fein)

Verarbeitung von Biopsien







Diagnose



Prognose



Behandlung

Lymphknotenschwellung: Ursache

1) Reaktiv:

Infekte

Medikamente

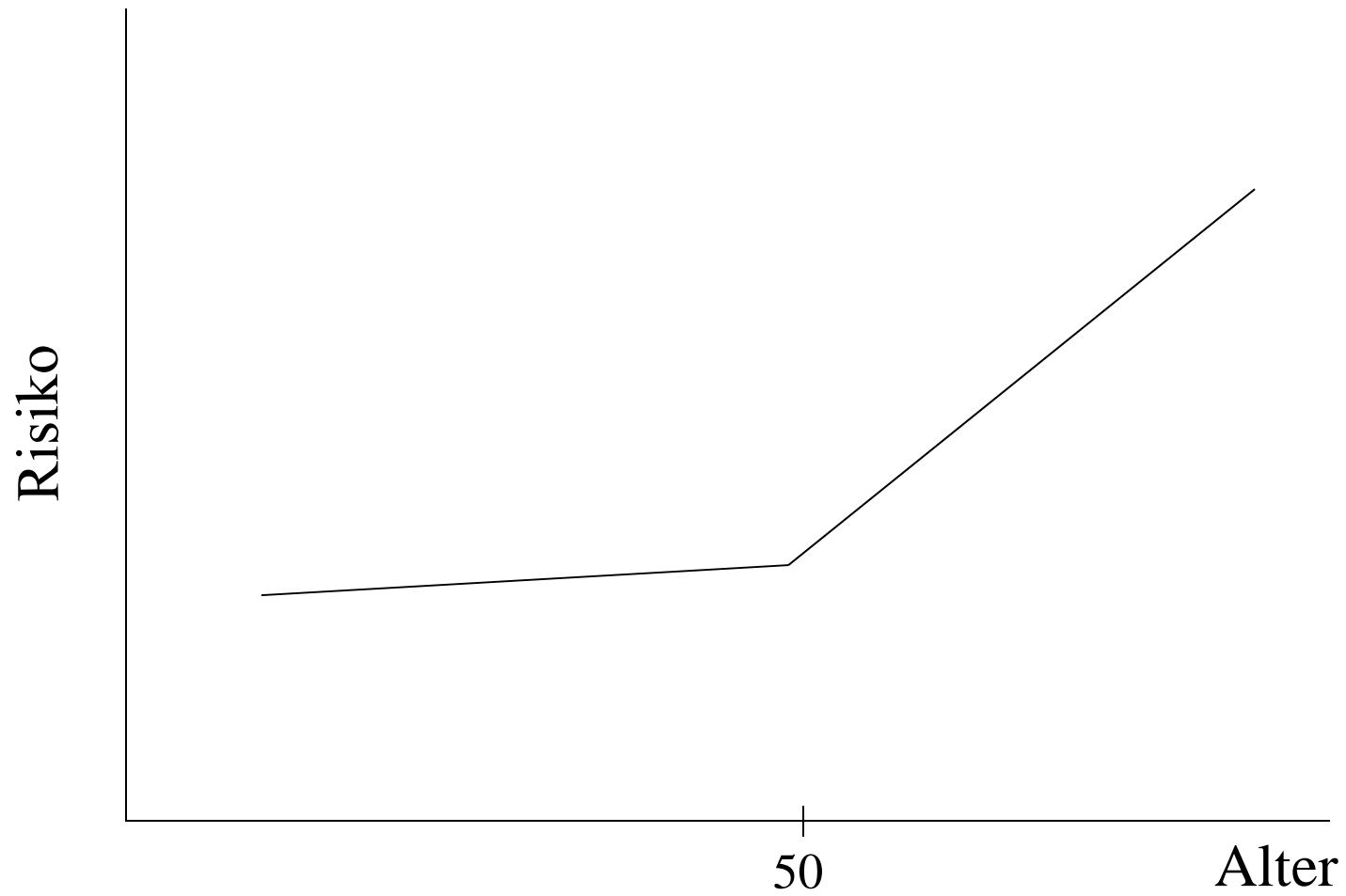
Immune-dysregulation

2) Neoplastisch

Lymphom

Metastase

Risiko, dass eine Lymphadenopathie maligne ist

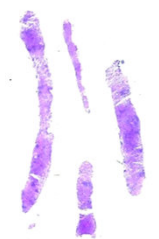
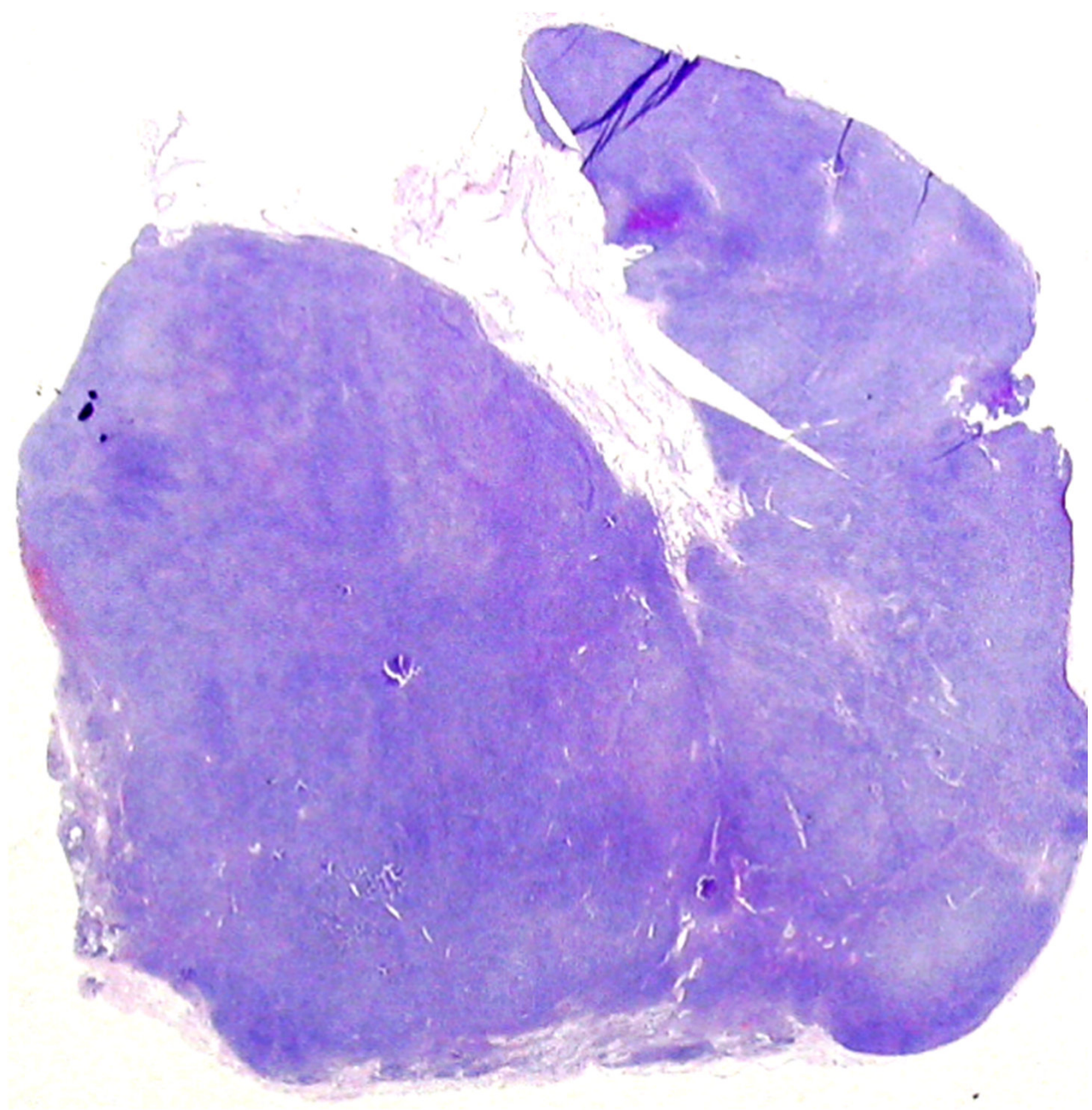


