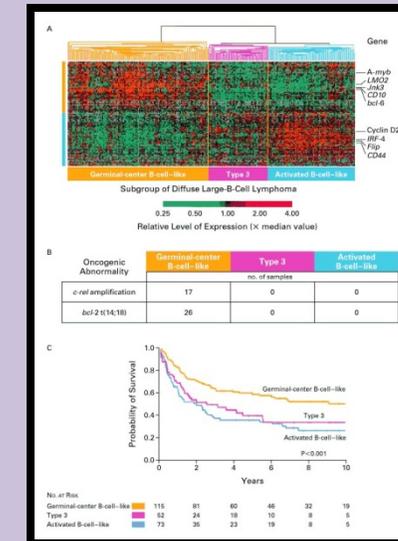
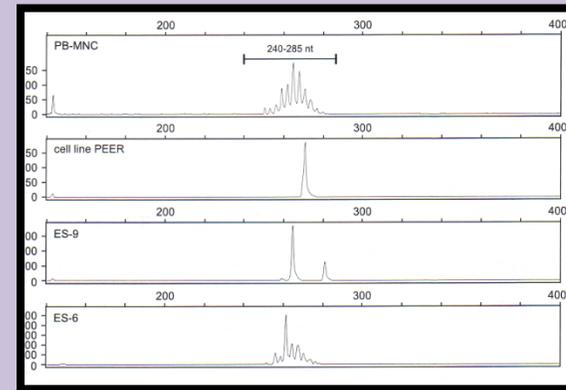
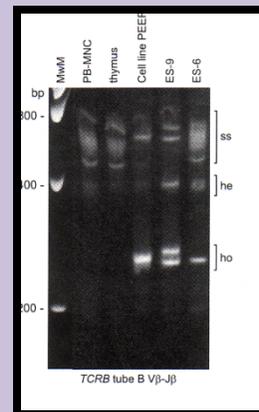
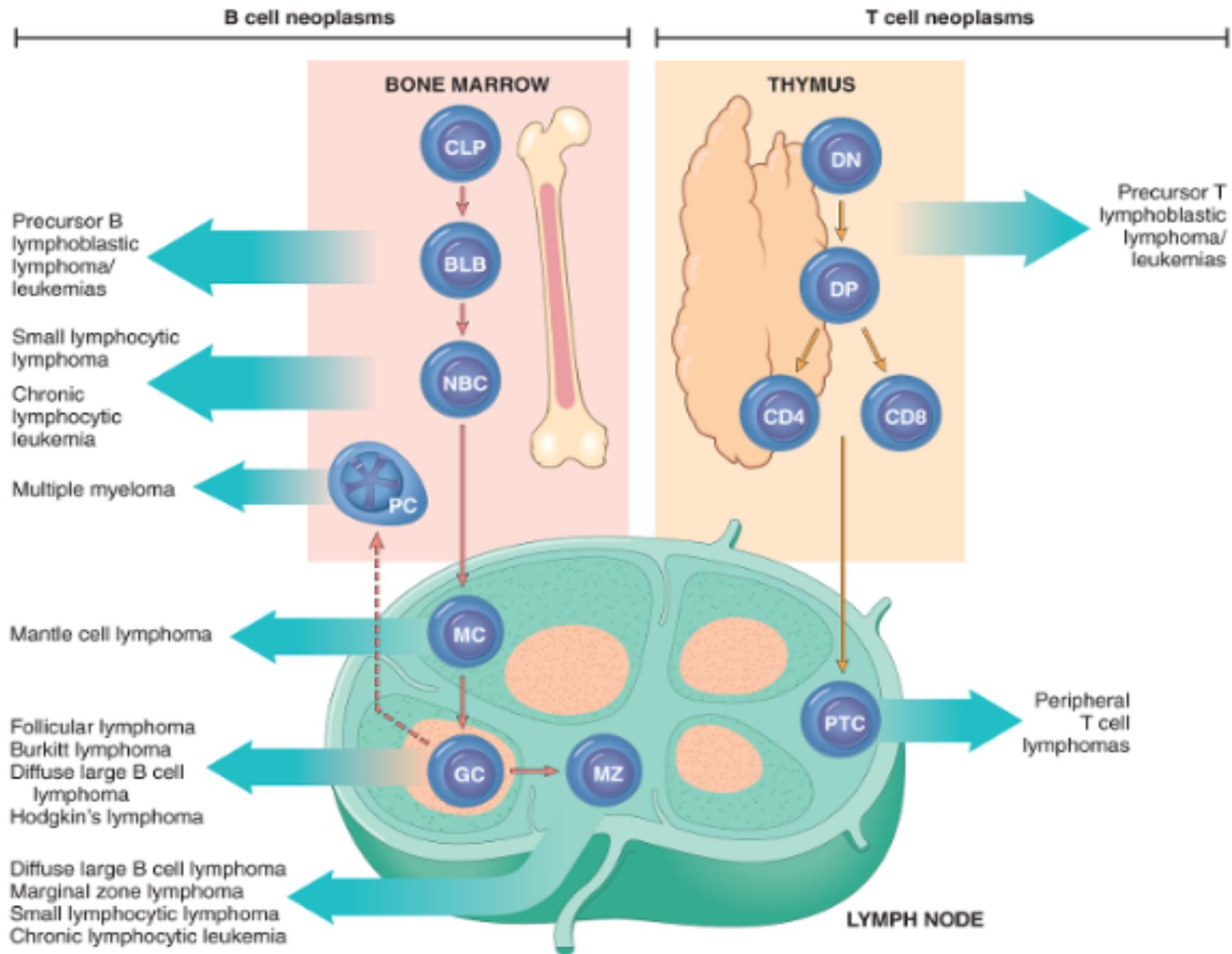


LENFOİD PRİMER NEOPLASTİK HASTALIKLAR

Prof. Dr. Işın Kuzu
Patoloji Anabilim Dalı
Dönem III Modül IV

16 MART 2017





Tarihteki Lenfoma Sınıflamaları

- Gall-Mallory (1940)
- Rappaport (1960)
- B.N.L.I (1973)
- Lukes-Collins (1974)
- Lennert (1974)
- WF (1980)
- REAL (1994)
- WHO (2001)
- **WHO GÜNCEL (2008)**



The International Lymphoma Study Group

Nancy Harris - Boston
 Elaine Jaffe - Bethesda
 Harald Stein - Berlin
 Peter Banks - San Antonio
 John Chan - Hong Kong
 Michael Cleary - Stanford
 Georges Delsol - Toulouse
 Chris De Wolf-Peeters - Leuven
 Brunangelo Falini - Perugia
 Kevin Gatter - Oxford

Thomas Grogan - Tucson
 Peter Isaacson - London
 Daniel Knowles - Cornell
 David Mason - Oxford
 Konrad Müller-Hermelink - Würzburg
 Stefano Pileri - Bologna
 Miguel Piris - Toledo
 Elizabeth Ralfkiaer - Copenhagen
 Roger Warnke - Stanford

PERSPECTIVE

A Revised European-American Classification of Lymphoid Neoplasms: A Proposal From the International Lymphoma Study Group

By Nancy Lee Harris, Elaine S. Jaffe, Harald Stein, Peter M. Banks, John K.C. Chan, Michael L. Cleary, Georges Delsol, Christine De Wolf-Peeters, Brunangelo Falini, Kevin C. Gatter, Thomas M. Grogan, Peter G. Isaacson, Daniel M. Knowles, David Y. Mason, Hans-Konrad Muller-Hermelink, Stefano A. Pileri, Miguel A. Piris, Elisabeth Ralfkiaer, and Roger A. Warnke

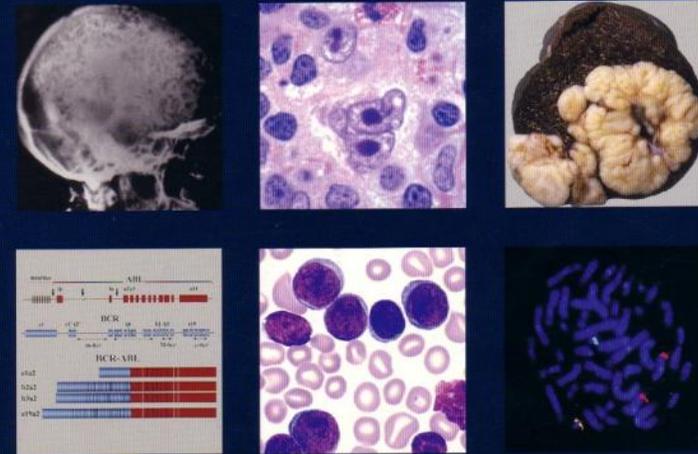
World Health Organization Classification of Tumours



Pathology & Genetics

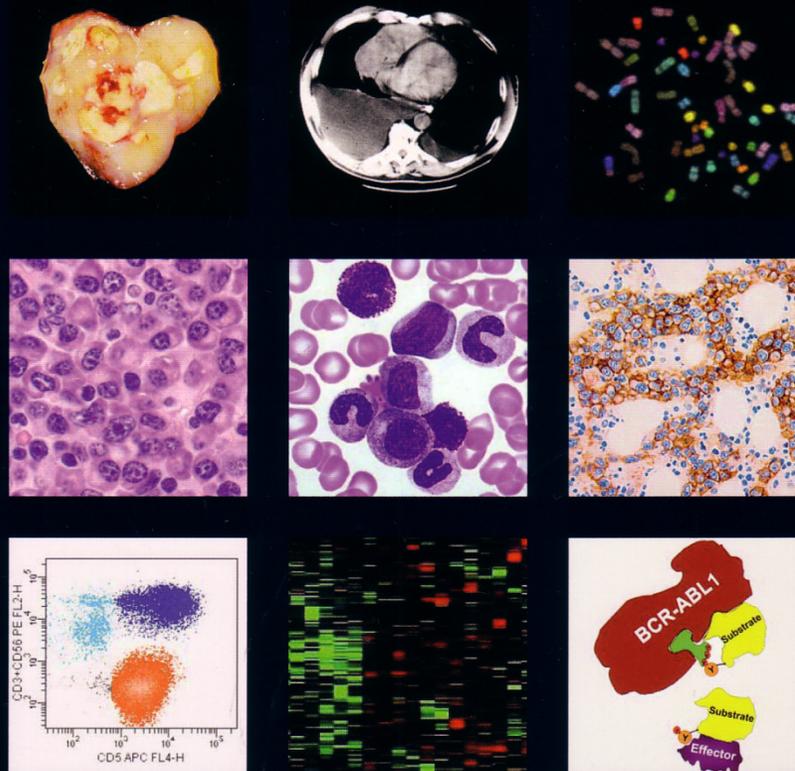
Tumours of Haematopoietic and Lymphoid Tissues

Edited by Elaine S. Jaffe, Nancy Lee Harris, Harald Stein, James W. Vardiman



WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

Edited by Steven H. Swerdlow, Elias Campo, Nancy Lee Harris, Elaine S. Jaffe, Stefano A. Pileri, Harald Stein, Jürgen Thiele, James W. Vardiman



WHO 2008

Onco-inflamamaları

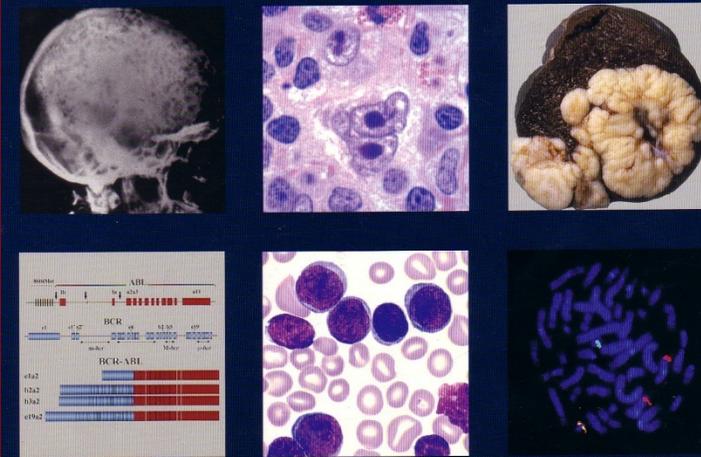
World Health Organization Classification of Tumours



Pathology & Genetics

Tumours of Haematopoietic and Lymphoid Tissues

Edited by Elaine S. Jaffe, Nancy Lee Harris, Harald Stein, James W. Vardiman



Classification of Lymphoid Neoplasms: International Lymphoma Study Group

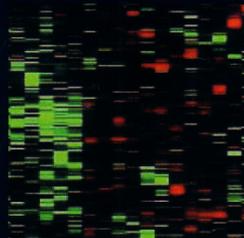
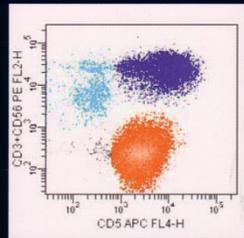
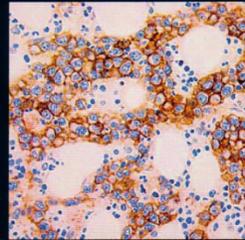
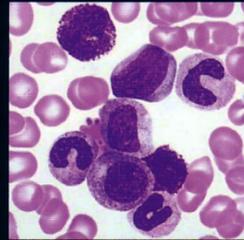
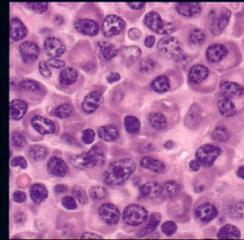
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WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues

Edited by Steven H. Swerdlow, Elias Campo, Nancy Lee Harris, Elaine S. Jaffe, Stefano A. Pileri, Harald Stein, Jürgen Thiele, James W. Vardiman



WHO 2016



WHO 2008

siniflamaları

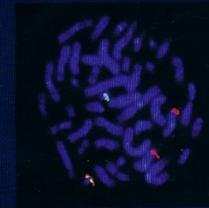
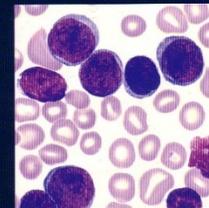
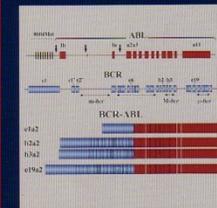
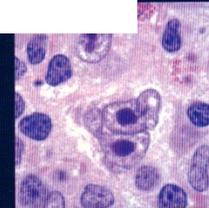
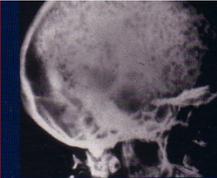
World Health Organization Classification of Tumours



Pathology & Genetics

Tumours of Haematopoietic and Lymphoid Tissues

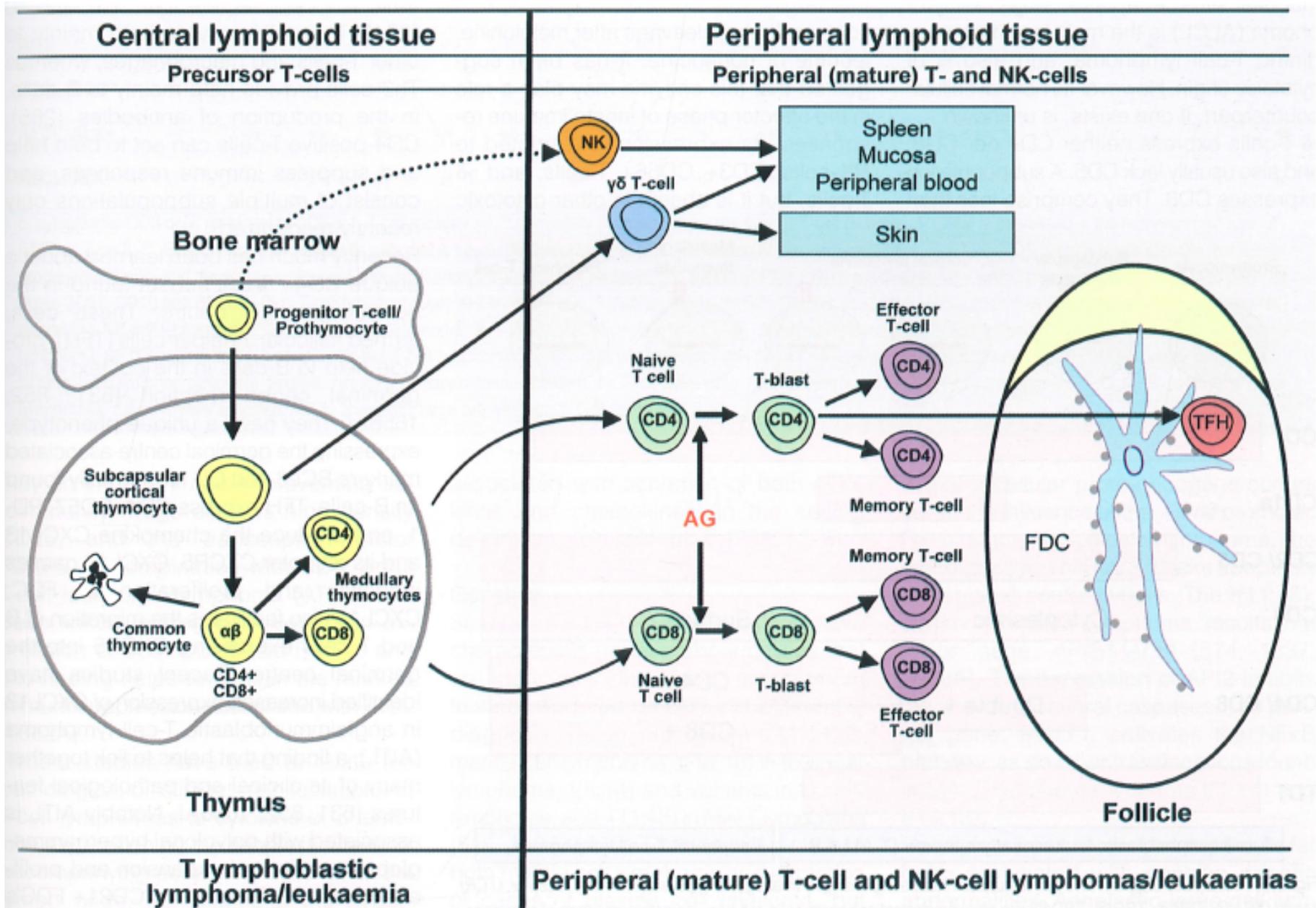
is, Harald Stein, James W. Vardiman



Classification of Lymphoid Neoplasms: International Lymphoma Study Group

ein, Peter M. Banks, John K.C. Chan, Michael L. Cleary, unangelo Falini, Kevin C. Gatter, Thomas M. Grogan, Mason, Hans-Konrad Muller-Hermelink, Stefano A. Pileri, Ralfkiaer, and Roger A. Warnke

T lenfositlerin gelişimi

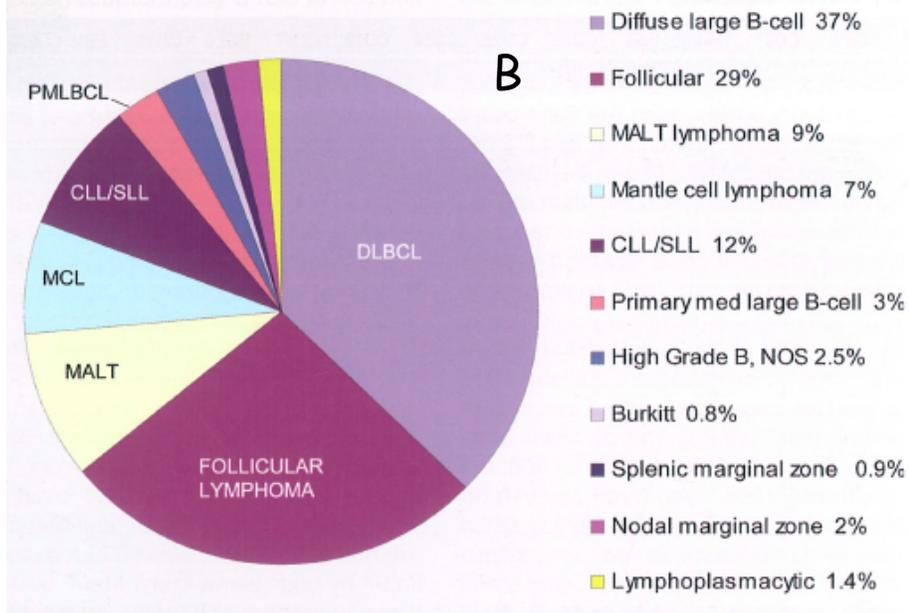


WHO Lenfoma Sınıflaması Ana Gruplar

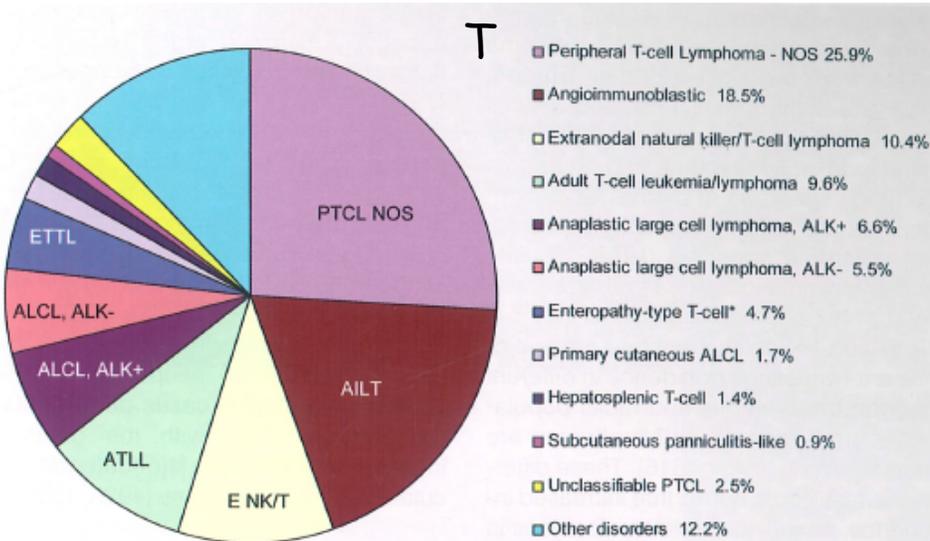
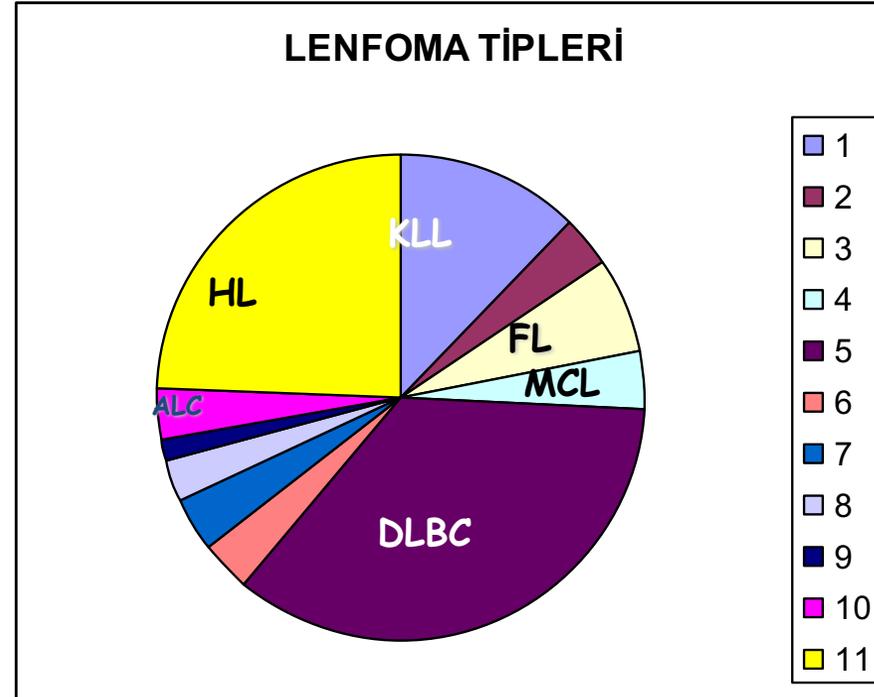
- 1- Prekürsor B ve T hücreli Lenfoma-Lösemi
- 2- Matür B hücreli Lenfomalar
- 3- Matür T-NK Hücreli Lenfomalar
- 4- Hodgkin Lenfoma
- 5- immünyetmezlikle ilişkili Lenfoproliferatif Hastalıklar
- 6- Histiyoitik Dendritik Hücreli Neoplaziler