Lymphom: Definition

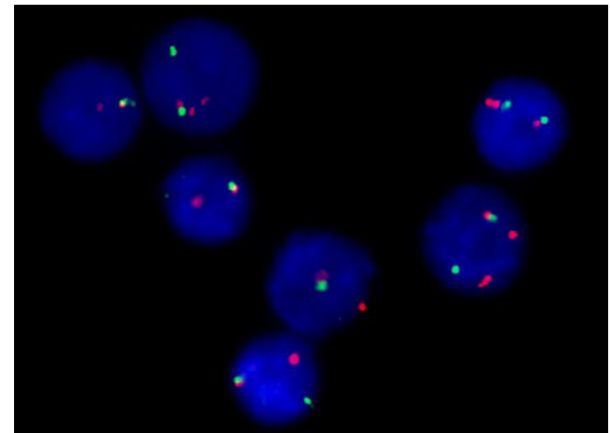
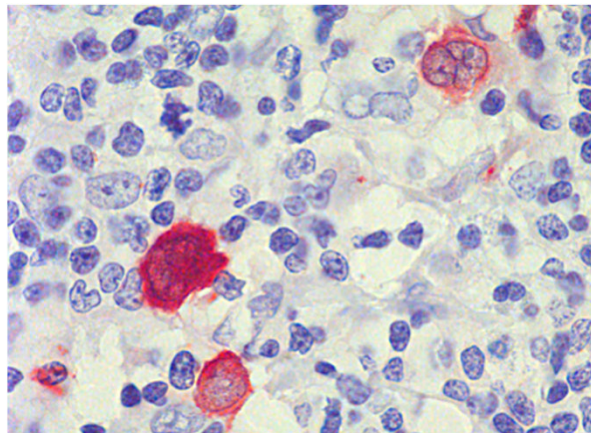
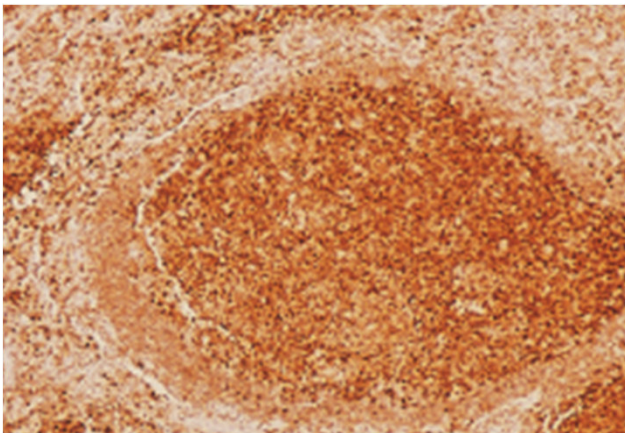
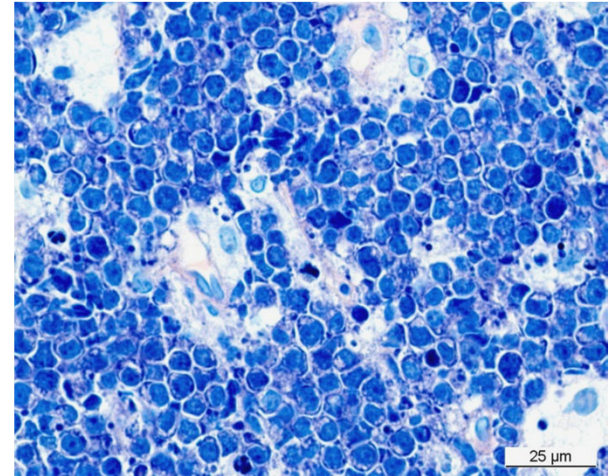
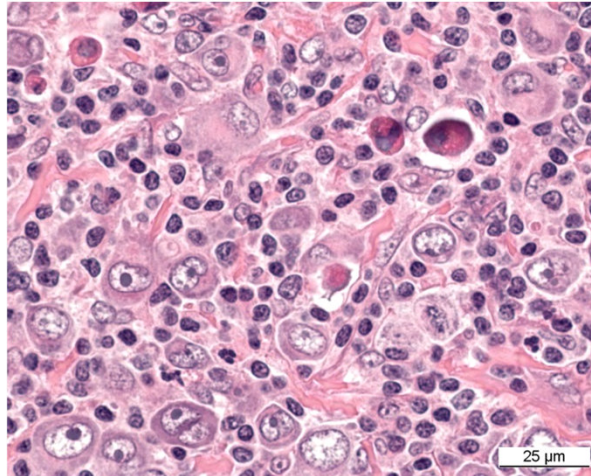
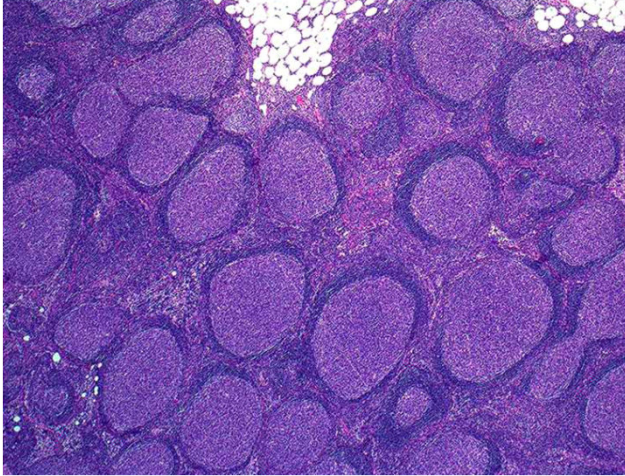
- Bösartige, neoplastische Erkrankungen der B-, T- oder NK-Lymphozyten
- in Organen des lymphatischen Systems (nodal)
- ausserhalb solcher Organe (extranodal)
- welche mit (leukämisch) oder ohne Ausschwemmung im Blut (Lymphome im engen Sinne) verlaufen

Gewebsbasierte Diagnostik für Lymphome unabdingbar

- Dignitätsbeurteilung
- Entitätsspezifische Diagnose
- Bestimmung von Prädiktionsparameter
- Exakte Diagnose - Grundvoraussetzung für eine spezifische onkologische Therapie



Lymphombefallene Lymphknoten

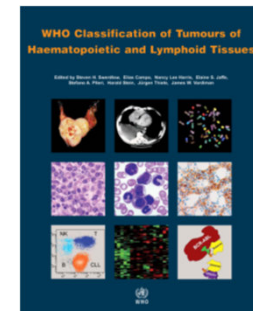


Geschichte der Lymphom-Klassifikation

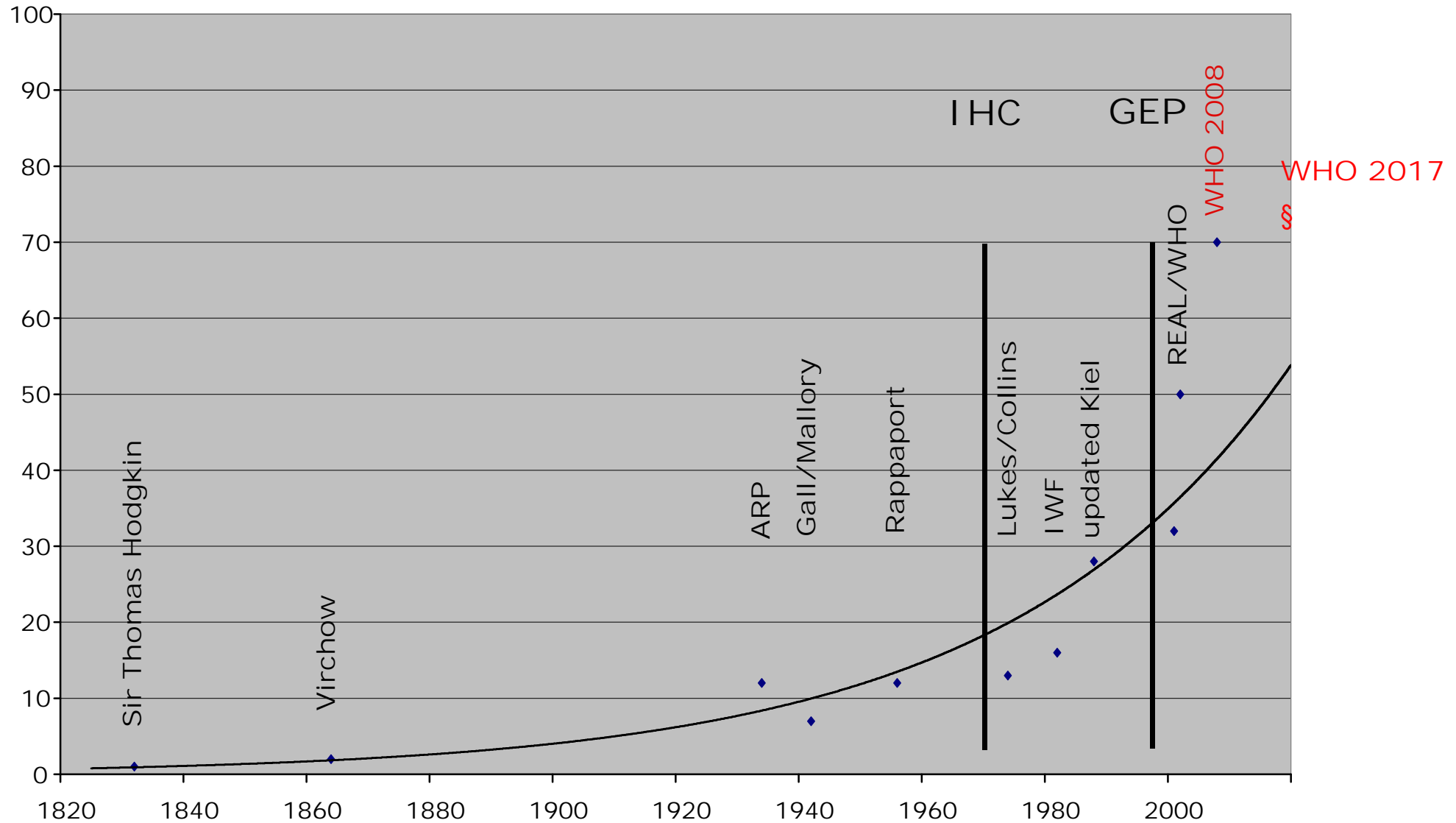
Willis, 1948

„nowhere in pathology has a chaos of names so clouded clear concepts as in the subject of lymphoid tumors“