Lenfomaların Görülme Sıklığı

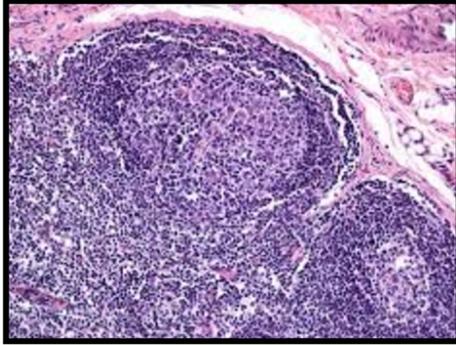
WHO 2008



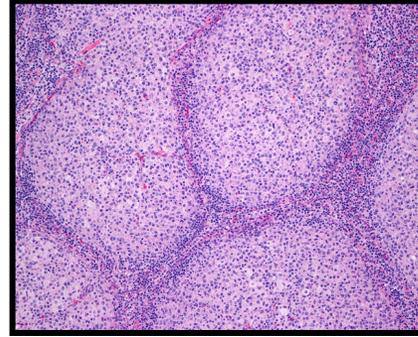
WHO Türkiye*
(*THD Lenfoma Kursu 2004)



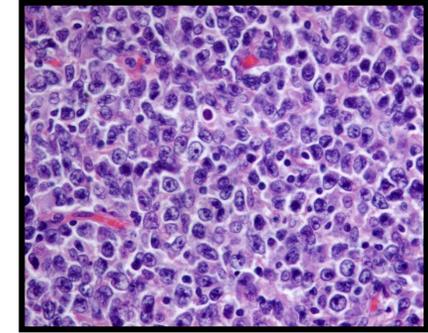
**LENFOMALARI ANLAMAK, TANIMAK VE
HASTALIKLA BAŞAÇIKMAK İÇİN
NORMAL LENFOSİT BİYOLOJİSİNİ BİLMELİYİZ**



REAKTİF



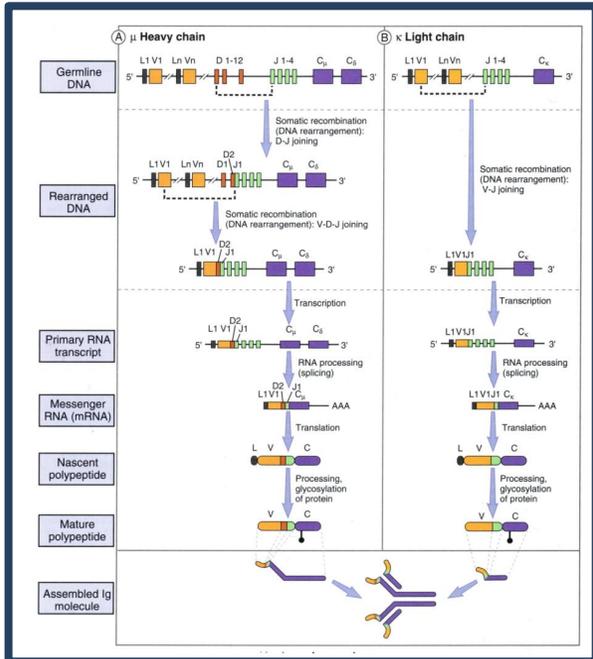
**FOLLİKÜLER
LENFOMA**



**DİFFÜZ BÜYÜK B
HÜCRELİ LENFOMA**

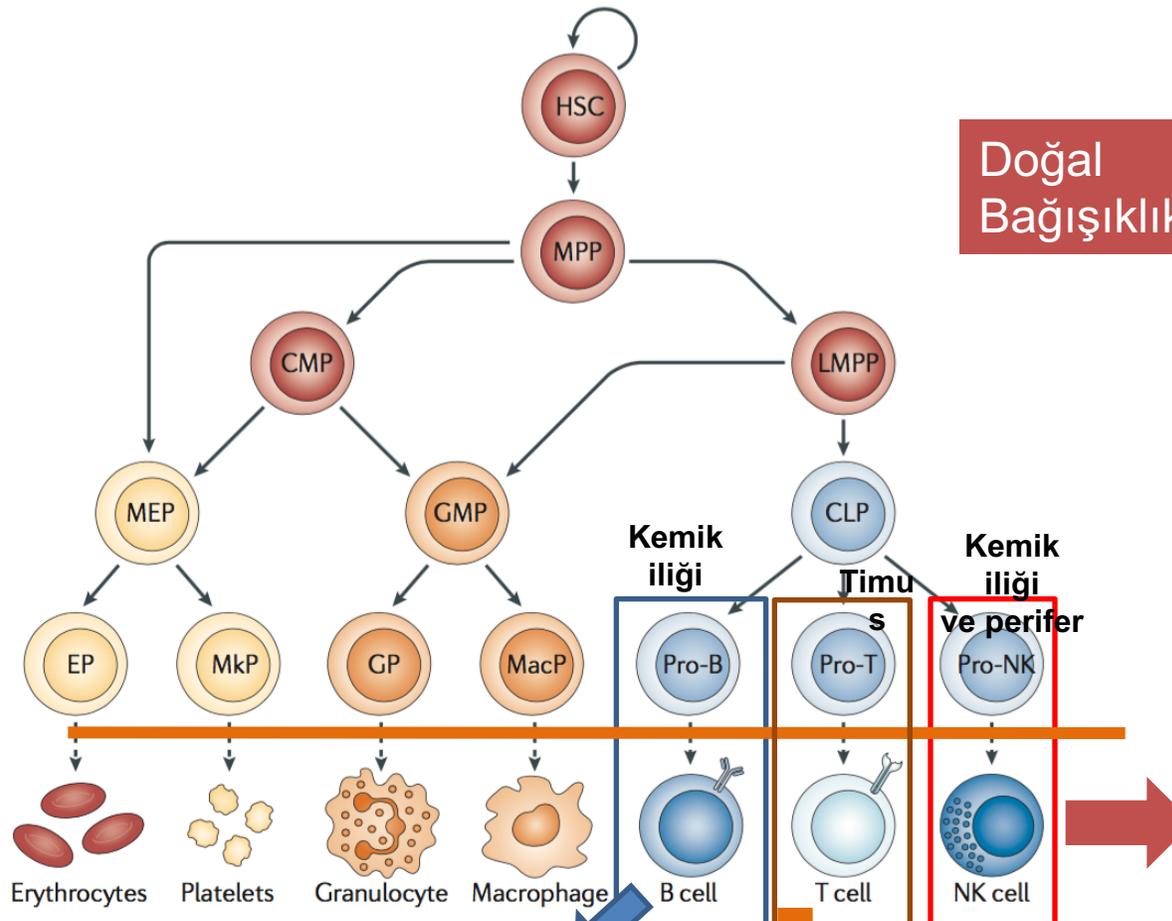
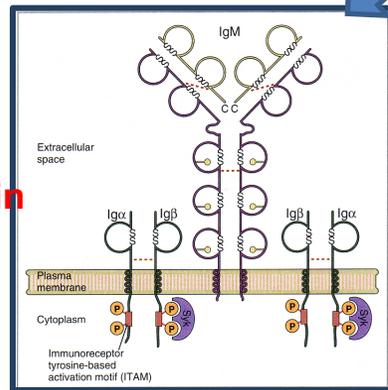
Lenfoid Hücreler

Hümmoral Bağışıklık

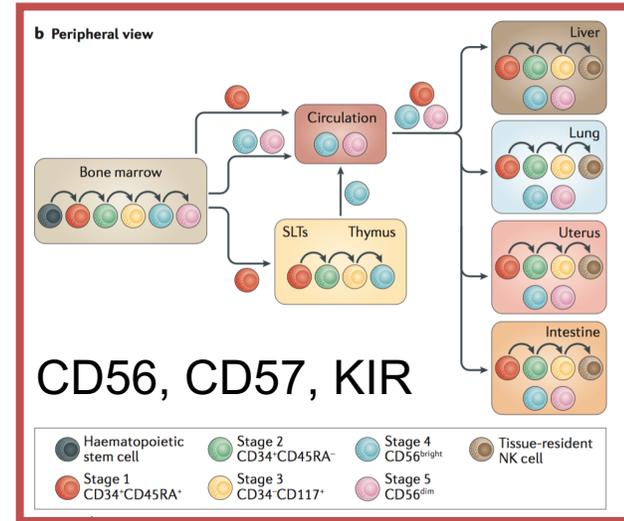
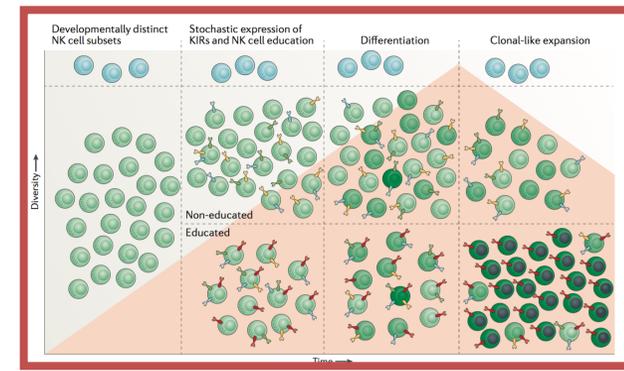


Cedar, Nat Rev Immunol 2015
 Björkström Nat Rev Immunol 2016
 Abbas, Cellular & Molecular Immunology

B hücre Reseptörü
Immunglobulin (Ig) Molekülü

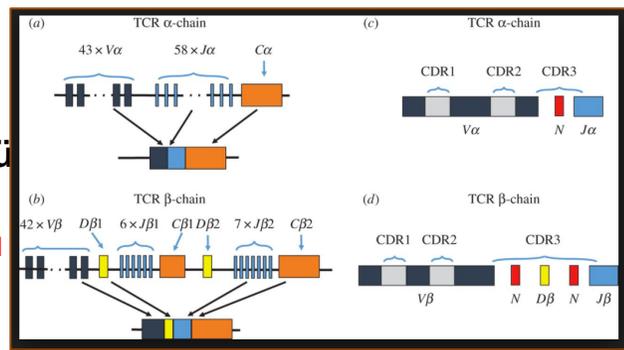
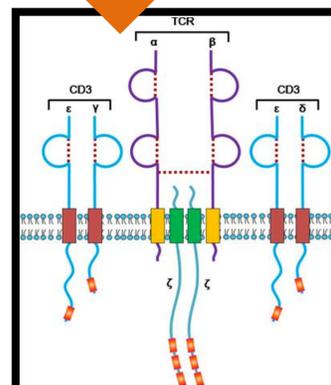


Doğal Bağışıklık



Hüresel Bağışıklık

T Hücre reseptörü
TCR Molekülü



Antijenden bağımsız B Hücre farklılaşması

KEMİK İLİĞ

ÖNCÜ B HÜCRELERİ



TdT



B hücre reseptörü (Ig)

Gen düzenlenmesi



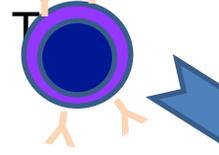
T(14:18)

Bcl2

T(11:14) **Siklin D1**

ÇEVRE LENFOİD DOKU

OLGUN B LENFOSİ



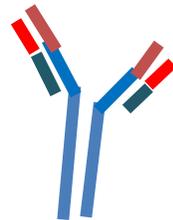
“NAİVE” OLGUN B LENFOSİ



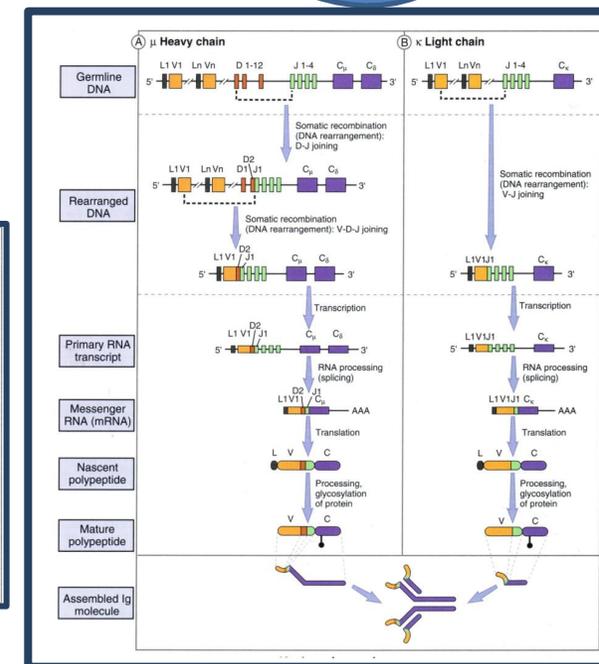
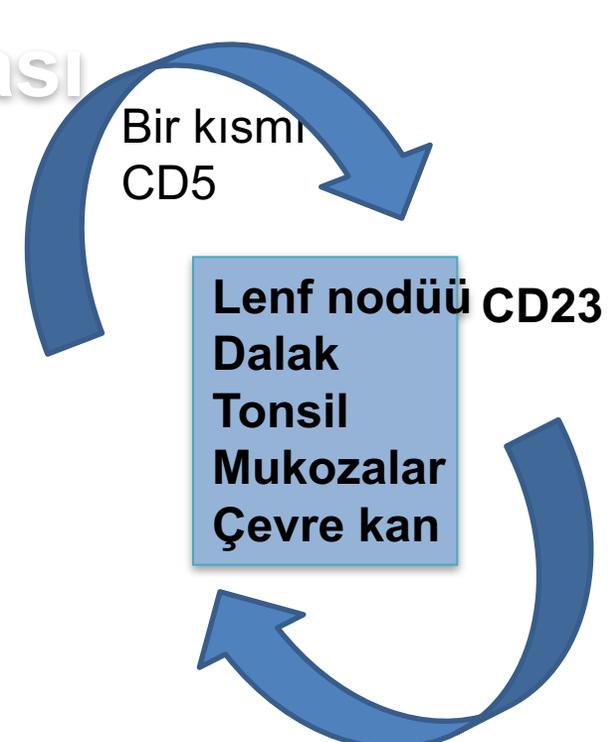
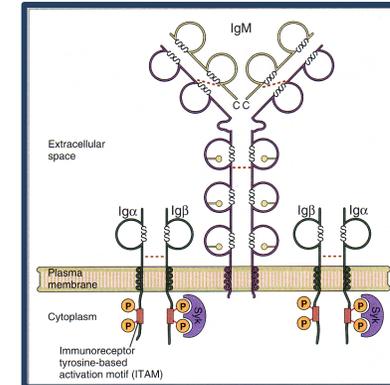
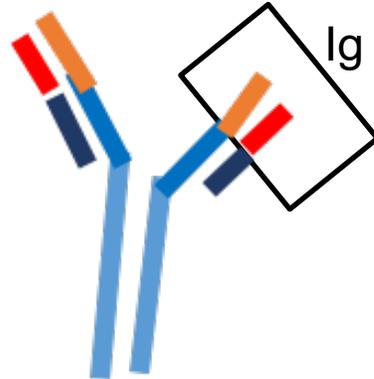
PRİMER FOLLİKÜL

IgD
IgM

Ig molekülü



Ig V bölgesi



Antijenden bağımsız B Hücre farklılaşması

KEMİK İLİĞ

ÖNCÜ B
HÜCRELERİ



TdT



B hücre reseptörü
(Ig)
Gen düzenlenmesi



ÇEVRE LENFOİD DOKU

OLGUN
B
LENFOSİ



“NAİVE”
OLGUN
B
LENFOSİ



PRİMER FOLLİKÜL



IgD
IgM

Bir kısmı
CD5+
(otoantikörlere
reaktif)

CD20+
CD19+
CD22+
CD40+
CD79A+
HLA C II+
CD21+
CD35+
CD23+

Lenf nodüü CD23
Dalak
Tonsil
Mukozalar
Çevre kan

Naive B hücre Alt grupları

- 1- CD23+ dolaşan non otoreaktif
- 2- CD23+ dolaşan düşük affinite otoreaktif (B1)
- 3- CD23 – otoreaktif olmayan

Antijen ile gelişen B Hücre farklılaşması

KEMİK İLİĞİ

ÖNCÜ B
HÜCRELERİ



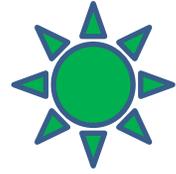
TdT



B hücre reseptörü (Ig)
Gen düzenlenmesi



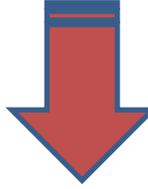
OLGUN B
LENFOSİT



ANTİJEN

Antijenle
Düşük
bağlanma
Yeteneğinde Ig

"NAİVE"
OLGUN B
LENFOSİT

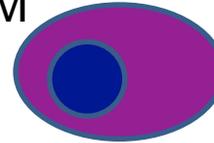


ÇEVRE LENFOİD DOKU

PRİMER FOLLİKÜL



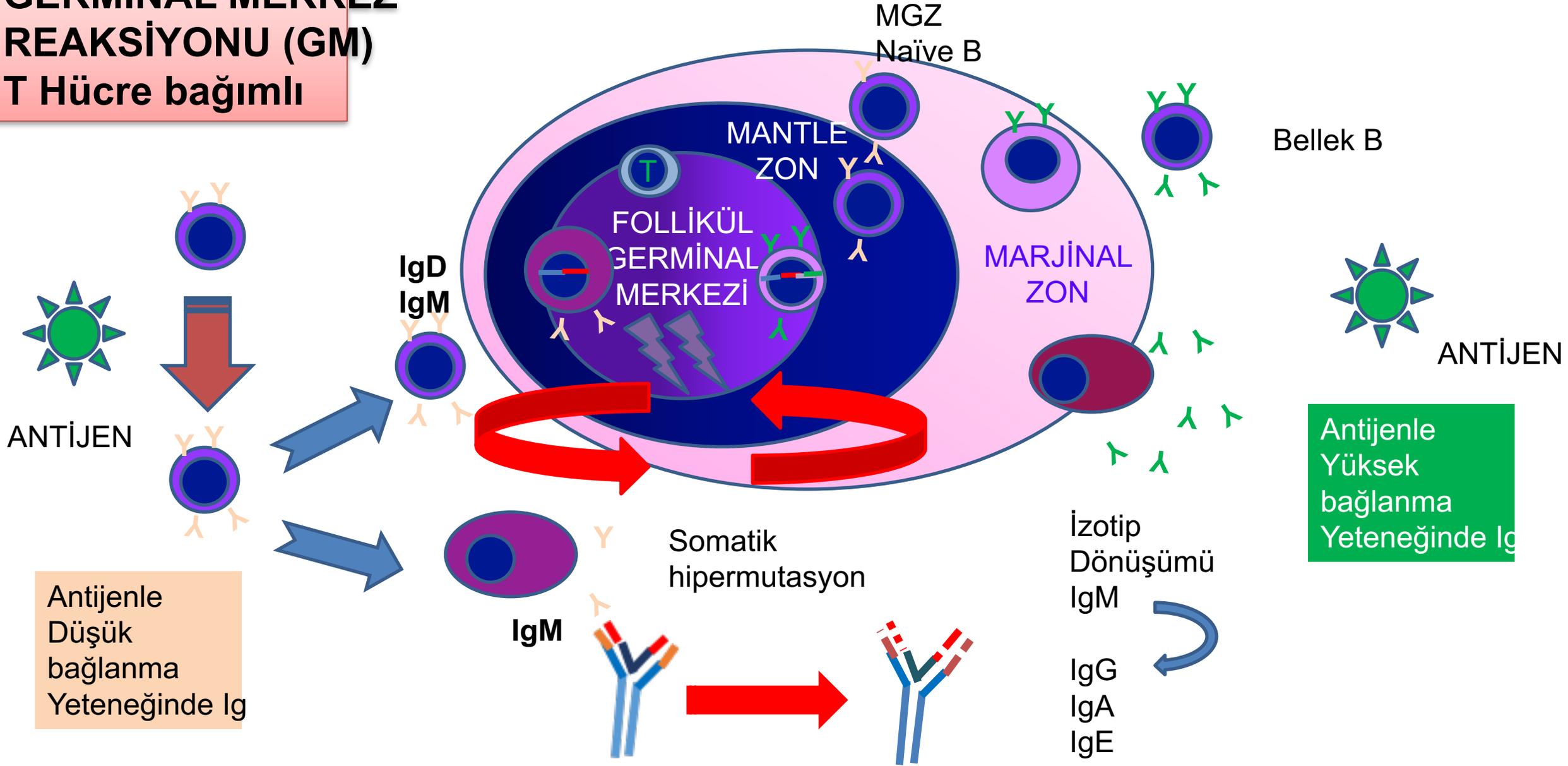
IgM



1. T Hücre bağımsız

GERMİNAL MERKEZ REAKSİYONU (GM) T Hücre bağımlı

AFİNİTE OLGUNLAŞMA



MATURE B-CELL NEOPLASMS

Chronic lymphocytic leukaemia/ small lymphocytic lymphoma	9823/3
B-cell prolymphocytic leukaemia	9833/3
Splenic marginal zone lymphoma	9689/3
Hairy cell leukaemia	9940/3
<i>Splenic B-cell lymphoma/leukaemia, unclassifiable</i>	9591/3
<i>Splenic diffuse red pulp small B-cell lymphoma</i>	9591/3
<i>Hairy cell leukaemia-variant</i>	9591/3
Lymphoplasmacytic lymphoma	9671/3
Waldenström macroglobulinemia	9761/3
Heavy chain diseases	9762/3
Alpha heavy chain disease	9762/3
Gamma heavy chain disease	9762/3
Mu heavy chain disease	9762/3
Plasma cell myeloma	9732/3
Solitary plasmacytoma of bone	9731/3
Extrasosseous plasmacytoma	9734/3
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)	9699/3
Nodal marginal zone lymphoma	9699/3
<i>Paediatric nodal marginal zone lymphoma</i>	9699/3
Follicular lymphoma	9690/3
<i>Paediatric follicular lymphoma</i>	9690/3
Primary cutaneous follicle centre lymphoma	9597/3

Mantle cell lymphoma	9673/3
----------------------	--------

Diffuse large B-cell lymphoma (DLBCL), NOS	9680/3
T-cell/histiocyte rich large B-cell lymphoma	9688/3
Primary DLBCL of the CNS	9680/3
Primary cutaneous DLBCL, leg type	9680/3
<i>EBV positive DLBCL of the elderly</i>	9680/3
DLBCL associated with chronic inflammation	9680/3
Lymphomatoid granulomatosis	9766/1
Primary mediastinal (thymic) large B-cell lymphoma	9679/3
Intravascular large B-cell lymphoma	9712/3
ALK positive large B-cell lymphoma	9737/3
Plasmablastic lymphoma	9735/3
Large B-cell lymphoma arising in HHV8- associated multicentric Castleman disease	9738/3
Primary effusion lymphoma	9678/3
Burkitt lymphoma	9687/3
B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma	9680/3
B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma	9596/3

MATURE B-CELL NEOPLASMS

Chronic lymphocytic leukaemia/
small lymphocytic lymphoma

B-cell prolymphocytic leukaemia

Splenic marginal zone lymphoma

Hairy cell leukaemia

Splenic B-cell lymphoma/leukaemia, unclassifiable

Splenic diffuse red pulp small B-cell lymphoma

Hairy cell leukaemia-variant

Lymphoplasmacytic lymphoma

Waldenström macroglobulinemia

Heavy chain diseases

Alpha heavy chain disease

Gamma heavy chain disease

Mu heavy chain disease

Plasma cell myeloma

Solitary plasmacytoma of bone

Extraosseous plasmacytoma

9823/3

9833/3

9689/3

9940/3

9591/3

9591/3

9591/3

9671

9761

9762

9762

9762

9762

9732

9731

9734

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

9699/3

Nodal marginal zone lymphoma

9699/3

Paediatric nodal marginal zone lymphoma

9699/3

Follicular lymphoma

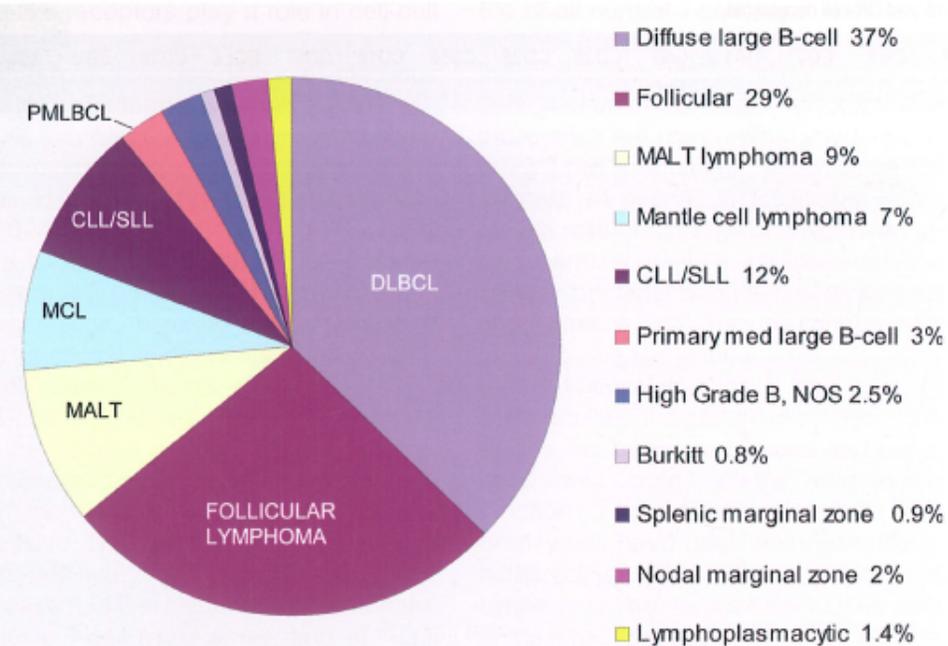
9690/3

Paediatric follicular lymphoma

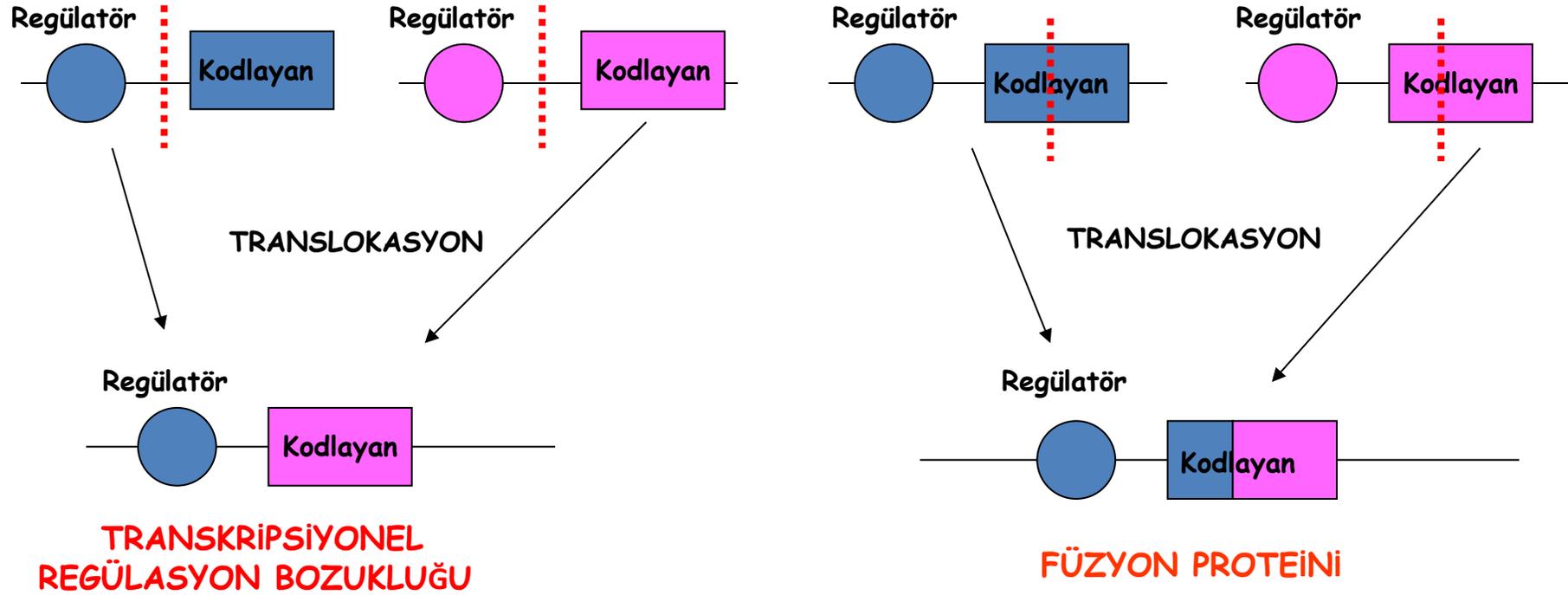
9690/3

Primary cutaneous follicle centre lymphoma

9597/3



INDOLENT B HÜCRELİ LENFOMALARDA GÖRÜLEN KROMOZOMAL TRANSLOKASYONLAR



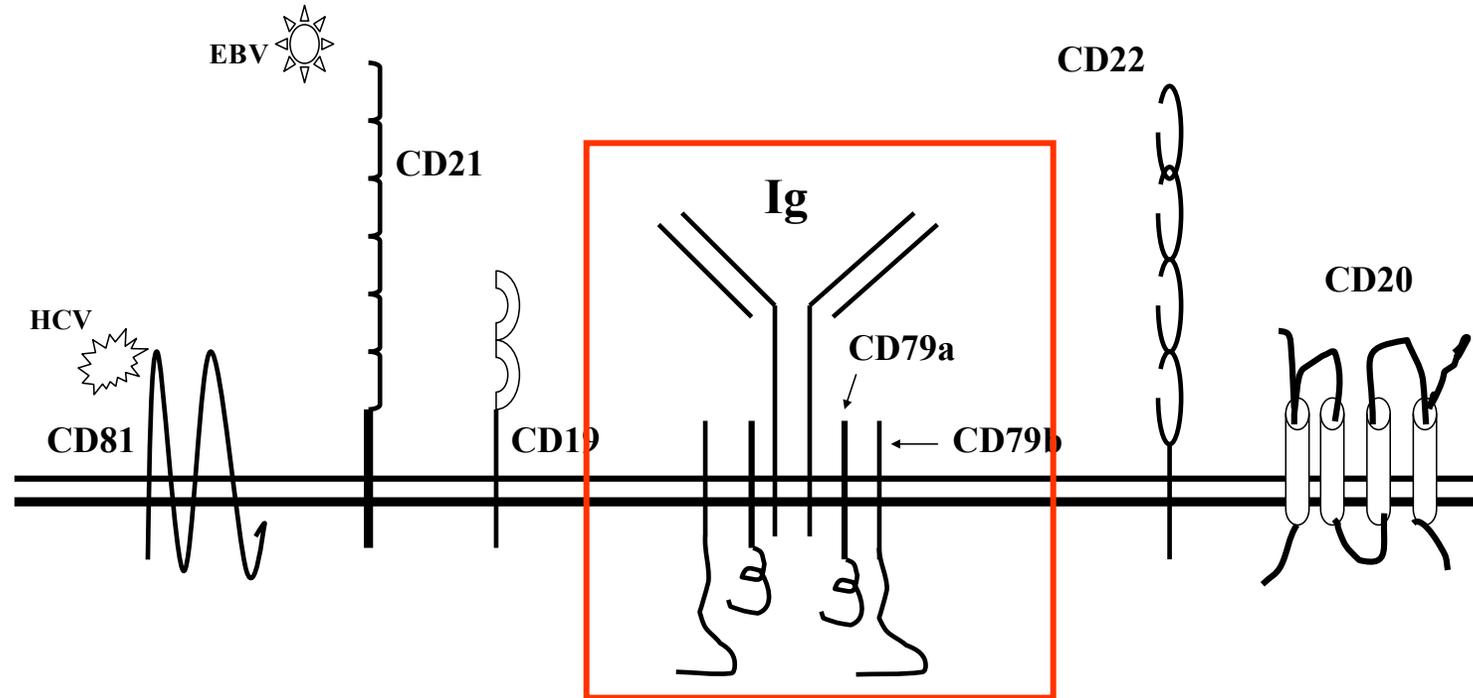
**TRANSKRİPSİYONEL
REGÜLASYON BOZUKLUĞU**

FÜZYON PROTEİNİ

t(14;18) IgH/Bcl-2
t(1;14) IgH/Bcl-10
t(11;14) IgH/Cyclin D1

t(11;18) API2/MALT1

B Hücre Reseptör Kompleksi "BCR"



B Hücre Reseptör (BCR) Kompleksi

Küçük lenfositik lenfoma / Kronik Lenfositik Lösemi (SLL/CLL). (ICQ=SLL: 9670/3 - CLL: 9823/3)

CLL : Kemik iliği ve periferik kan tutulumuyla karakterli prezentasyon

SLL : Periferik kan tutulumu olmayan, Lenf Nodülü ile birlikte kemik iliği tutulumunun bulunabildiği prezentasyon

Tutulum patternleri:

Lenf Nodülü:

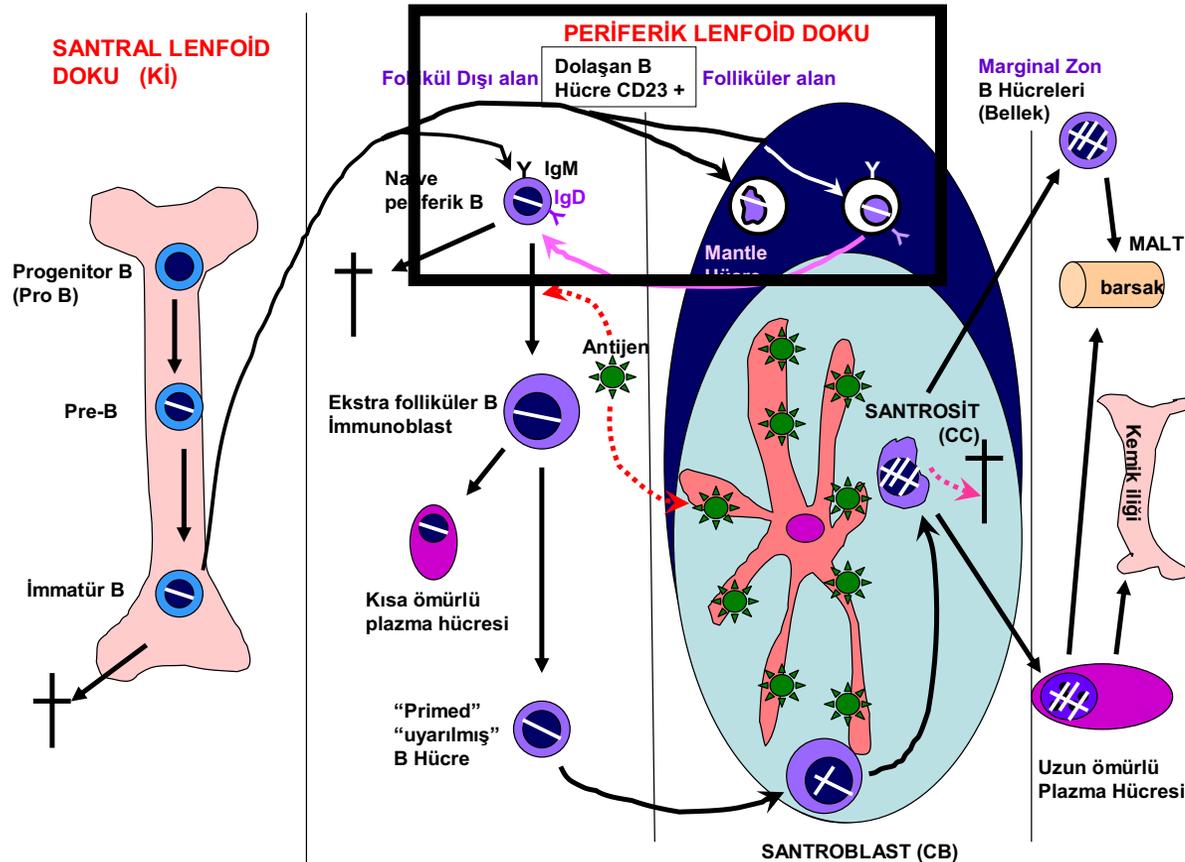
Diffüz

Kemik iliği:

Diffüz, Nodüler, interstisyel veya kombine

Küçük lenfositik lenfoma / Kronik Lenfositik Lösemi (SLL/CLL). (ICQ=SLL: 9670/3 - CLL: 9823/3)

Ig gen rearanjmanı (düzenlenmesi) +
Ig VH gen somatik mutasyon - (%40-50)
CD5+, CD23+, IgD ve IgM birlikte + **Naive B lenfositleri**

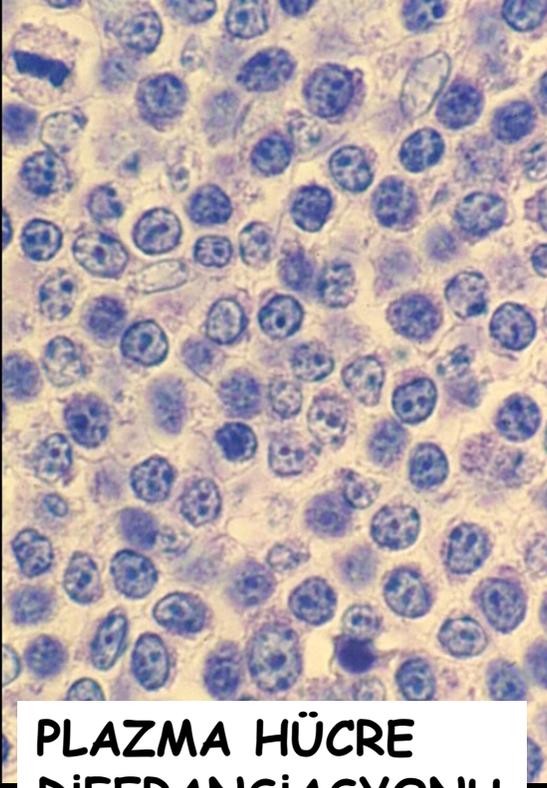


Hücre Kökeni

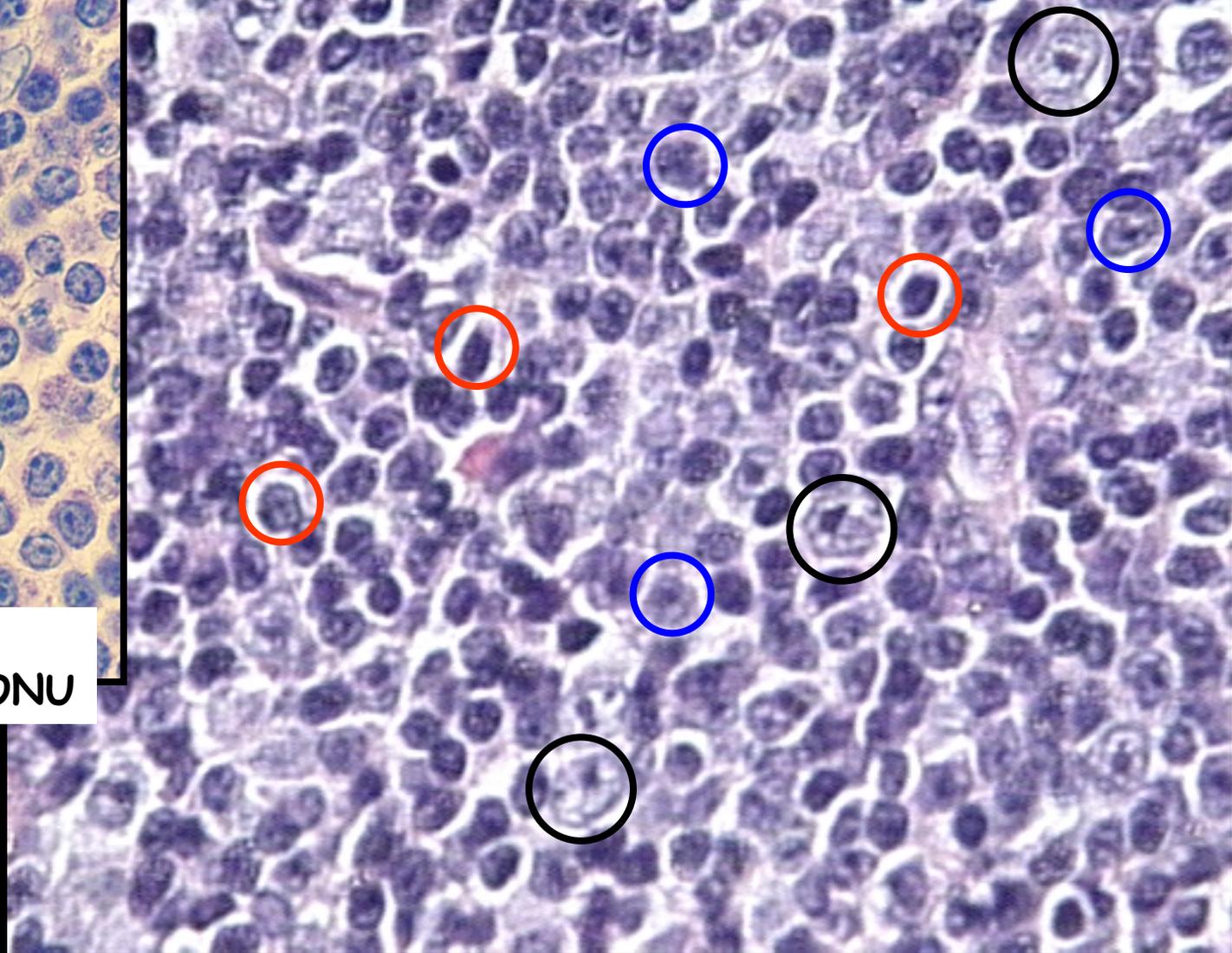
Ig gen rearanjmanı (düzenlenmesi) + /
Ig VH genlerinde somatik mutasyon +
(%50-60)

CD5+, IgM+
**Periferik kan
Memory B
hücreleri**

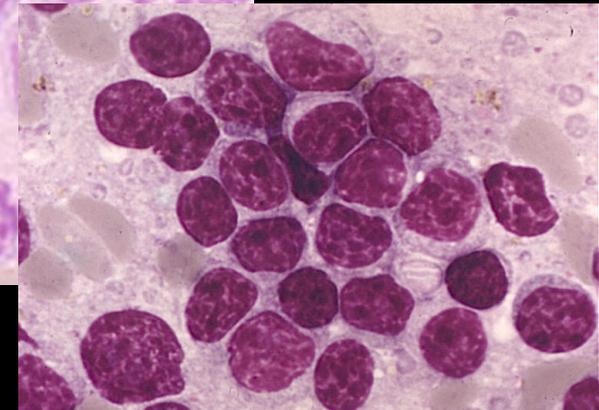
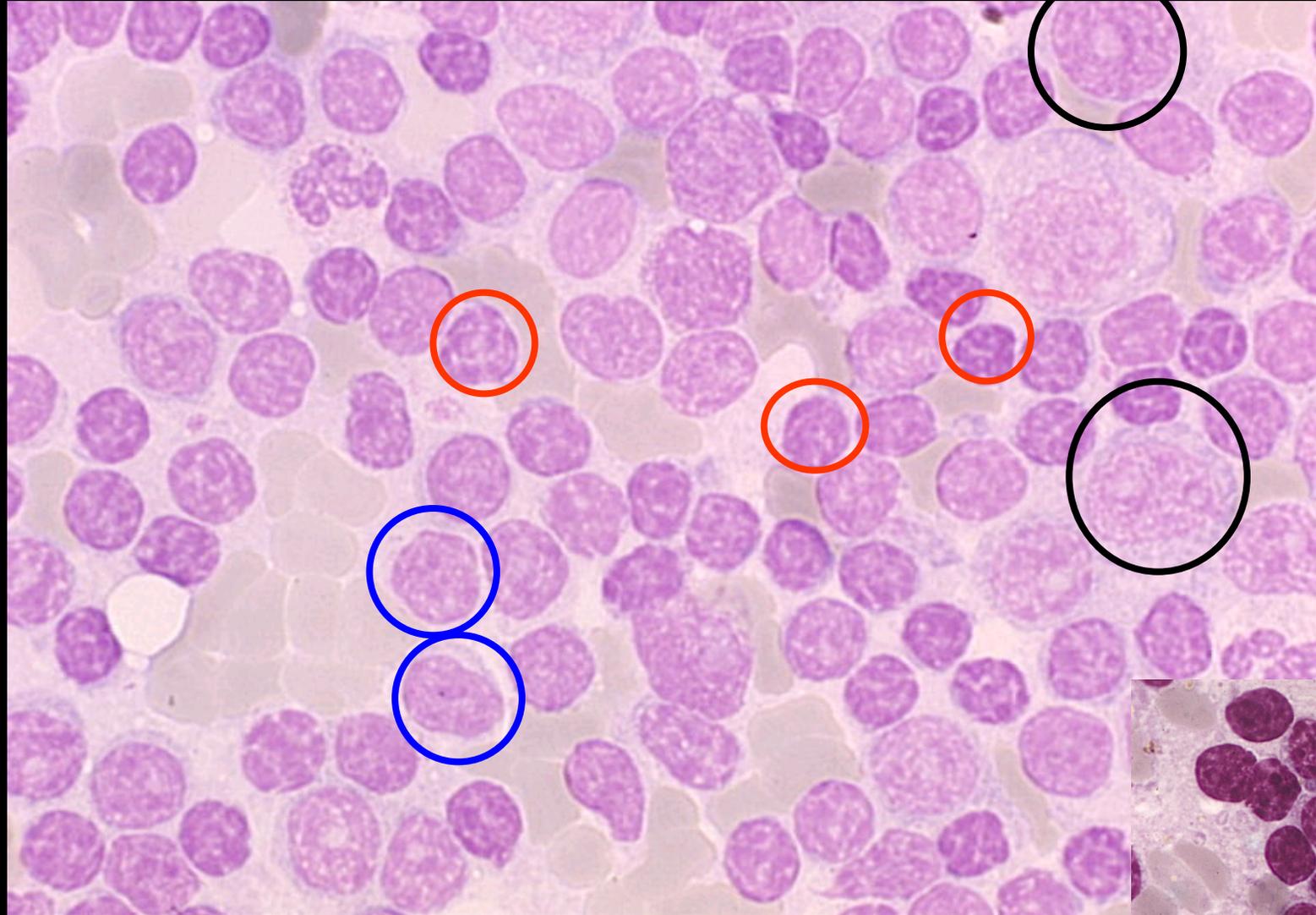
**Küçük lenfositik lenfoma / Kronik Lenfositik Lösemi
(SLL/CLL). (ICQ=SLL: 9670/3 - CLL: 9823/3)**