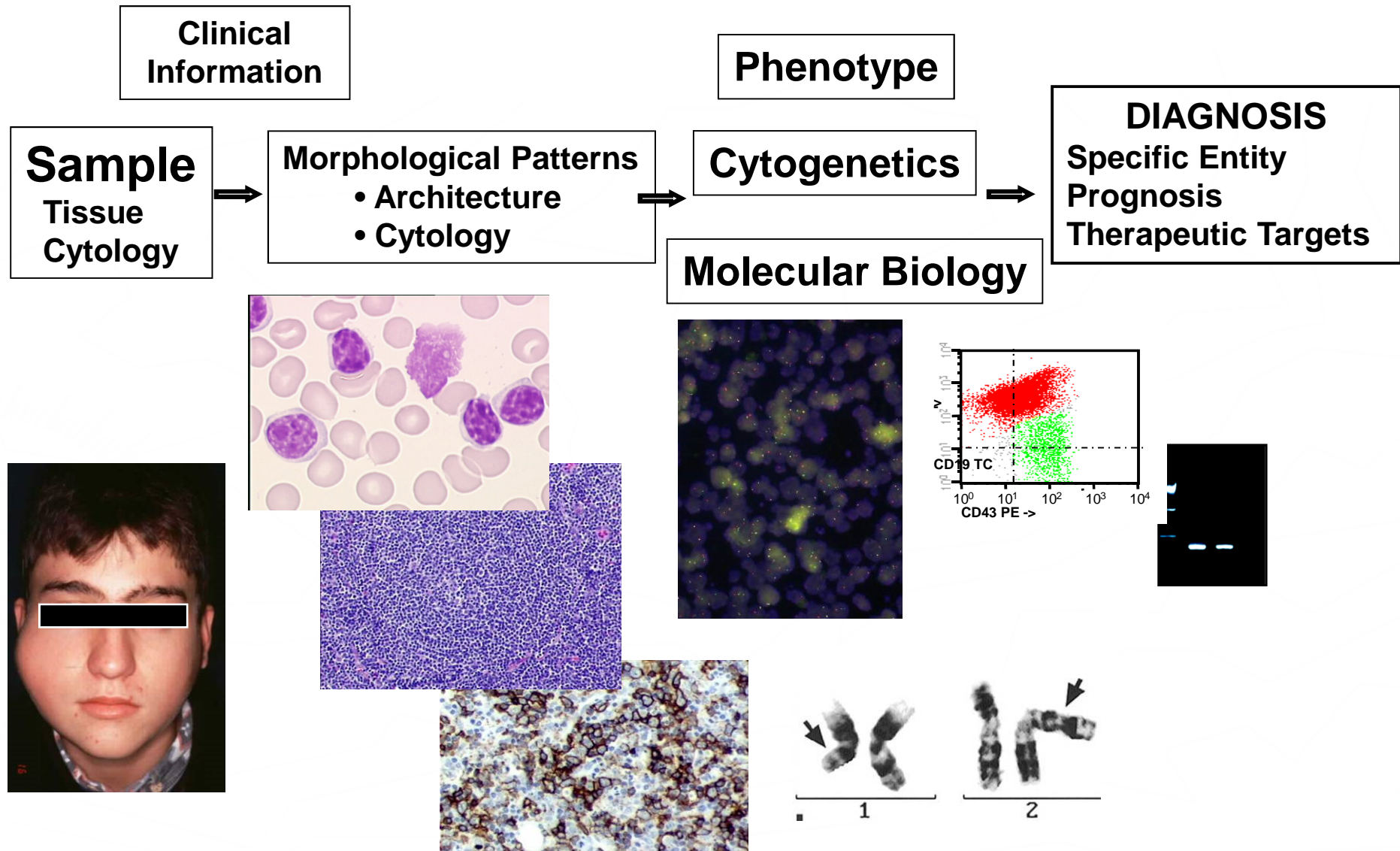
- **Rappaport/Lukes-Collins 1975**
- **Kiel 1974, updated 1992**
- **International Working Formulation (IWF) 1982**
- **Revised European American Lymphoma-Classif. (REAL) 1994**
- **WHO: 2001, 2008 & 2017**