**PLAZMA HÜCRE
DİFERANSİASYONU**



**Küçük lenfositik lenfoma / Kronik Lenfositik Lösemi
(SLL/CLL). (ICQ=SLL: 9670/3 - CLL: 9823/3)**

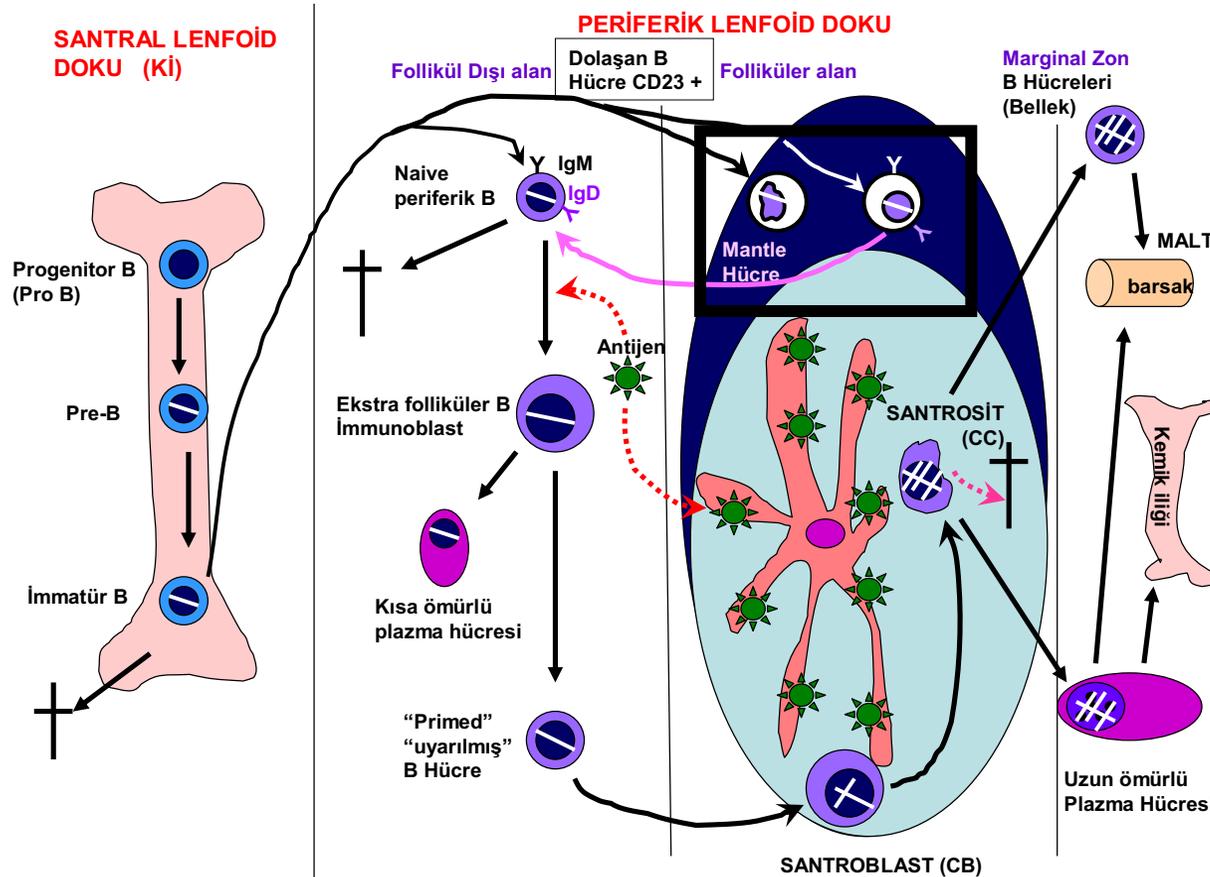


Mantle Hücreli Lenfoma (MCL) (ICQ= 9673/3)

Genetik Özellikler:

Ig gen düzenlenmesi +
Ig HV genleri somatik mutasyon -

Hücre Kökeni:
Foliküllerin
Mantle zon
alanlarındaki
küçük çentikli
naive B
lenfositler

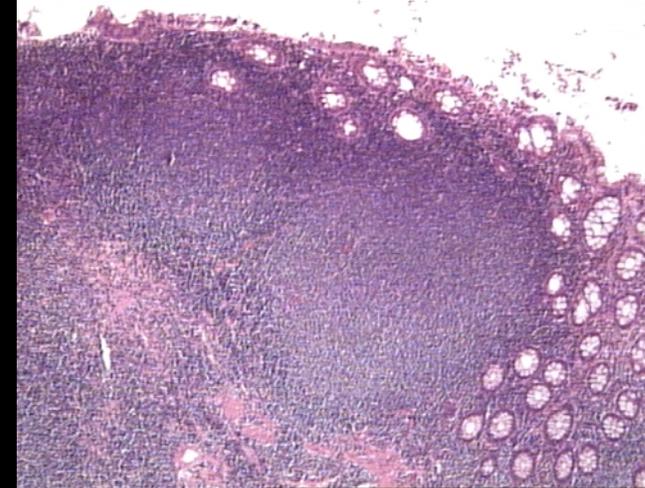
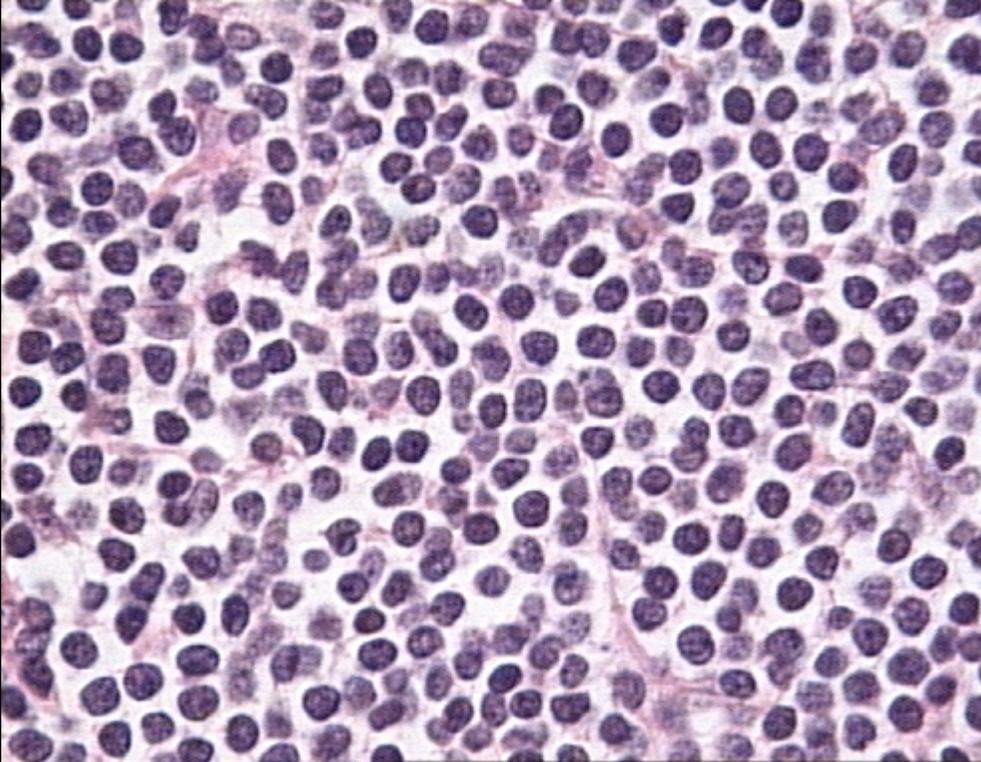


Mantle Hücreli Lenfoma (MCL) (ICQ= 9673/3)

LN,

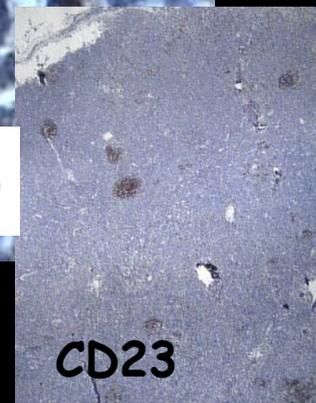
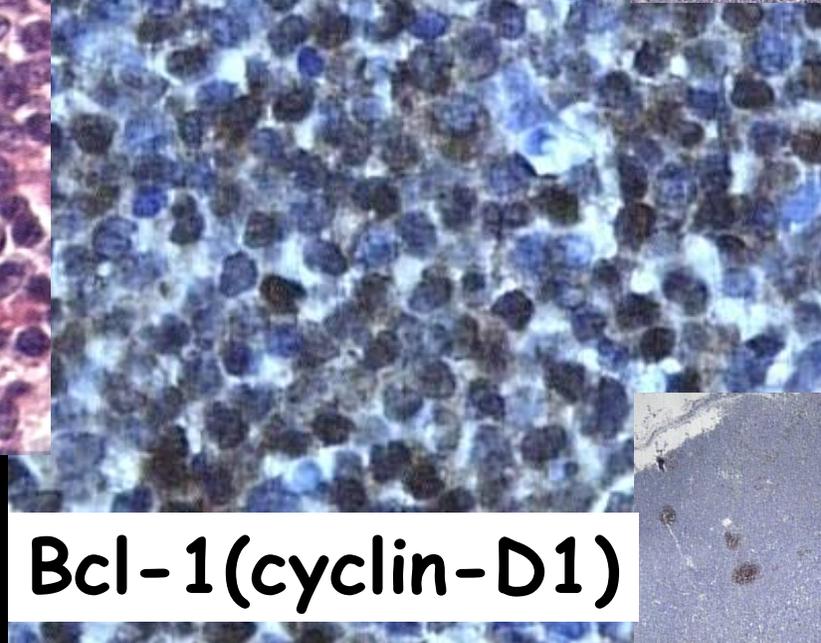
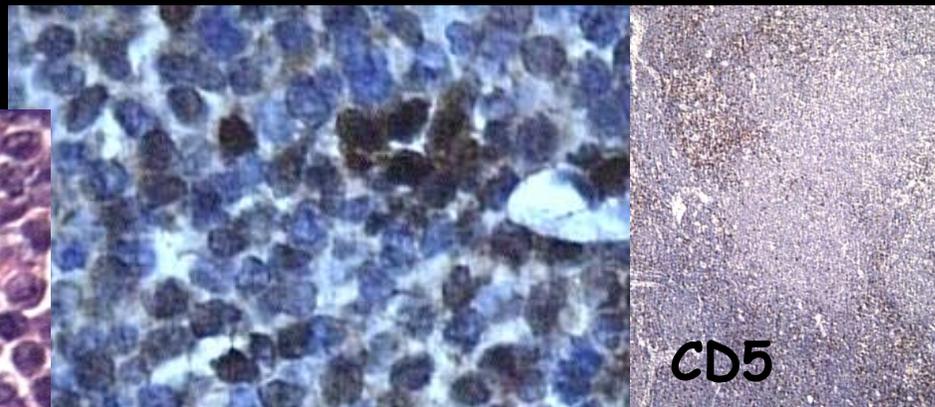
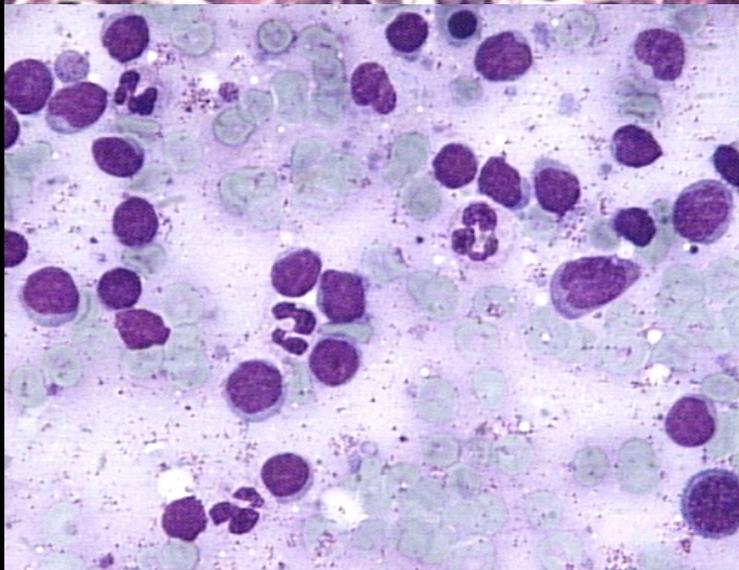
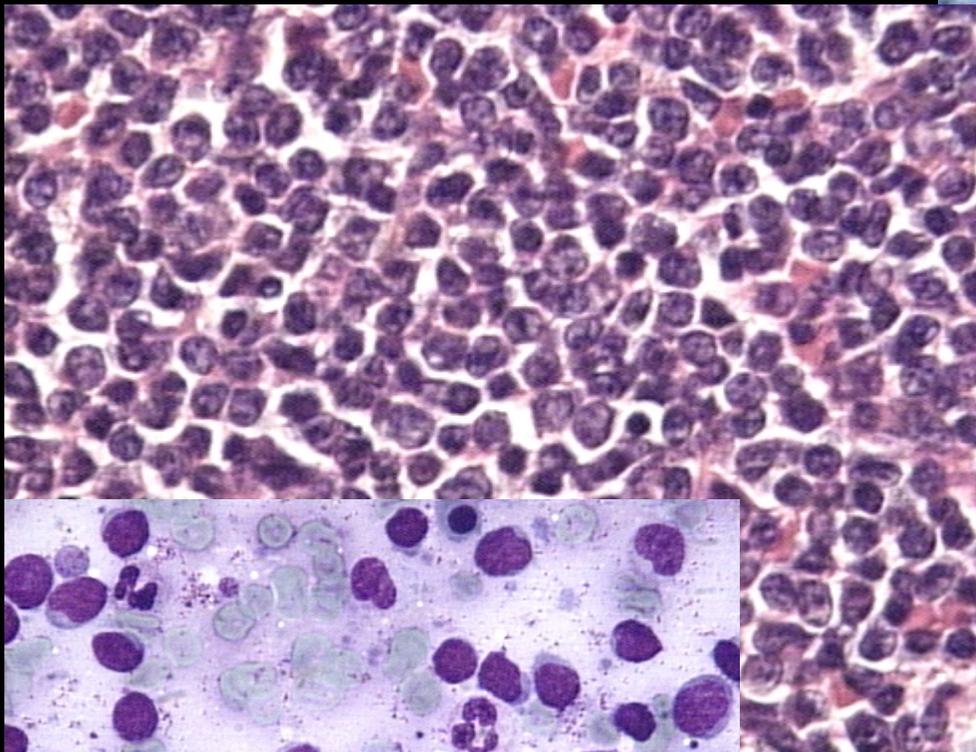
Kemik iliği, Dalak, Periferik Kan +/-

Ekstranodal (%30) (Lenfomatöz polipozis, Waldeyer halkası)



Mantle Hücreli Lenfoma (MCL) (ICQ= 9673/3)

immunfenotip: IgM+, IgD+



Mantle Hücreli Lenfoma (MCL) (ICQ= 9673/3)

Genetik Anomaliler:

t(11;14) (q13;q32)

(cyclin D1= PRAD1= BCL-1= CCND1)

(IgH)

FISH %100

Blastoid varyantlarda:

P53

P16

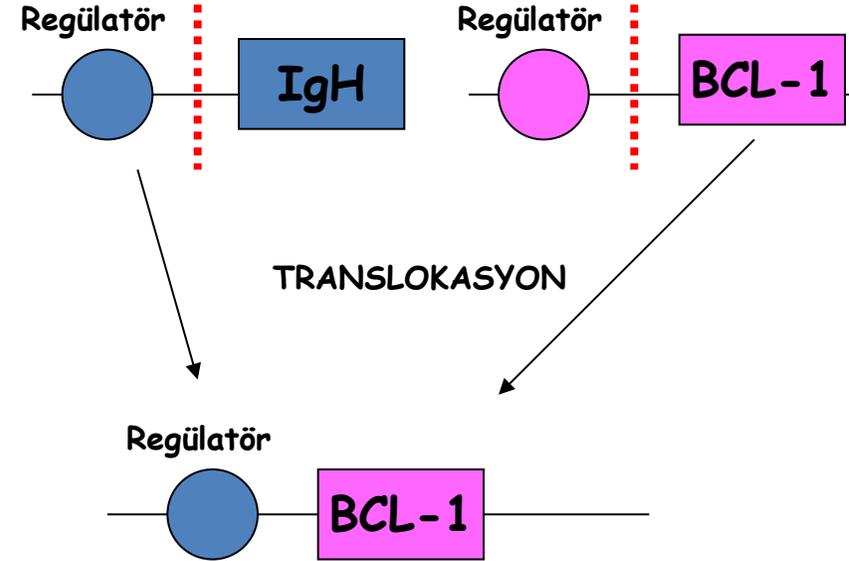
P18

Del 13q14

Trizomi 12

t(8;14) c-myc

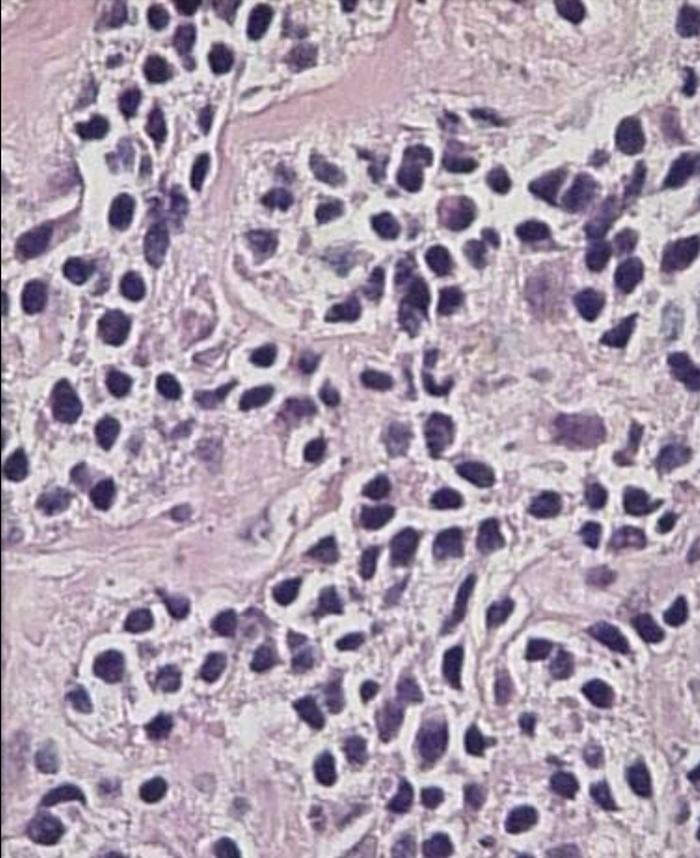
t(14;18) BCL-2



**TRANSKRİPSİYONEL
REGÜLASYON BOZUKLUĞU
BCL-1 nükleer ekspresyonu**

Lenfoplazmasitik Lenfoma / Waldenström Makroglobulinemisi (LPL) (ICQ= 96/3)

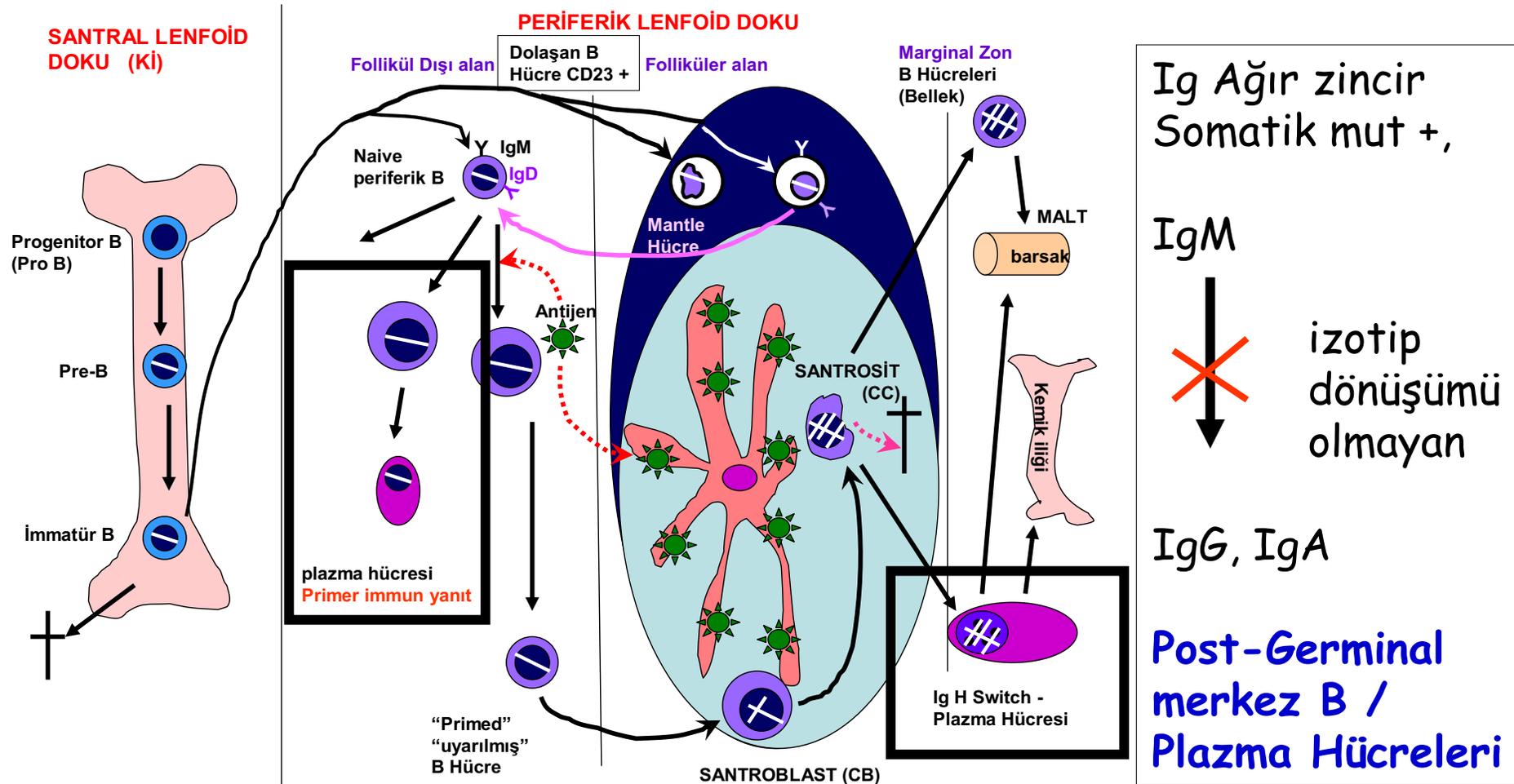
Plazma hücre diferansiasyonu gösteren diğer lenfomalar dışındaki,
Küçük lenfositler (CD5-), Plazmasitoid lenfositler ve plazma hücreleri +
Kemik iliği, Lenf nodülü ve Dalak tutulumu +
Serum monoklonal hafif zincir artışı + Lenfomalar



Lenfoplazmatik Lenfoma / Waldenström Makroglobulinemisi (LPL) (ICQ= 96/3)

Plazma hücrelerine dönüşme uyarısı almış
Pre-Germinal Merkez B lenfositleri

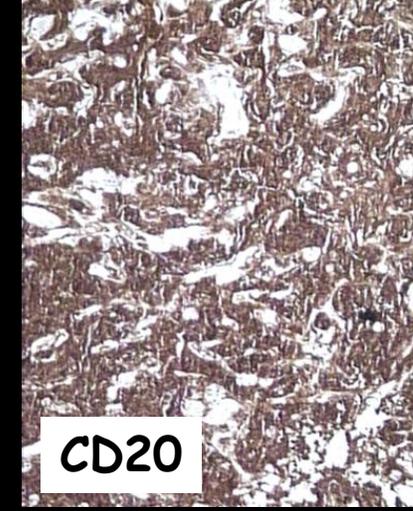
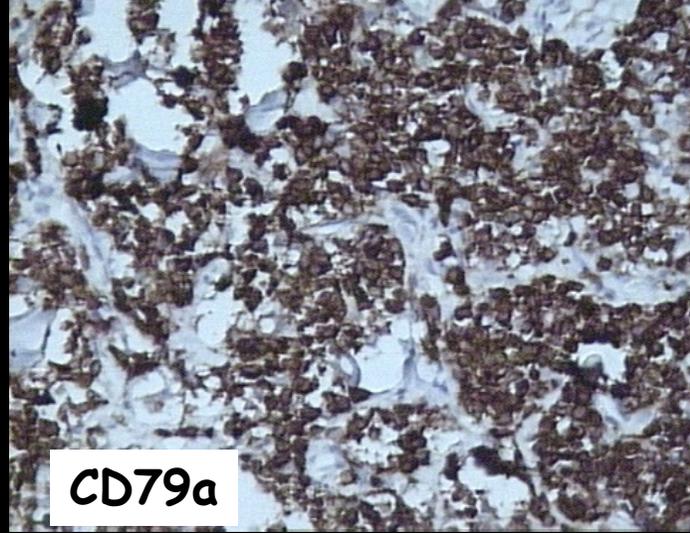
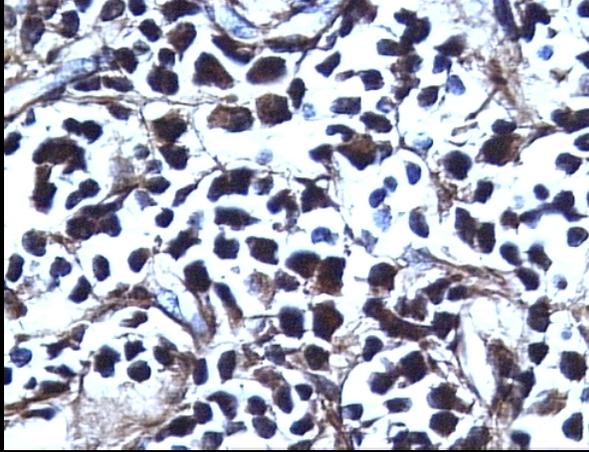
Hücre Kökeni



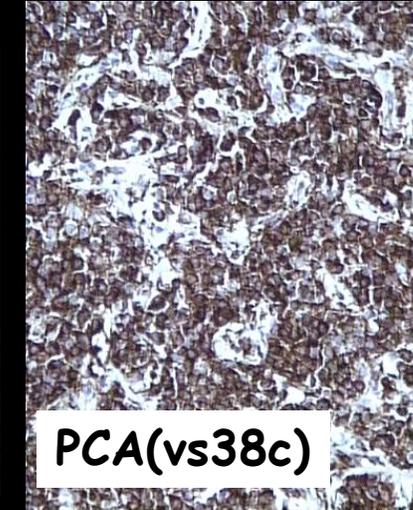
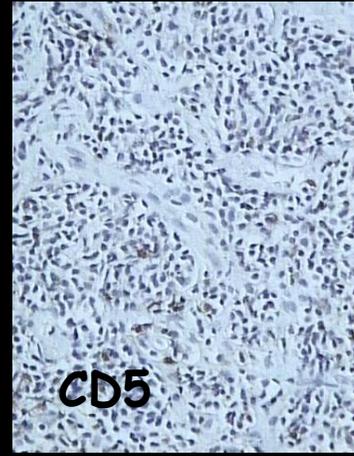
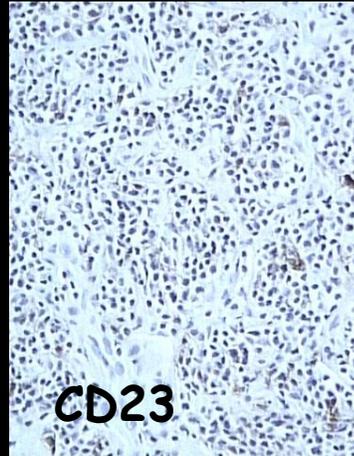
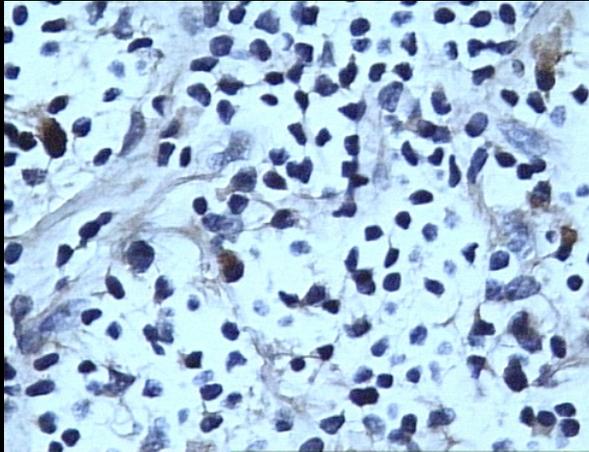
Lenfoplazmatik Lenfoma / Waldenström Makroglobulinemisi (LPL) (ICQ= 96/3)

Yüzey IgM+ (çok seyrek IgG+ veya IgA+) (IgD-)

κ



λ

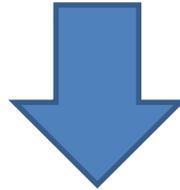


**Lenfoplazmasitik Lenfoma /
Waldenström Makroglobulinemisi (LPL) (ICQ= 96/3)**

Ig gen düzenlenmesi +

Ig VH gen somatik mutasyon +

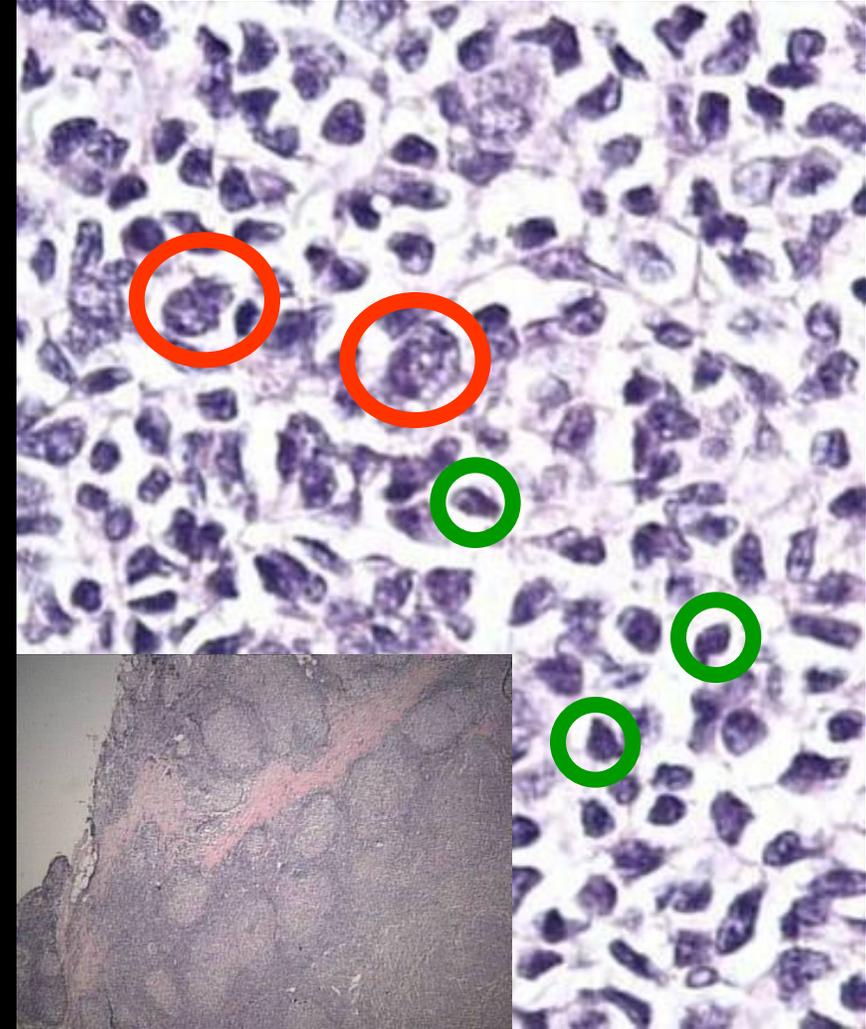
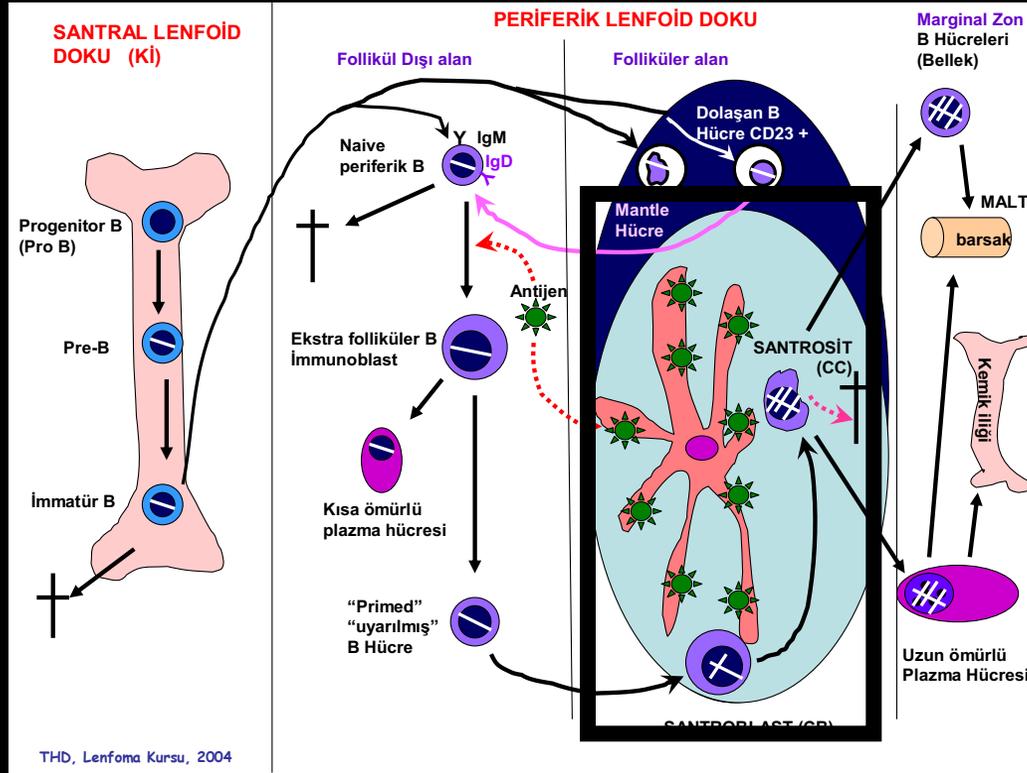
t(9;14)(p13;q32) : PAX-5 geni düzenlenmesi (%50)



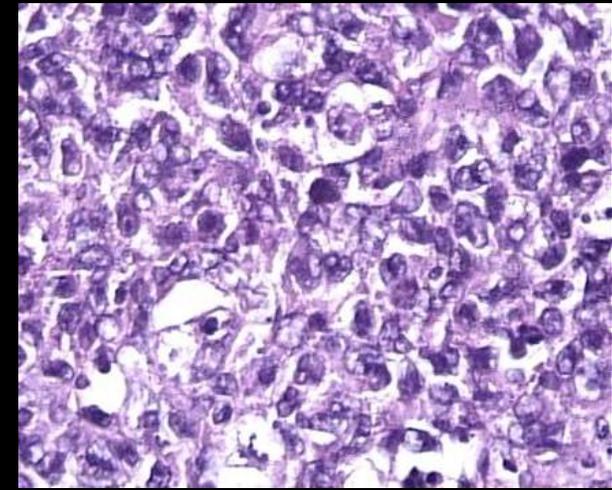
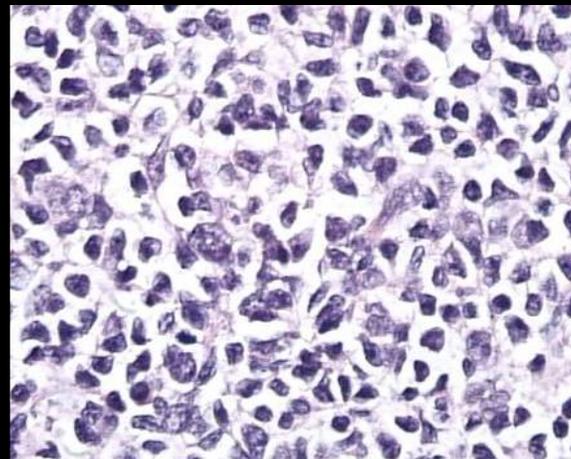
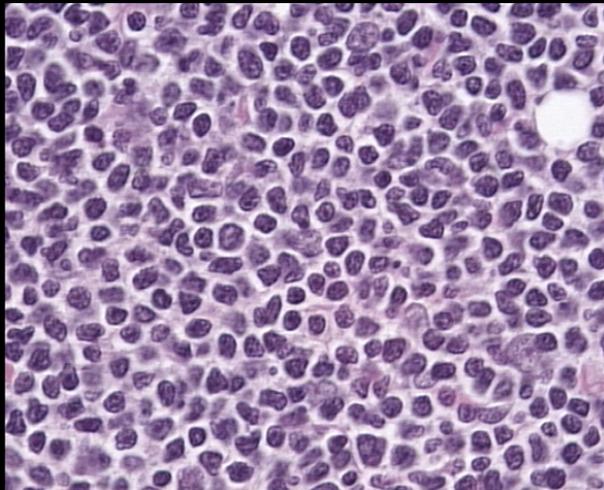
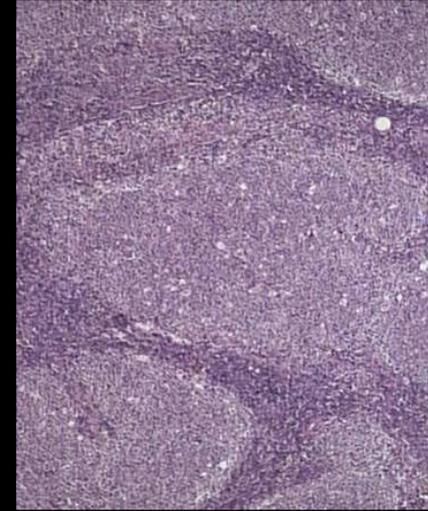
MYD88 GENİ NOKTA MUTASYONU

Foliküler Lenfoma (FL) (ICQ= 9690/3)

Kısmen de olsa follikül şeklinde organizasyonu bulunan, follikül merkezinin B Hücrelerinin "**Santrosit (CC)** ve **Santroblast (CB)**" lenfoması.



Folikulärer Lymphom (FL) (ICQ= 9690/3)



FL I

0-5 CB /hpf

FL II

6-15 CB/hpf

FL III

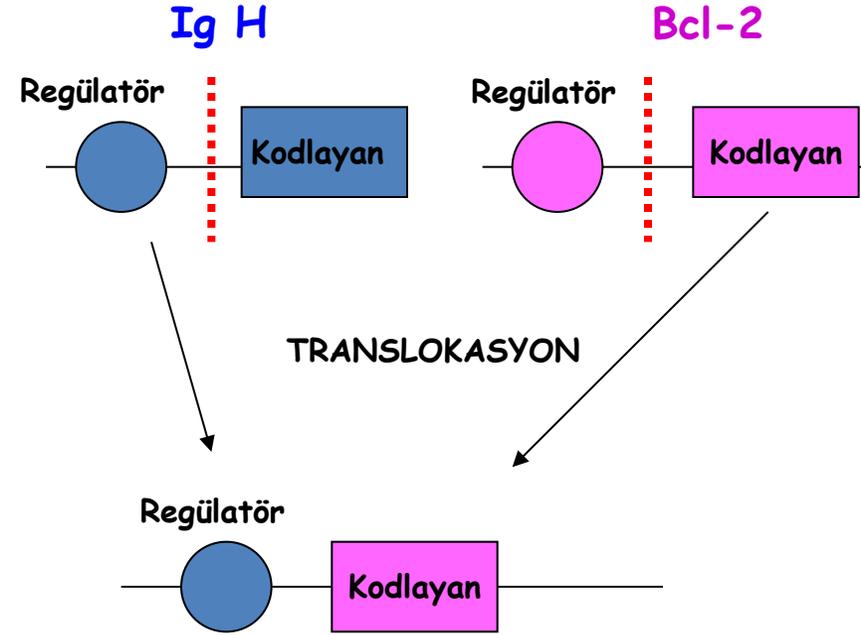
> 15 CB/hpf

Foliküler Lenfoma (FL) (ICQ= 9690/3)

Genetik Anomaliler

† (14:18) (q32:q21) %70-95
† (2:18) (p11:q21)
† (18:22) (q21:q11)

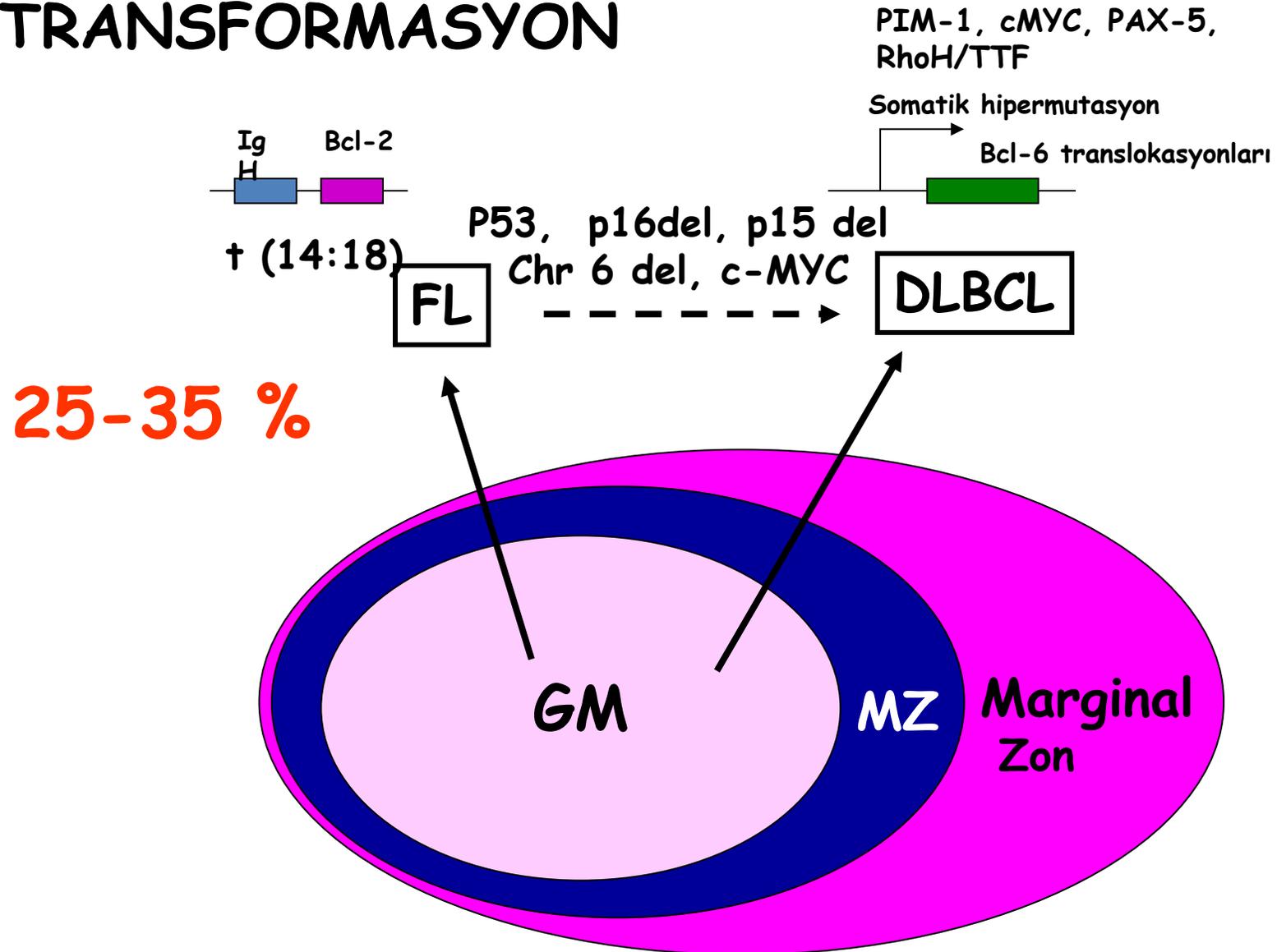
Bcl-2	18 q21
IgH	14 q32
Igκ	2 p11
Igλ	22 q11



TRANSKRİPSİYONEL
REGÜLASYON BOZUKLUĞU
BCL-2 ekspresyonunda artış

Foliküler Lenfoma (FL) (ICQ= 9690/3)

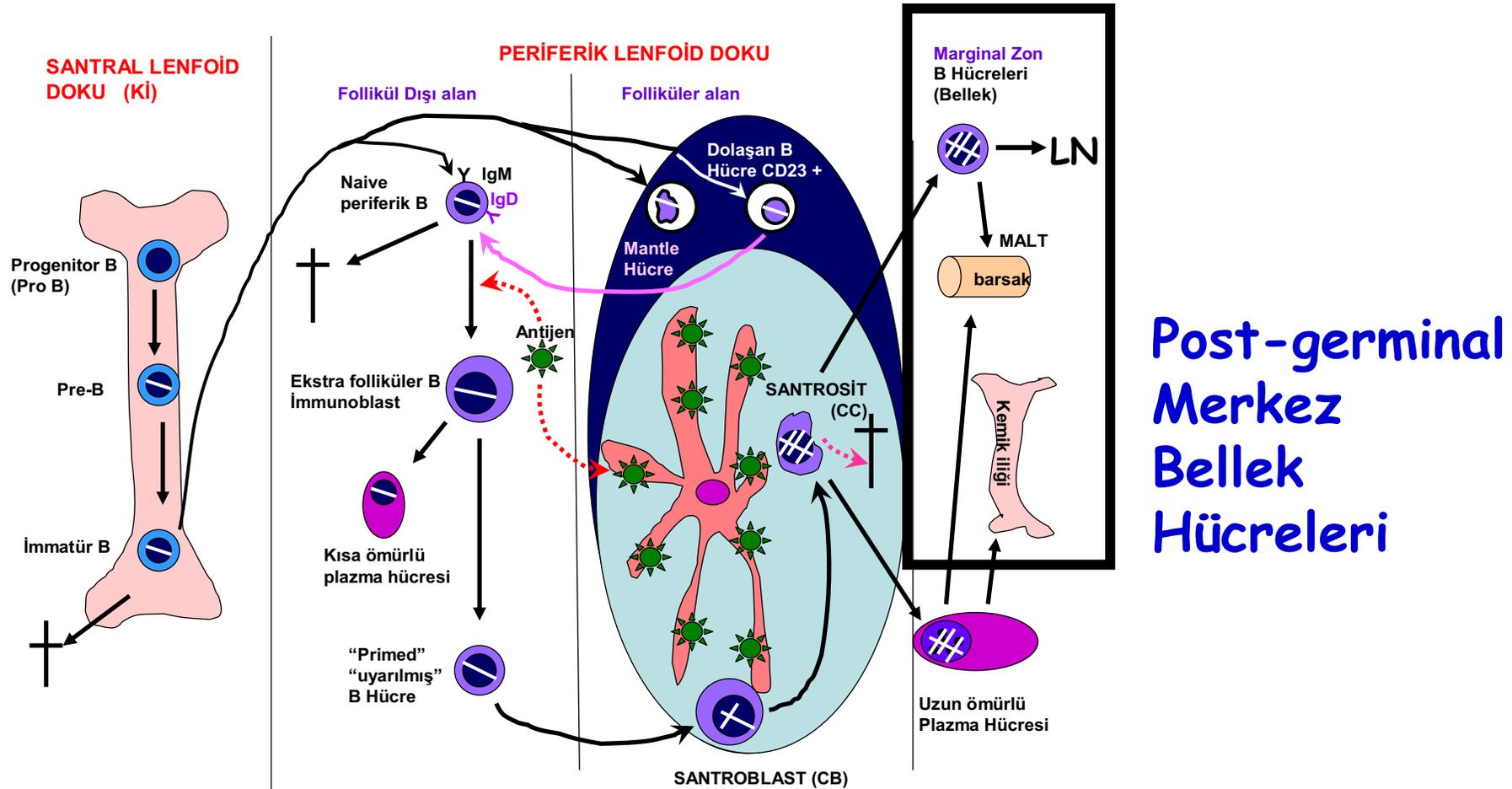
TRANSFORMASYON



Marginal Zon Lenfomalar

Hücre Kökeni

Periferik kan, Lenf Nodülü veya Ekstra-Nodal Lenfoid Doku
Post-Germinal Merkez / Marginal zon B hücreleri