Zunahme der Lymphom-Entitäten



WHO 2017: Integrative Diagnosis





Hodgkin Lymphoma

Hodgkin Lymphoma - Introduction

Nodular lymphocyte predominant Hodgkin lymphoma

Classical Hodgkin lymphoma, introduction


Nodular sclerosis classical Hodgkin lymphoma

Mixed cellularity classical Hodgkin lymphoma

Lymphocyte-rich classical Hodgkin lymphoma

Lymphocyte-depleted classical Hodgkin lymphoma

Mature T- and NK-cell Neoplasms



T-cell prolymphocytic leukaemia

T-cell large granular lymphocytic leukaemia

Chronic lymphoproliferative disorders of NK cells

Aggressive NK cell leukaemia

EBV-positive T-cell lymphoproliferative disorders of childhood

Adult T-cell leukaemia/lymphoma

Extranodal NK/T cell lymphoma, nasal type

Enteropathy-associated T-cell lymphoma

Hepatosplenic T-cell lymphoma

Subcutaneous panniculitis-like T-cell lymphoma

Mycosis fungoides

Sézary syndrome

Primary cutaneous CD30 positive T-cell lymphoproliferative disorders


Primary cutaneous gamma-delta T-cell lymphomas

Peripheral T-cell lymphoma, NOS


Angioimmunoblastic T-cell lymphoma

Anaplastic large cell lymphoma (ALCL), ALK positive

Anaplastic large cell lymphoma (ALCL), ALK negative



Mature B-cell Neoplasms



Chronic lymphocytic leukaemia /small lymphocytic lymphoma

B-cell prolymphocytic leukaemia

Splenic marginal zone lymphoma

Hairy cell leukaemia

Splenic lymphoma/leukaemia, unclassifiable

Lymphoplasmacytic lymphoma

Heavy chain diseases

Plasma cell neoplasms

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)

Nodal marginal zone lymphoma

Follicular lymphoma

Primary cutaneous follicle centre lymphoma

Mantle cell lymphoma

Diffuse large B-cell lymphoma (DLBCL), NOS

T-cell/histiocyte-rich large B-cell lymphoma

Primary DLBCL of the CNS

Primary cutaneous DLBCL, leg type

EBV positive DLBCL of the elderly

DLBCL associated with chronic inflammation

Lymphomatoid granulomatosis

Primary mediastinal (thymic) large B-cell lymphoma

Intravascular large B-cell lymphoma

ALK positive large B-cell lymphoma

Plasmablastic lymphoma

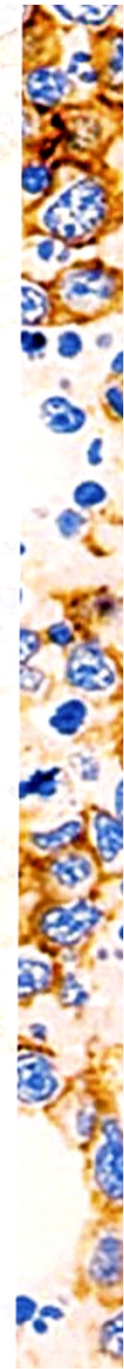
Large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease

Primary effusion lymphoma

Burkitt lymphoma

B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and Burkitt lymphoma

B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classical Hodgkin lymphoma



Lymphomdiagnose - Lymphomtherapie

- Watch & wait
- PUVA, Antibiotics
- Rituximab (R), Brentuximab, Alemtuzumab
- (R-)COP, (R-)CHOP, R-Benda, R², R-ICE, Fludara
- Crizotinib
- Bortezomib
- CODOX, Hyper-CVAD
- EPOCH, EPOCH(-R)
- ABVD, BEACOP
- RT
- HD-autoSZT/ HD-alloSZT

Large B-cell lymphomas – WHO 2017

- DLBCL, NOS
 - Morphological variants: Centroblastic, Immunoblastic, Anaplastic
 - Molecular subtypes: GCB-type, non GCB-type (ABC-type)
- T-cell/histiocyte-rich large B-cell lymphoma
- Intravascular large B-cell lymphoma
- Primary DLBCL of the CNS
- Primary cutaneous DLBCL, leg-type
- Primary mediastinal (thymic) large B cell lymphoma
- EBV-positive DLBCL, NOS
- *Large B cell lymphoma with IRF4 rearrangements*
- DLBCL associated with chronic inflammation
- ALK+ large B-cell lymphoma
- Plasmablastic lymphoma
- HHV8-positive DLBCL
- Primary effusion lymphoma
- **High grade B-cell lymphoma**
 - HGBCL, with MYC and BCL2 and/or BCL6 rearrangements
 - HGBCL, NOS
- B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and cHL