Splenik Marginal Zon Lenfoma (Sp-MZL) (ICQ= 9689/3)

Genetik Özellikler:

Ig gen düzenlenmesi +

Ig VH gen somatik mutasyon + veya sürmekte

IgM+ / IgD+

Hücre Kökeni :

Diferansiasyon evresi bilinmeyen Post-germinal merkez B Hücreleri

Genetik Anomali

Del 7q21-32 (%40)

Sonuç

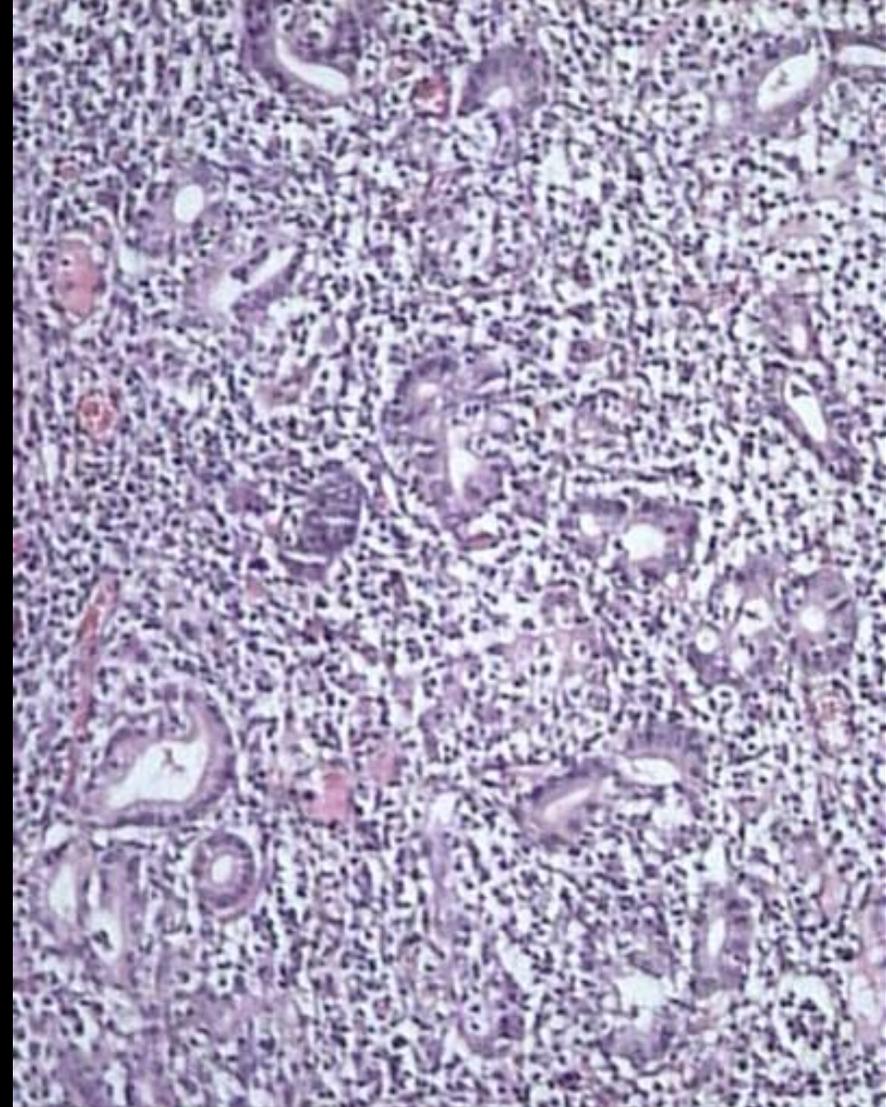
CDK6 regülasyonu bozukluğu
(mitoz bölünme kontrolü)

Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

Mukozalarla ilişkili lenfoid dokudan (MALT) gelişen Ekstranodal Lenfomalar

Heterojen Morfoloji

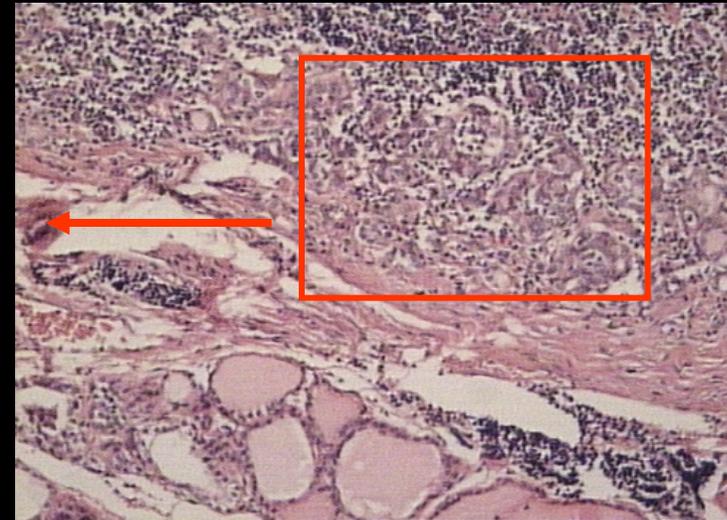
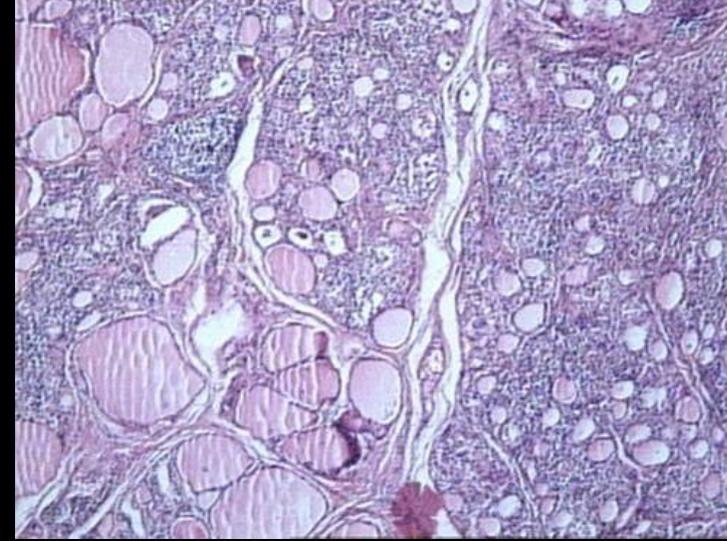
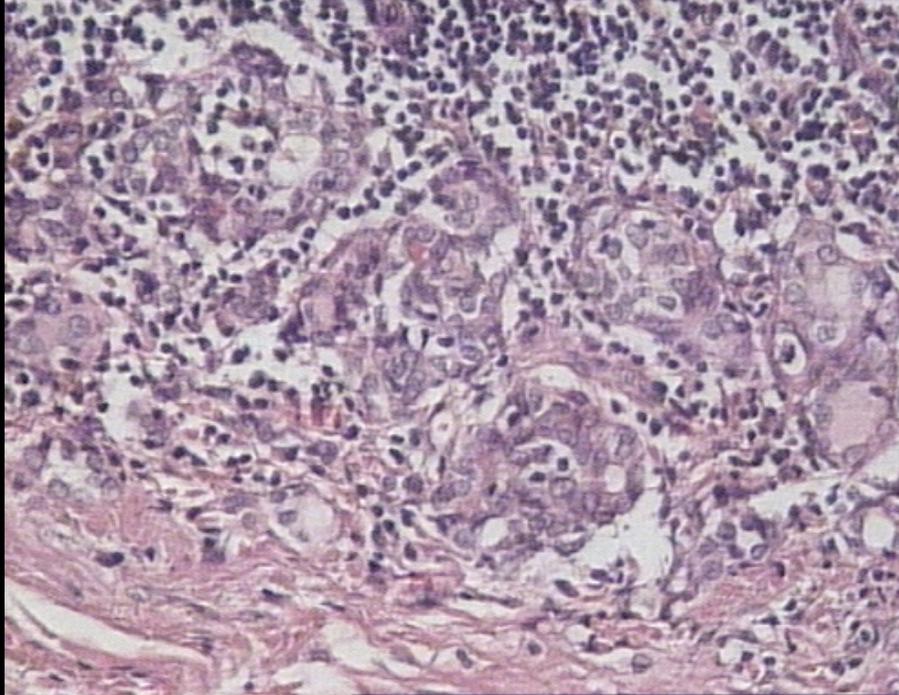
- marginal zon hücrelerine benzeyen küçük B lenfositleri
- Küçük lenfositler
- Dağınık santroblast
- İmmunoblast
- Plazma hücre diferansiasyonu



Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

Öncü lezyonlar ve durumlar

- H pylori gastriti
- Kronik intestinal infeksiyonlar (IPSID)
- Sjögren Sendromu
- Hashimoto tiroiditi



Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

Genetik özellikler:

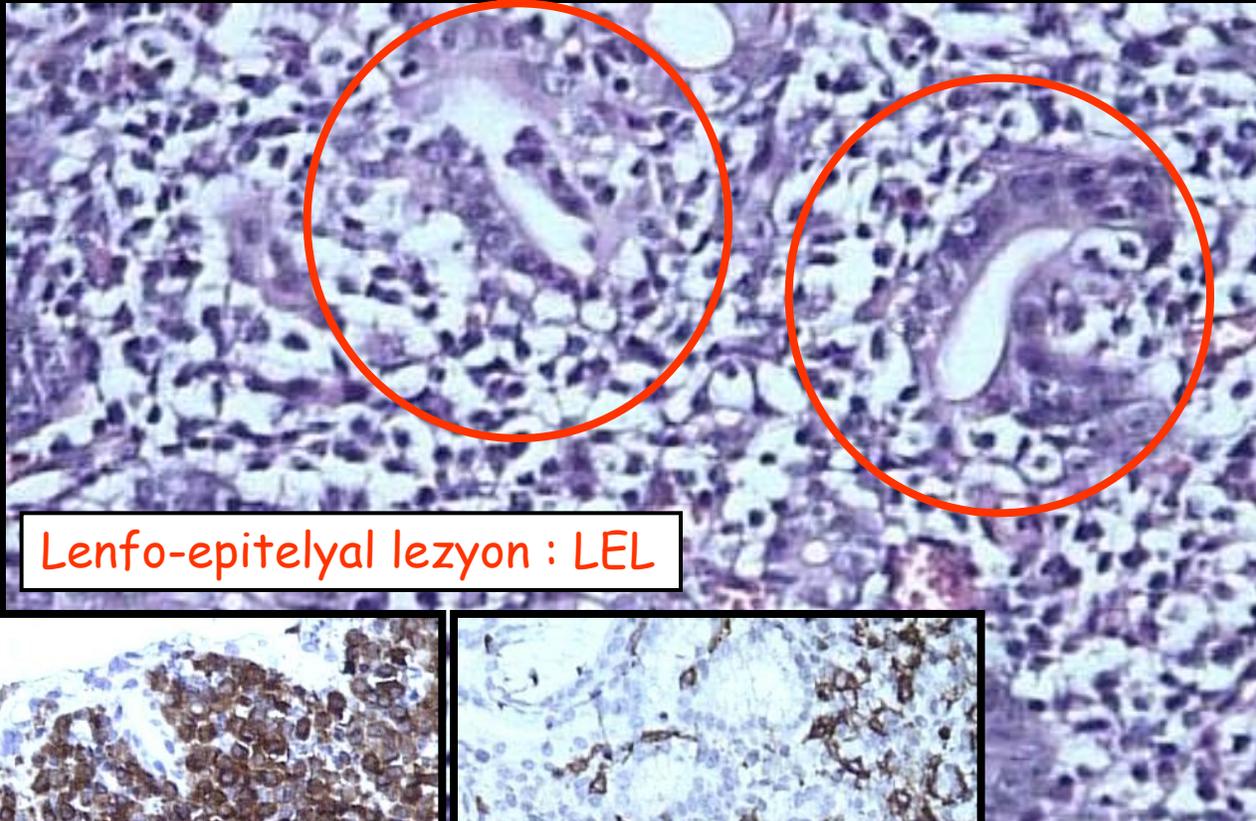
Ig gen düzenlenmesi +

Ig VH gen somatik mutasyon +

Hücre Kökeni :

Post-germinal Merkez Memory B hücreleri

Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

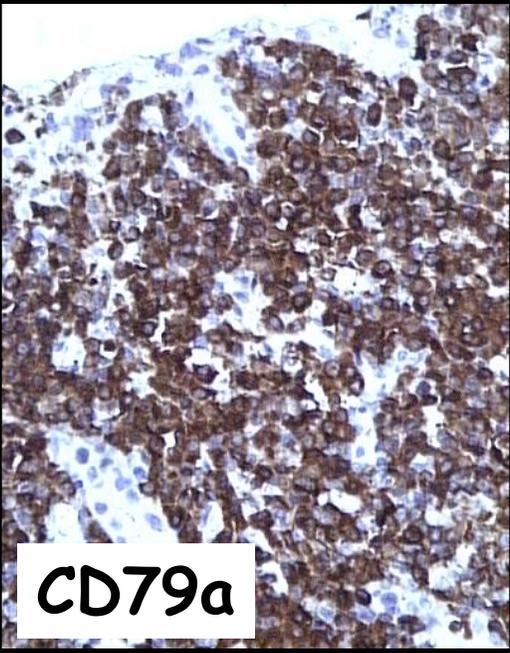


Lenfo-epitelyal lezyon : LEL

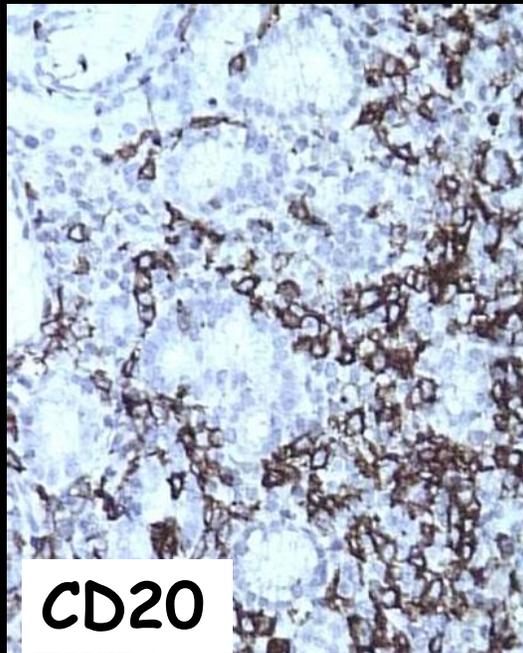
Mide mukozası



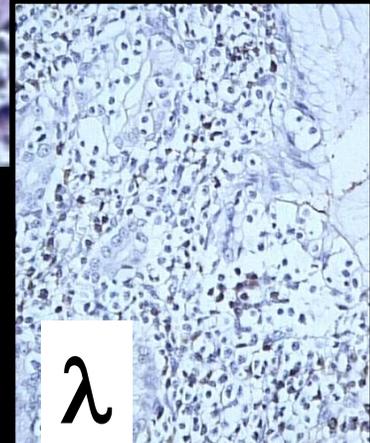
sitokeratin



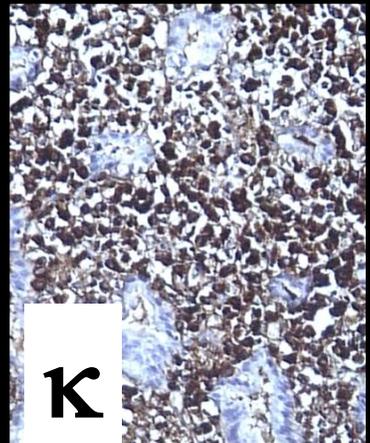
CD79a



CD20



λ



κ

Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

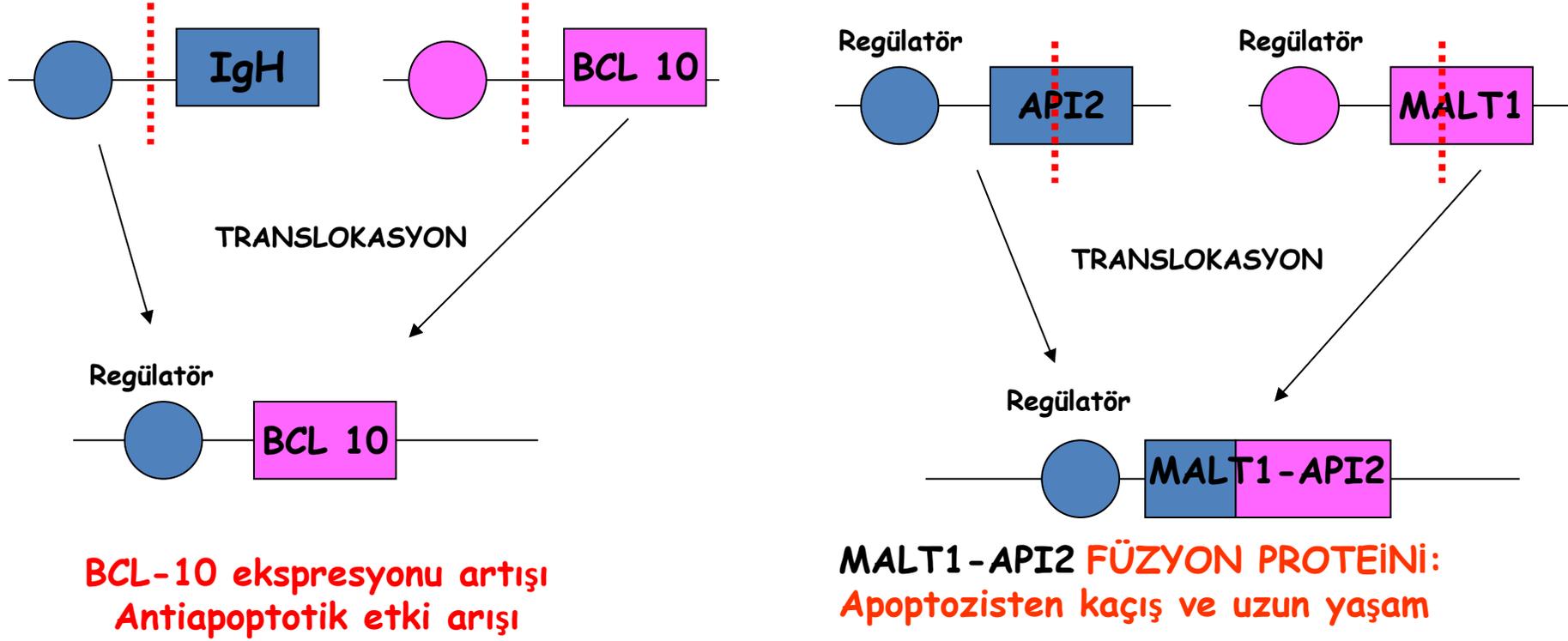
immunfenotipik özellikler

IgM+ > IgA+ veya IgG+, klonal λ veya κ zincir
CD20+, CD79a+, CD43 +/-, CD11c +/-
CD5, CD10, CD23, Bcl-1 (Cyclin D1) Negatif

**SPESİFİK OLAN BİR İMMUNFENOTİPİK ÖZELLİK
YOKTUR.**

**DiĞER LENFOMALARIN SPESİFİK İMMUNFENOTİPİK
ÖZELLİKLERİYLE AYIRICI TANI**

Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)

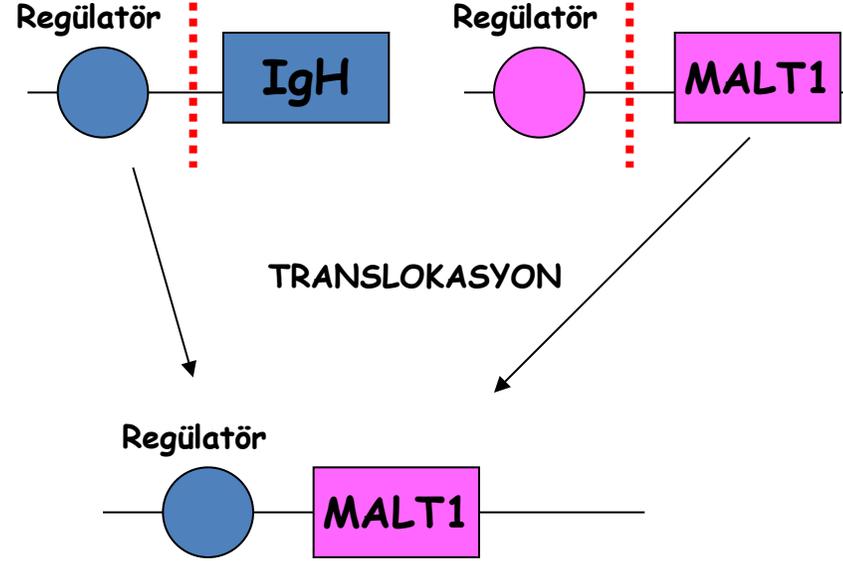


t(1;14) (p22;q32)
(% 5-7)

t(11;18)(q21;q21)
(%22-50)

Genetik anomaliler

Ekstranodal Marginal Zon Lenfoma (E-MZL) (ICQ= 9699/3)



MALT1 ekspresyonunda artış
Caspase benzeri proteaz (parakaspaz)
ekspresyonunda artış, apoptozisin engellenmesi

t(14;18) MALT1/IgH
(10%)

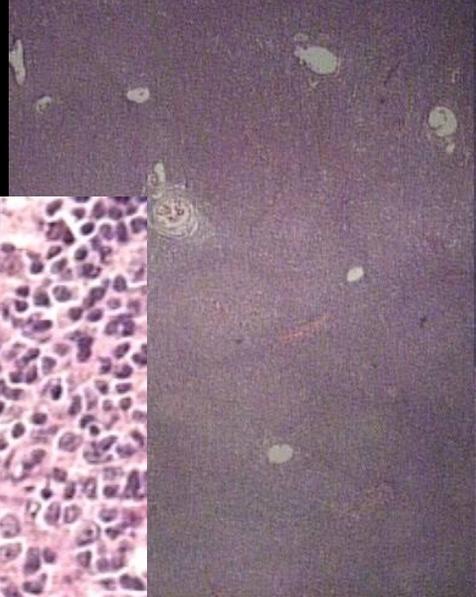
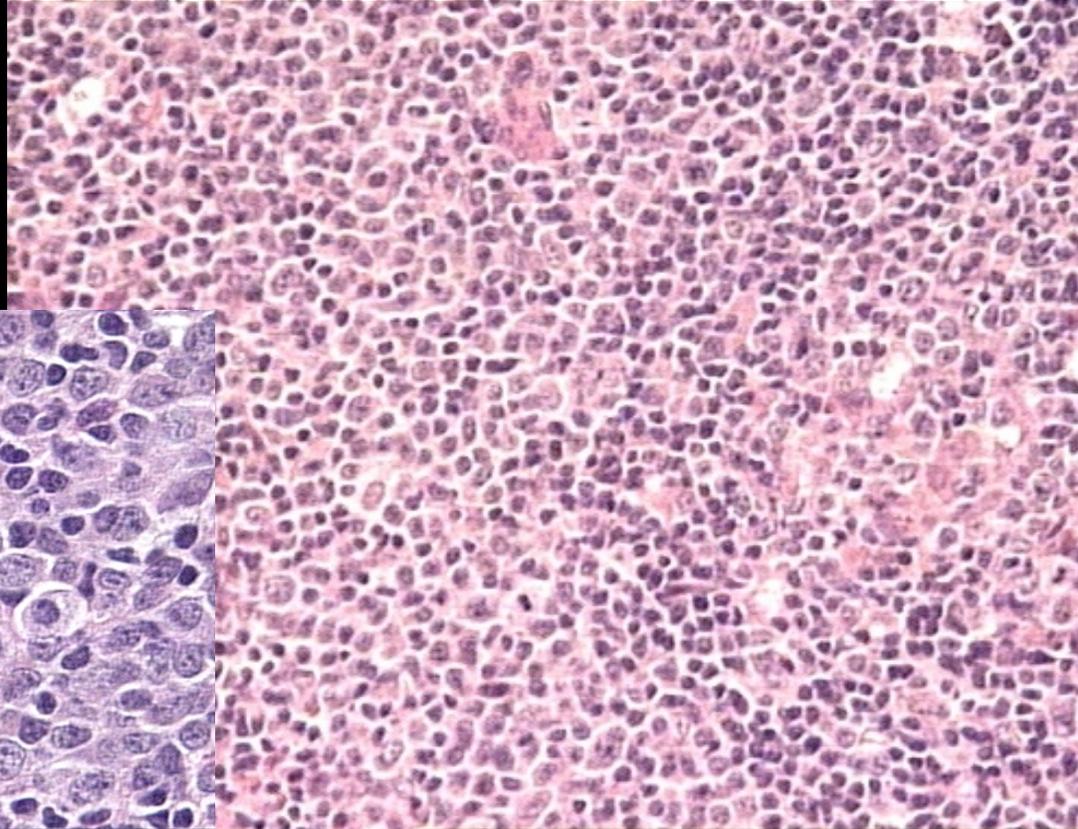
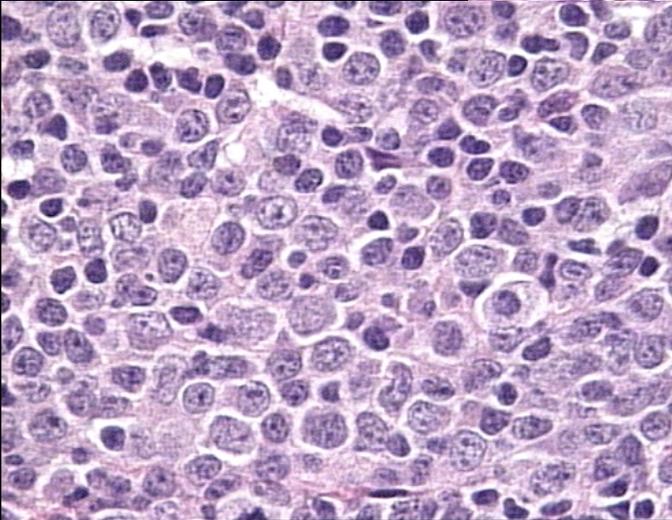
Genetik anomaliler

Nodal Marginal Zon Lenfoma (N-MZL) (ICQ= 9699/3)

Primer lenf nodülünde gelişen, marginal zon hücrelerinden meydana gelen lenfomalar. Ekstranodal veya dalakta tutulumun bulunmaması tanı için gerekli Kemik iliği ve periferik kan tutulumu çok seyrek.

immünofenotipik özellikler E-MZL ile aynıdır.