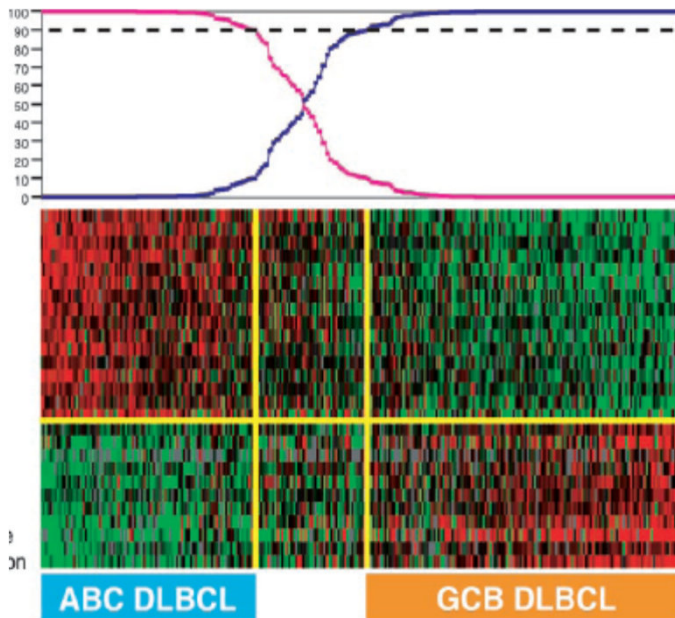
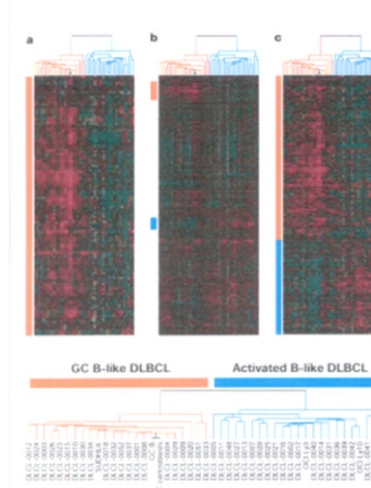


Molekulare Subtypen des DLBCL: CoO-classification

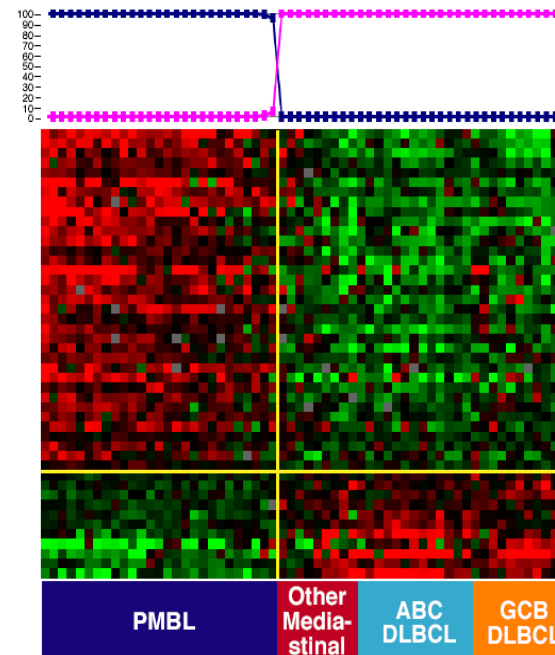
Nature, 2000 articles

Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling

Ash A. Alizadeh^{1,2}, Michael B. Eisen^{2,3,4}, R. Eric Davis⁵, Chi Ma⁵, Izidore S. Lossos⁶, Andreas Rosenwald⁵, Jennifer C. Boldrick¹, Hajeer Sabet⁵, Truc Tran⁵, Xin Yu⁵, John I. Powell⁷, Liming Yang⁷, Gerald E. Marti⁸, Troy Moore⁹, James Hudson Jr⁹, Lisheng Lu¹⁰, David B. Lewis¹⁰, Robert Tibshirani¹¹, Gavin Sherlock⁴, Wing C. Chan¹², Timothy C. Greiner¹², Dennis D. Weisenburger¹², James O. Armitage¹³, Roger Warnke¹⁴, Ronald Levy⁶, Wyndham Wilson¹⁵, Michael R. Grever¹⁶, John C. Byrd¹⁷, David Botstein⁴, Patrick O. Brown^{1,18} & Louis M. Staudt⁵

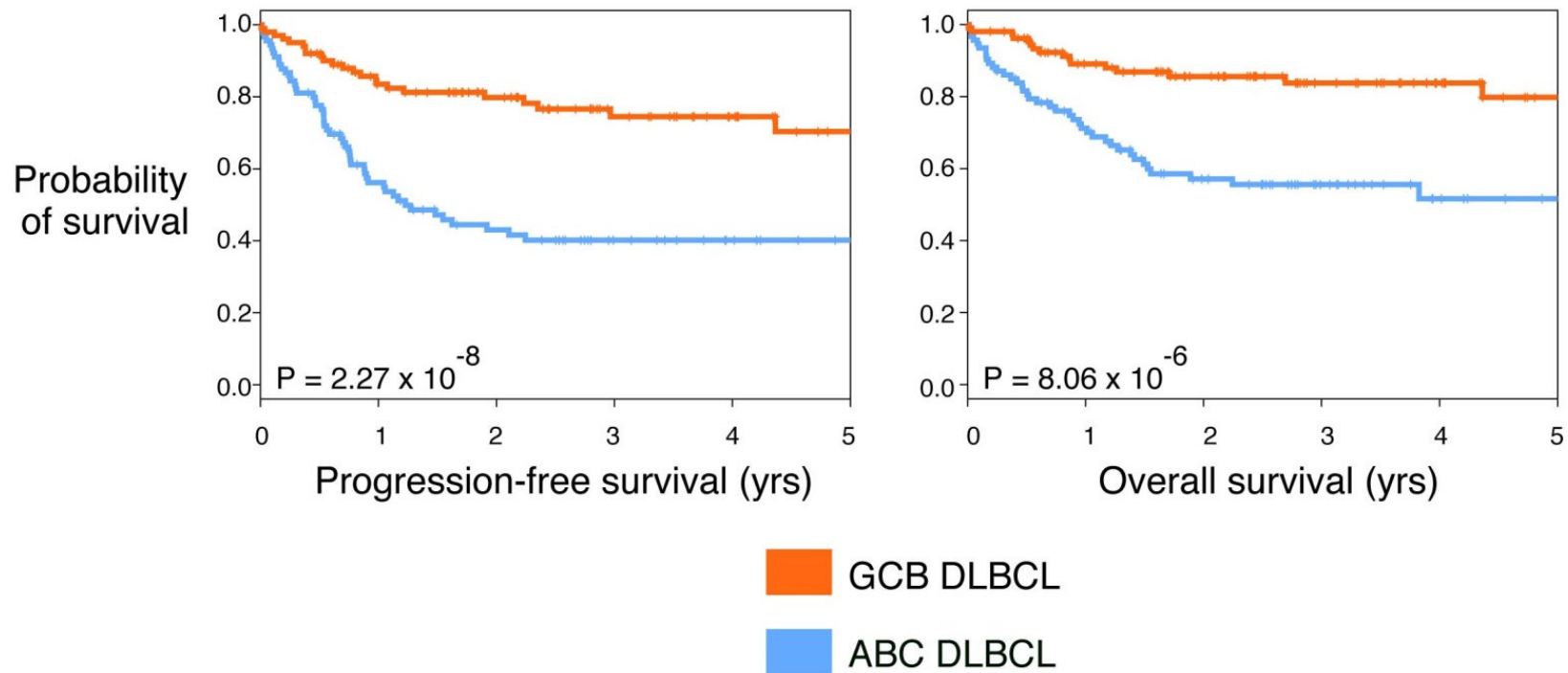


Wright et al., PNAS 2003



Rosenwald et al., J Exp Med 2003

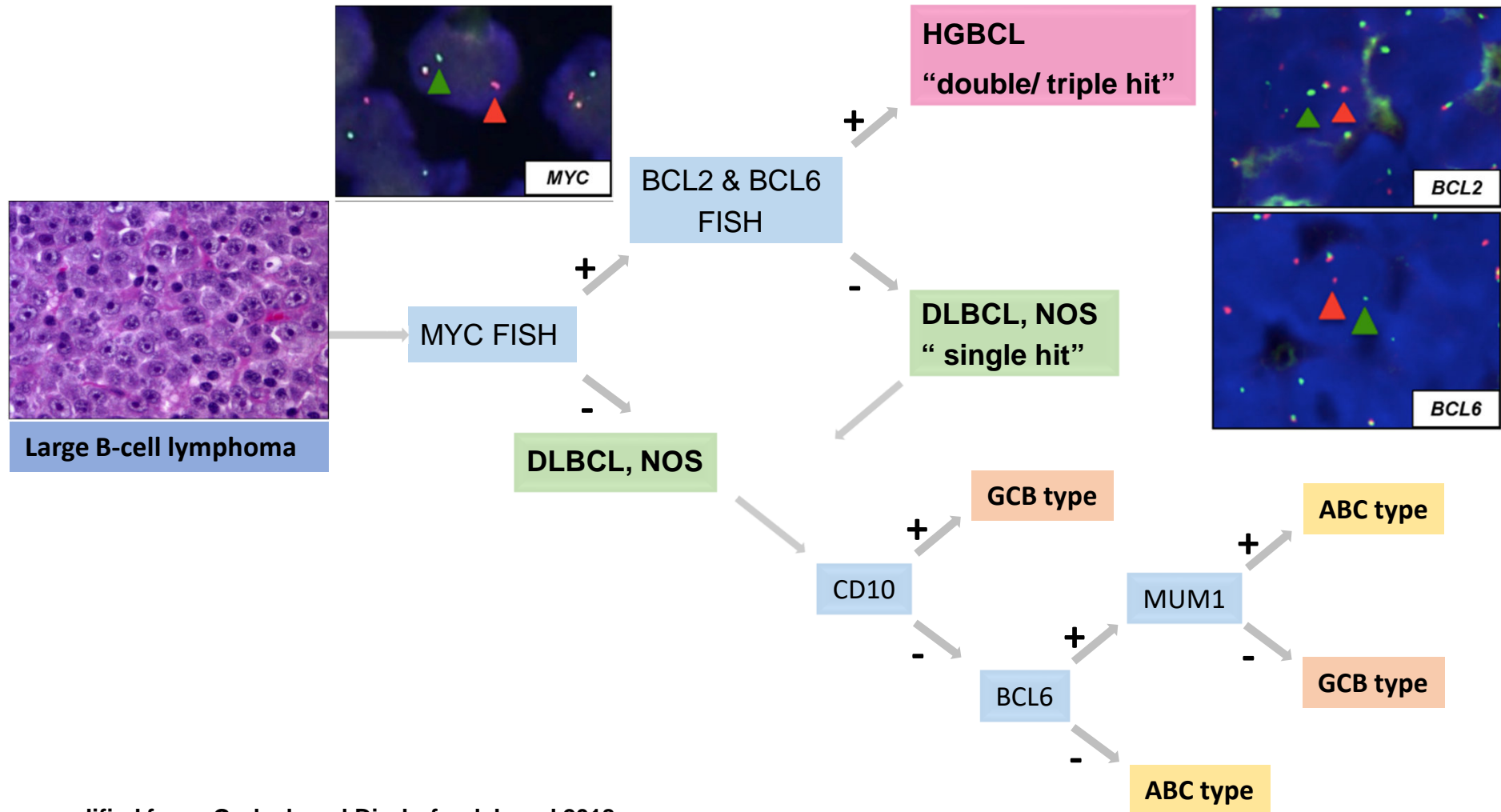
Unterschiedliche Prognose ABC vs. GCB-DLBCL (R-CHOP)