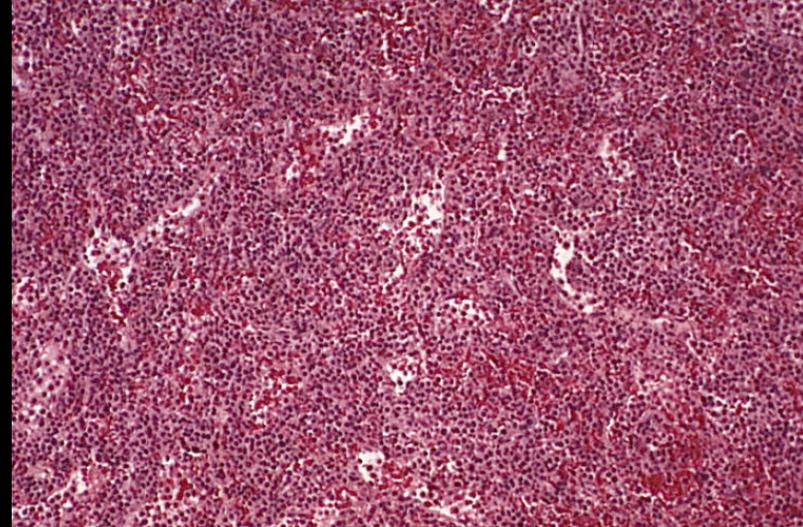
Genetik anomalilerle ilgili iyi dökümanite edilmiş veriler - .



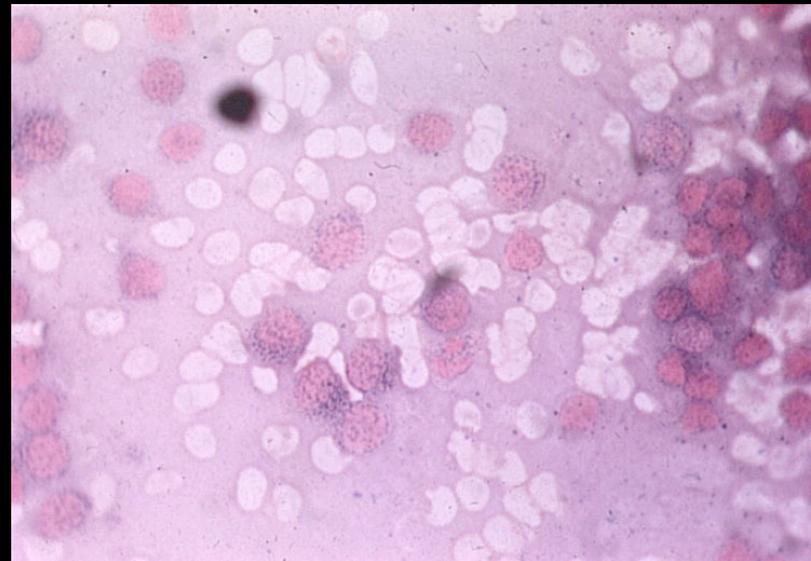
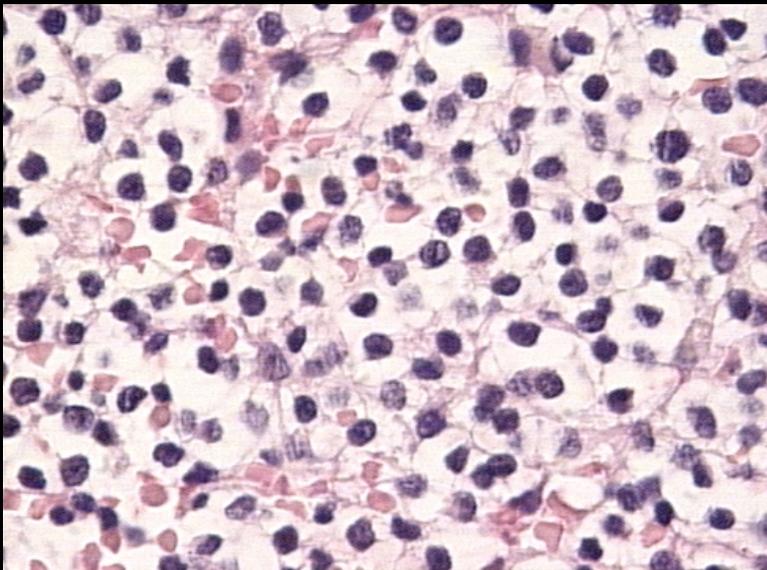
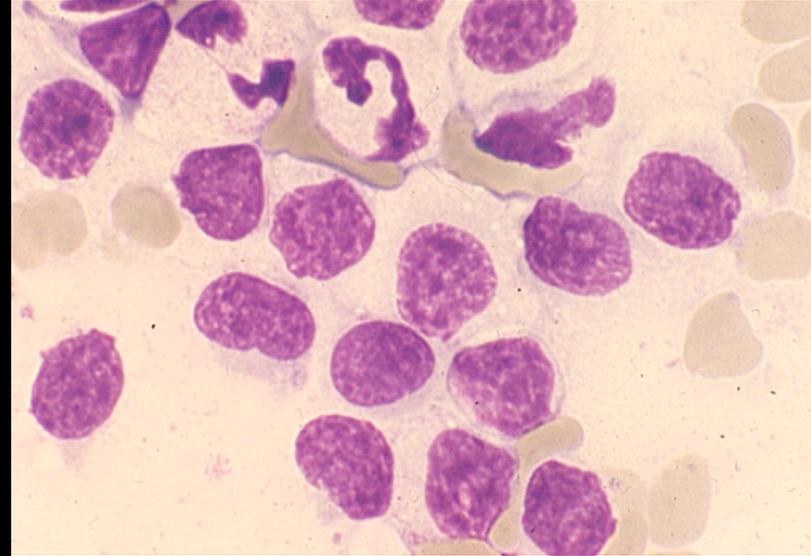
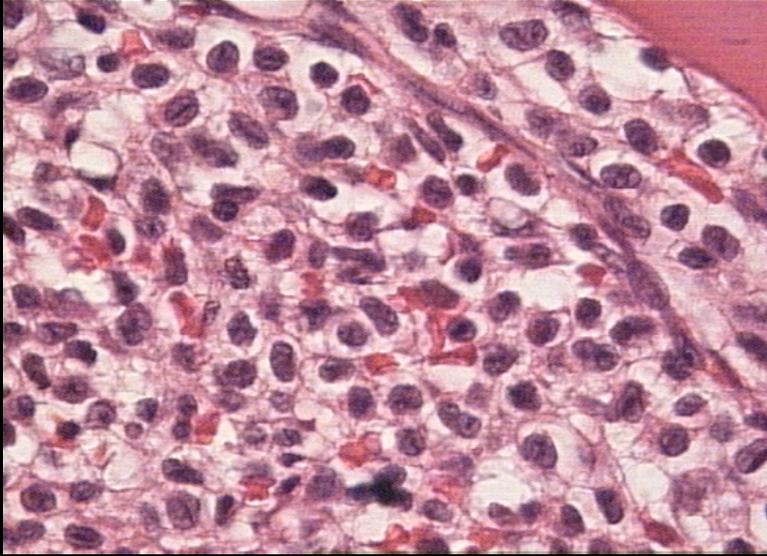
Hairy Cell Lösemi (HCL) (ICQ= 9940/3)

Periferik kanda, kemik iliği ve dalakta tipik sitoplazmik çıkıntıları olan neoplastik küçük B lenfositleri

Dalakta diffüz
(kırmızı pulpada-sinüoidlerde)
tutululum karakteristik



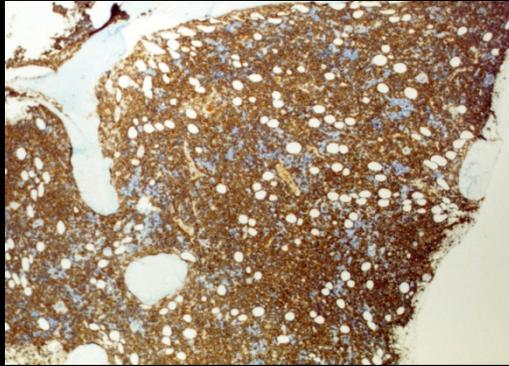
Hairy Cell Leukemia (HCL) (ICQ= 9940/3)



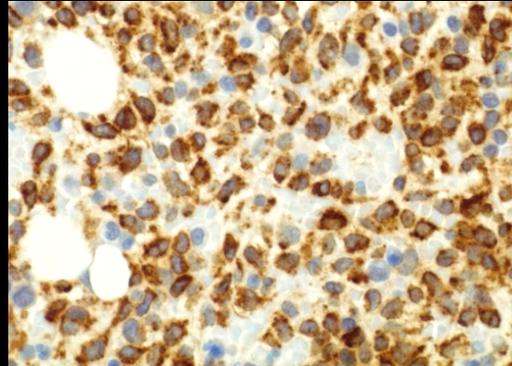
TRAP

Hairy Cell Lösemi (HCL) (ICQ= 9940/3)

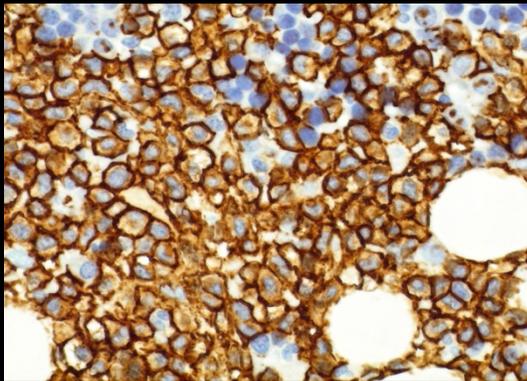
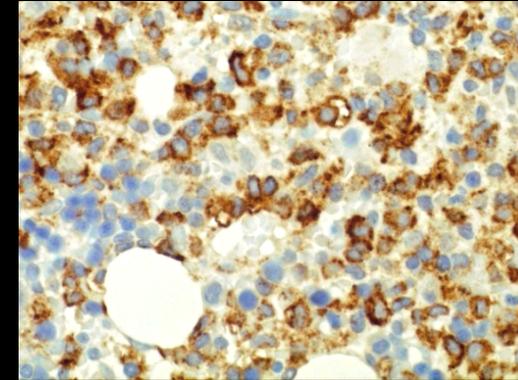
CD20



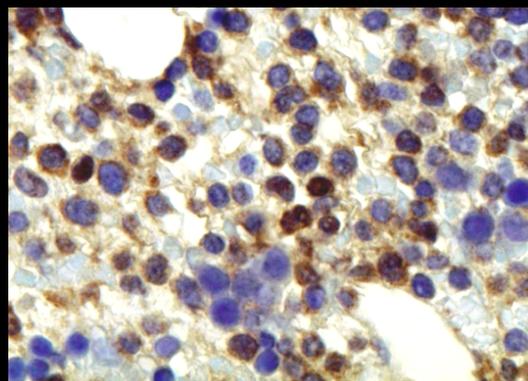
TRAP



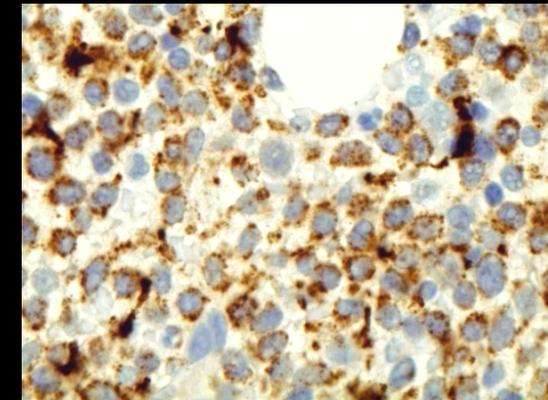
DBA 44



CD20



Cyclin D1



CD68

Membranöz IgM+/ IgG+ veya IgA +, IgD -

Hairy Cell Lösemi (HCL) (ICQ= 9940/3)

Genetik Özellikler:

Ig gen düzenlenmesi +

Ig HV genleri somatik mutasyon düşük oranda +

*Aynı klon içinde farklı Ig ağır izotipleri+ (IgM,IgG,IgA)
m-RNA düzeyinde transkripsiyon aşamasında düzenlenme

%100 BRAF V600E MUTASYONU

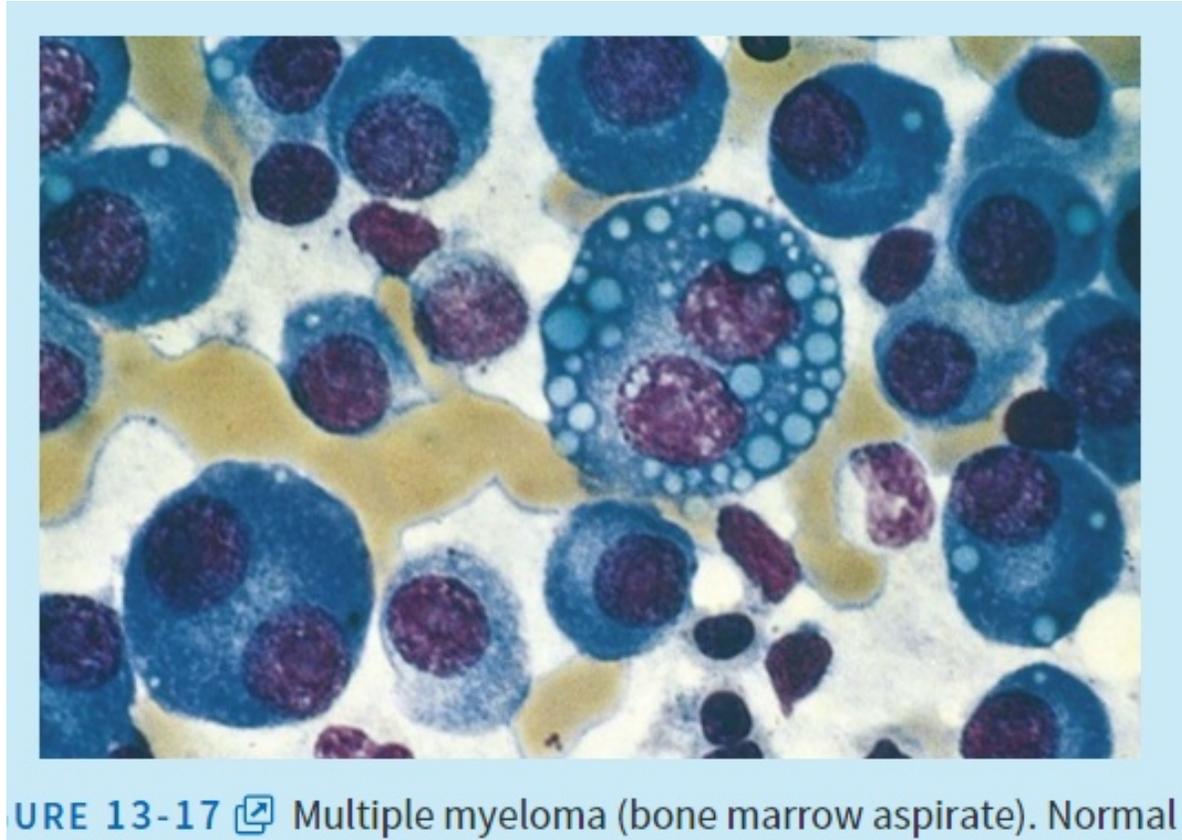
Hücre Kökeni :

Diferansiasyon evresi bilinmeyen

Post-germinal Merkez B hücreleri

PLAZMA HÜCRELİ MİYELOM

- Plazma hücrelerinin neoplazisi
- Kemik iliğinde yaygın- lokalize



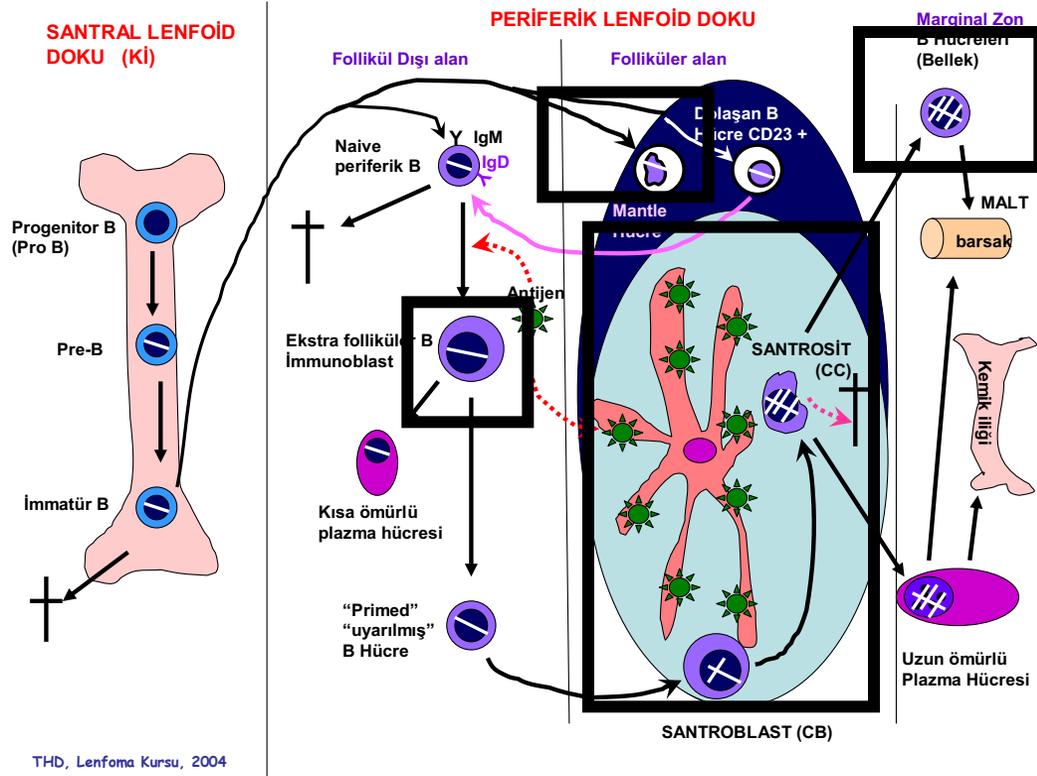
Plasma Cell Neoplasms /Multiple Myeloma

- Plasma cell tumor that manifests with multiple lytic bone lesions associated with pathologic fractures and hypercalcemia
- Neoplastic plasma cells suppress normal humoral immunity and secrete partial immunoglobulins that are nephrotoxic
- Associated with diverse translocations involving the IgH locus; frequent dysregulation and overexpression of D cyclins
- May be associated with AL amyloidosis (as may other neoplasms later)



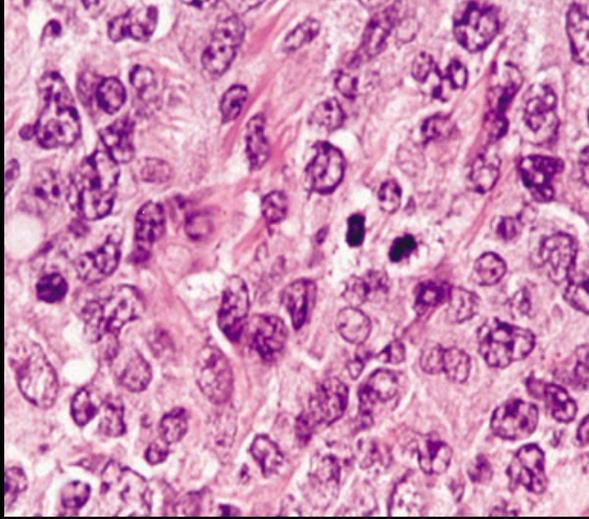
Diffüz Büyük B Hücreli Lenfoma

De-novo (Primer) - Transforme (sekonder)