Lenz et al., NEJM, 2008



Diagnostischer Algorithmus: "large B-cell lymphoma"



modified from: Gerlach and Dirnhofer; labmed 2018

Klapper et al; Der Pathologe 2018

Scott et al; Blood 2018

Reinke et al; Virchows Archive 2018



Zusammenfassung

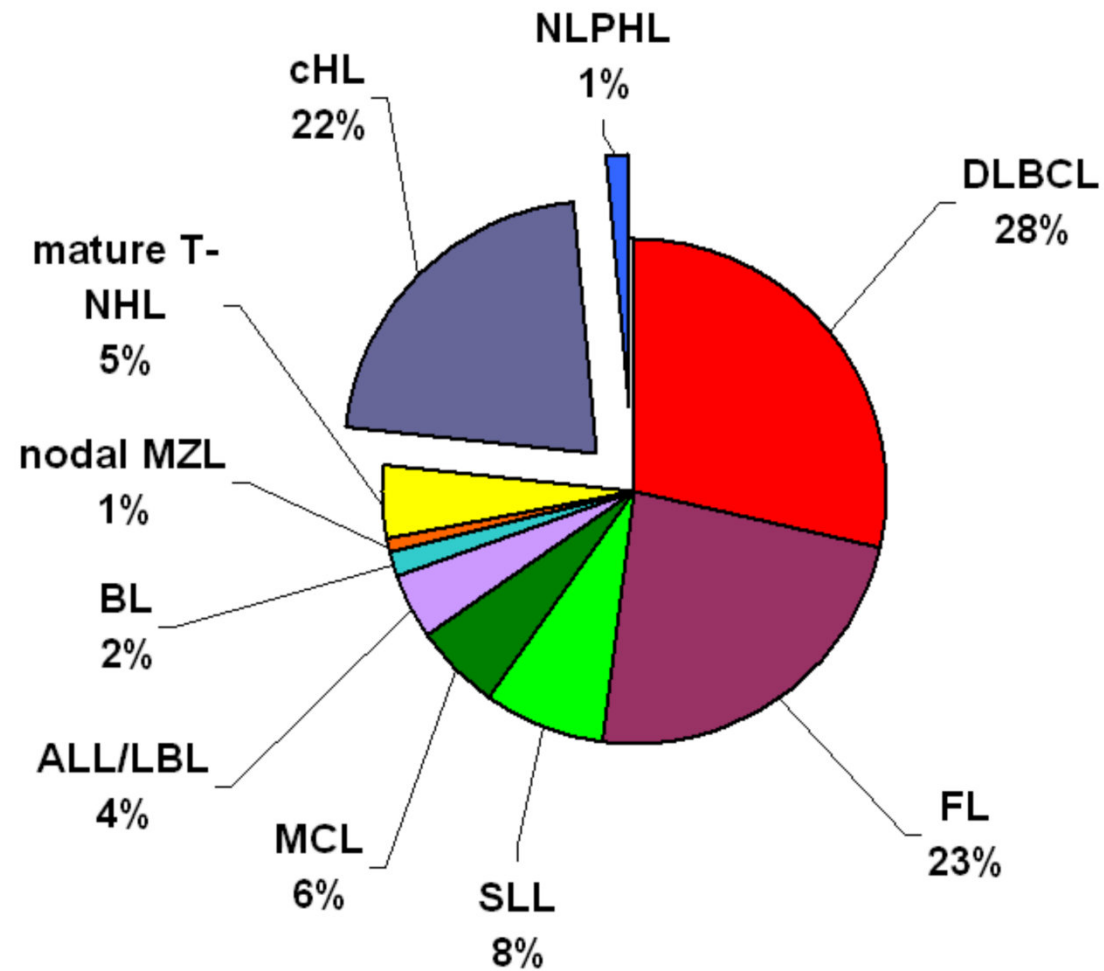
- **Pathologie – gewebebasierte Diagnostik**
- **Therapie**
- **Prognose**
- **Prädiktion**

- **Lymphomdiagnose durch Pathologie (WHO 2017)**
- **Klassifikation (>75 Lymphomtypen)**
- **WHO 2017: neue Varianten beim «Grosszelligen Lymphom»**

Vielen Dank

J

Was und in welcher Häufigkeit kommt vor?



Nodal



Prognostische Relevanz der Klassifikation