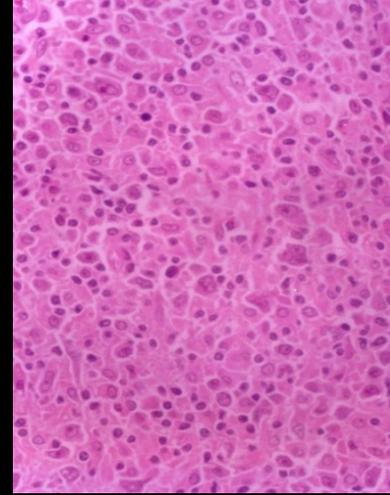


DLBCL Morfolojik Varyantlar

Santroblastik



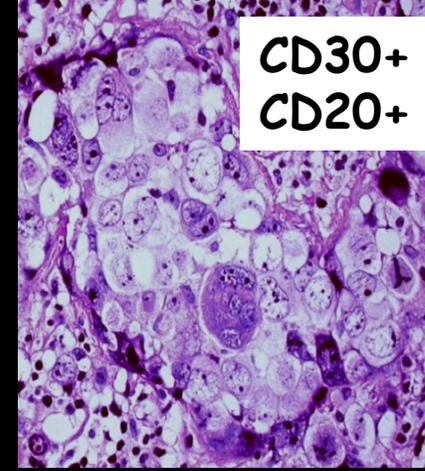
CD20 +
CD79a+



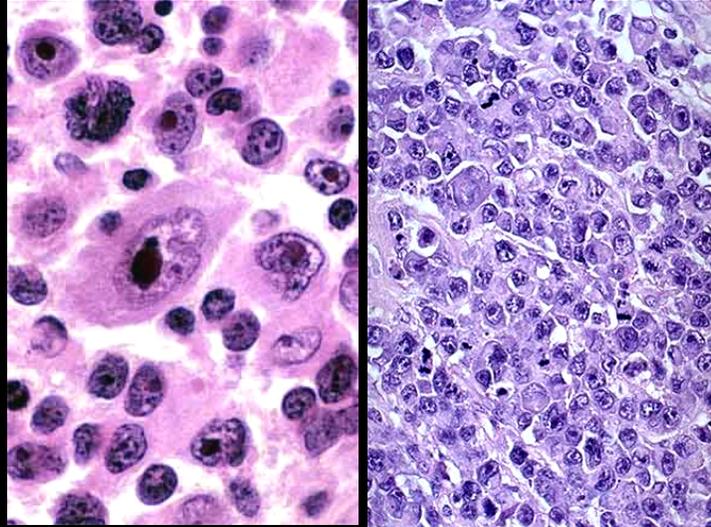
T Hücreden Zengin
Büyük B Hücreli

Neoplastik B Hücr % 10 altında

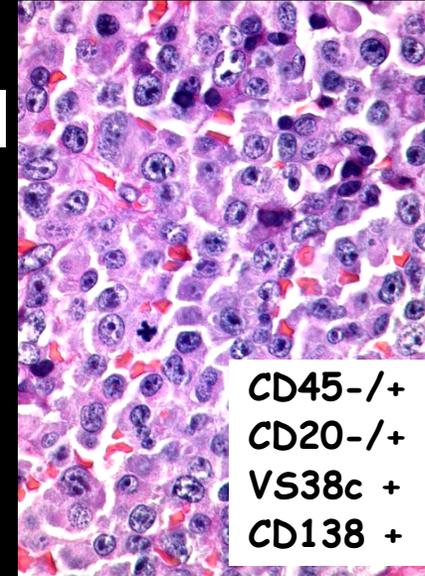
Anaplastik



CD30+
CD20+



immunoblastik



CD45-/+
CD20-/+
VS38c +
CD138 +

Plazmablastik

DIFFÜZ BÜYÜK B HÜCRELİ LENFOMALARIN MOLEKÜLER KLASİFİKASYONUNUN "TISSUE MICROARRAY" KULLANILARAK İMMÜNHİSTOKİMYA İLE DOĞRULANMASI

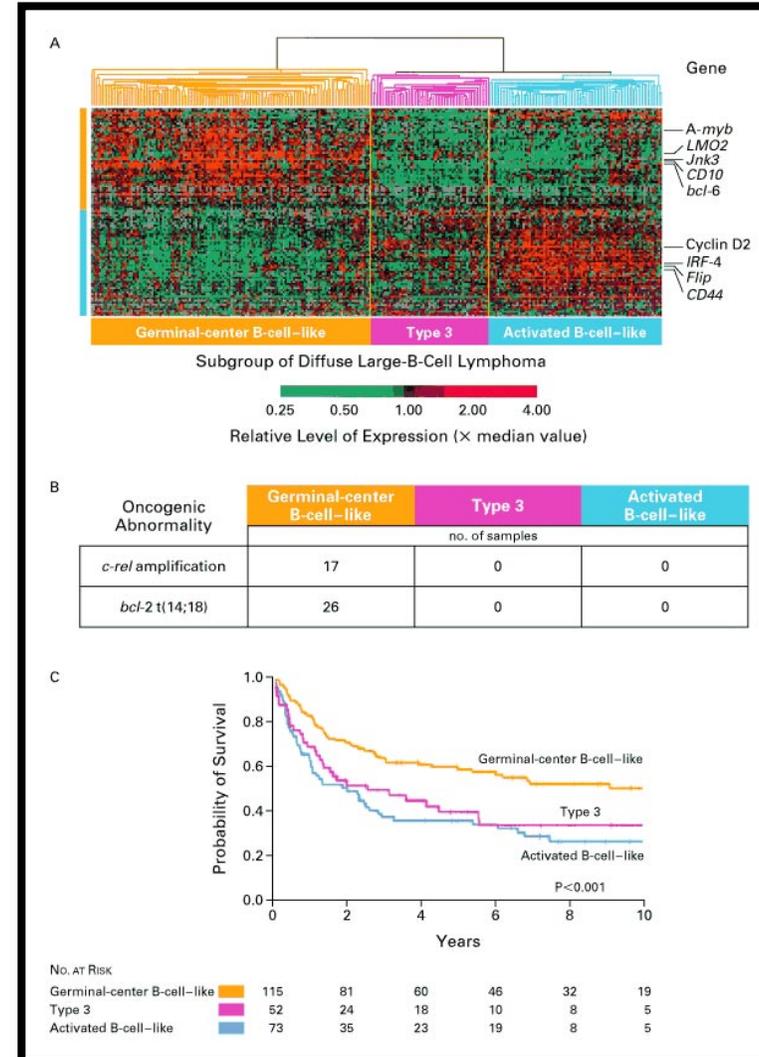
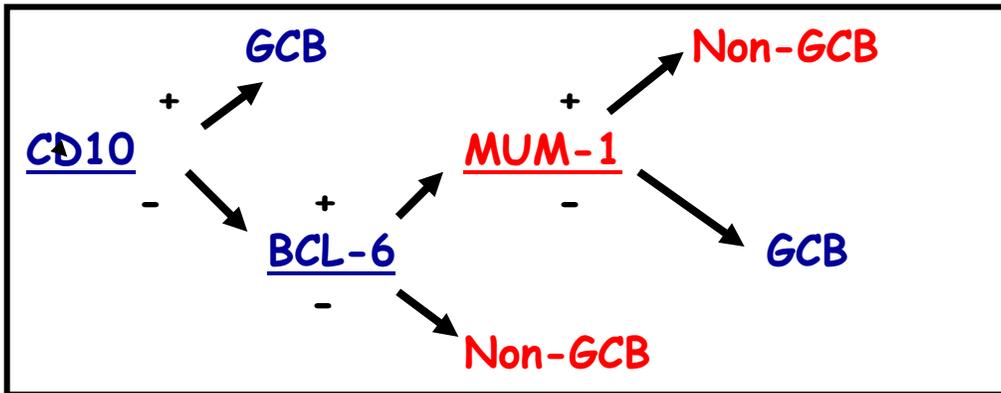
(Weisenburger, Armitage et al, Blood, September 22, 2003)

IHK: CD20, CD10, bcl-6, MUM-1, bcl-2, siklin D2, FOX P1

Tissue Microarray

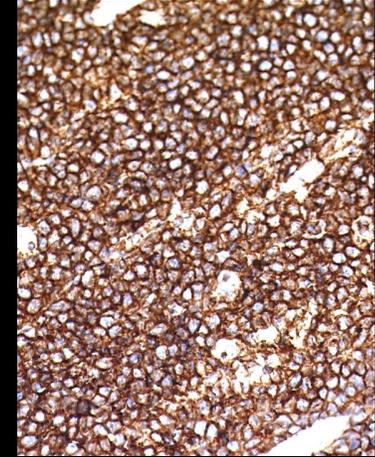
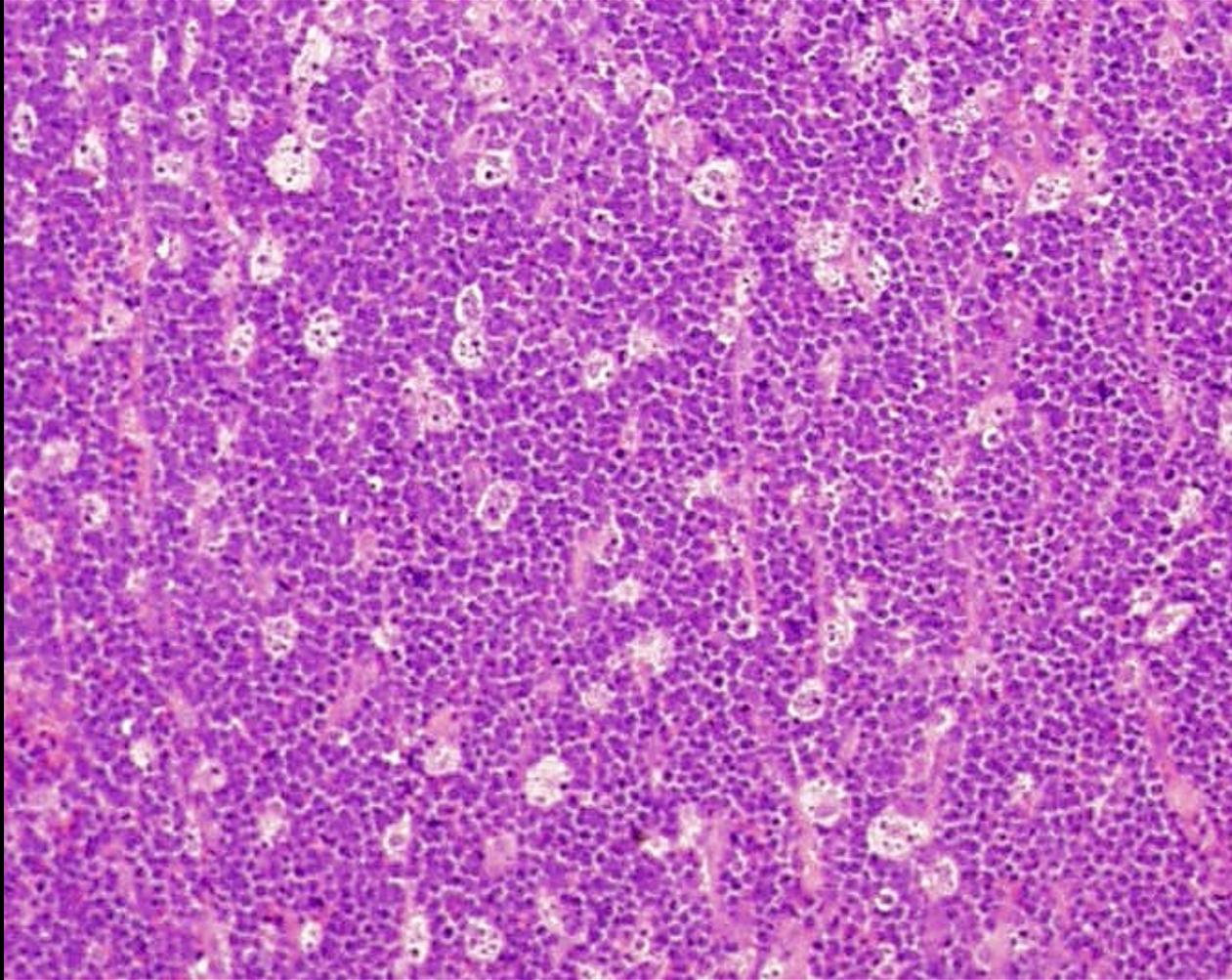
CD10, bcl-6, MUM 1 sonuçlarına göre olgular 2 subgruba ayrılmış.

- 1- GCB
- 2- Non-GCB

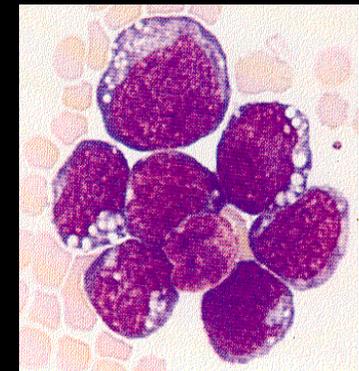


Rosenwald A ve ark., N Eng J Med 2002

Burkitt Lenfoma Histopatoloji



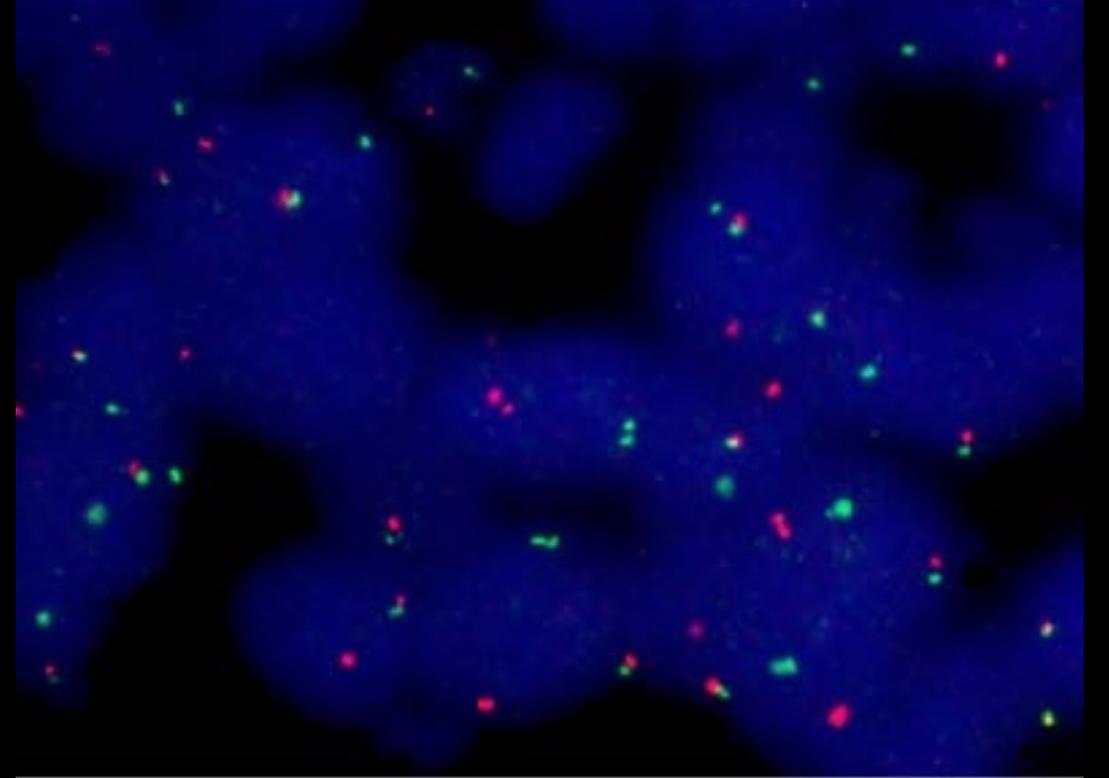
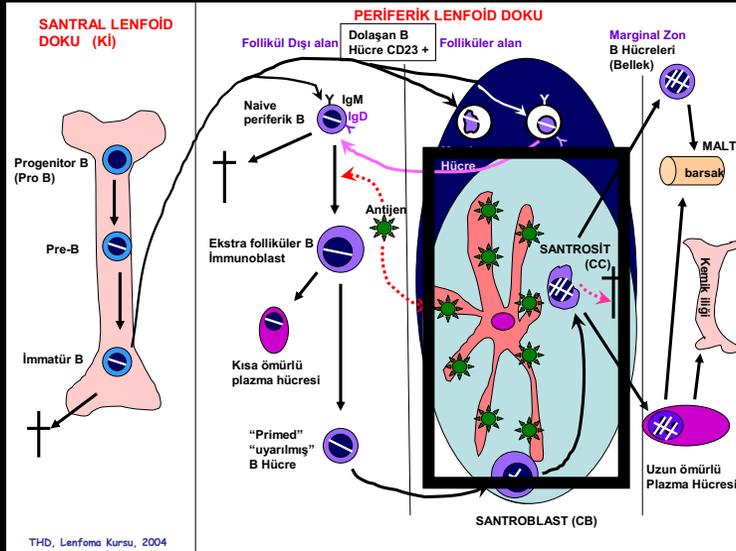
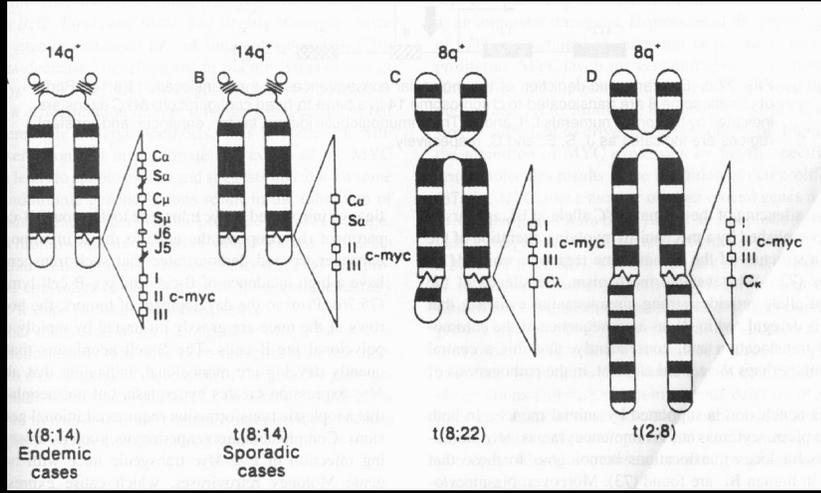
CD20



Burkitt Lenfoma

Genetik anomali

C-MYC Translokasyonu
Myc gen ürünü
ekspresyonunda artış



Hodgkin Lymphoma WHO 2008-2016

HODGKIN LYMPHOMA

Nodular lymphocyte predominant
Hodgkin lymphoma

Classical Hodgkin lymphoma

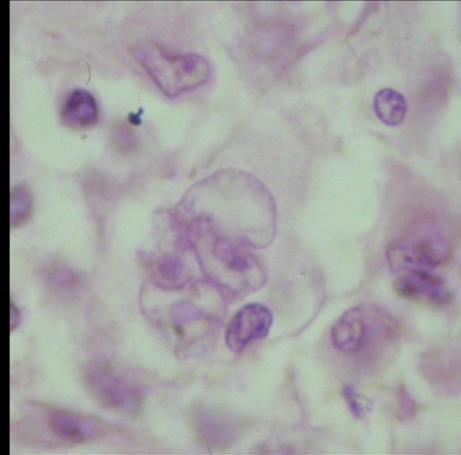
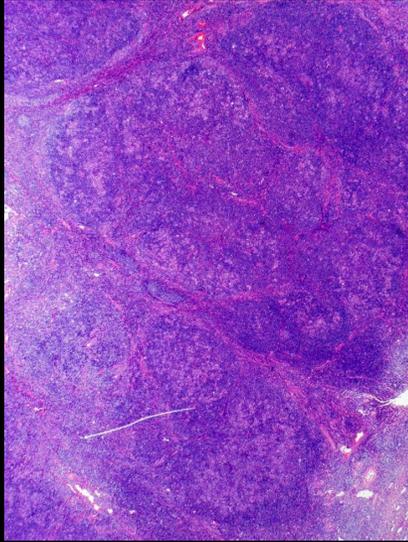
Nodular sclerosis classical
Hodgkin lymphoma

Lymphocyte-rich classical
Hodgkin lymphoma

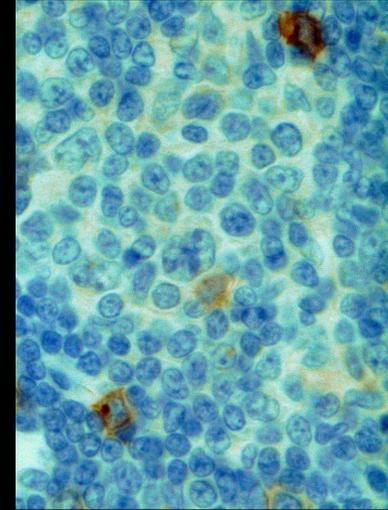
Mixed cellularity classical
Hodgkin lymphoma

Lymphocyte-depleted classical
Hodgkin lymphoma

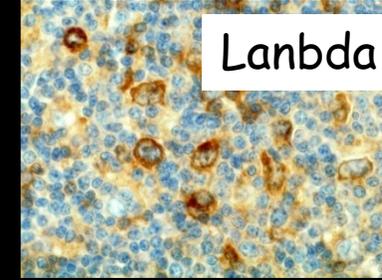
Nodüler Lenfosit Predominant HL



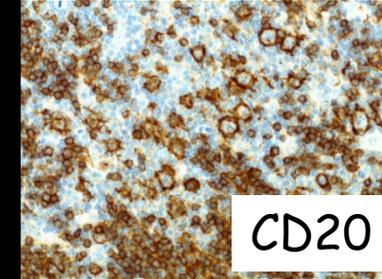
Popcorn Hücreleri



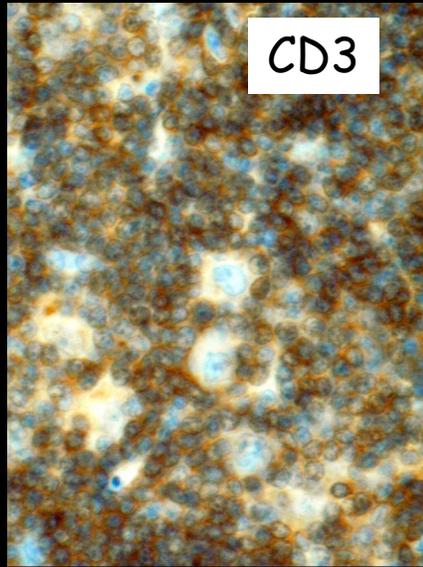
CD30



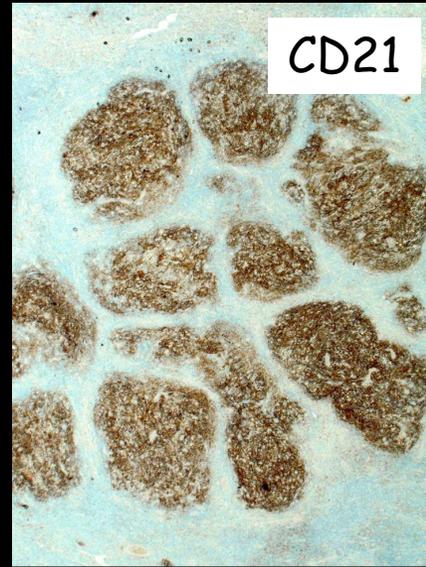
Lambda



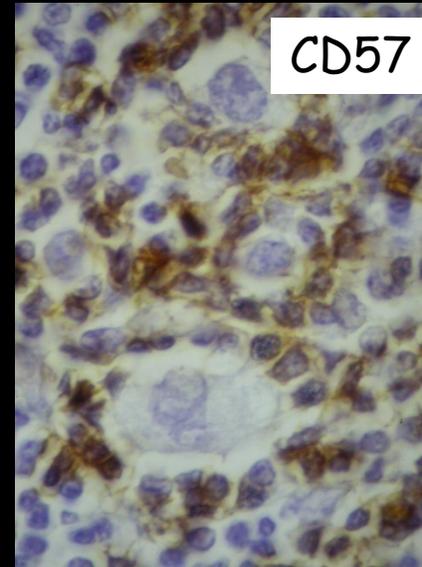
CD20



CD3



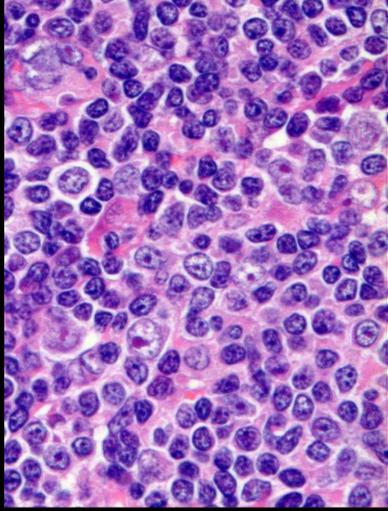
CD21



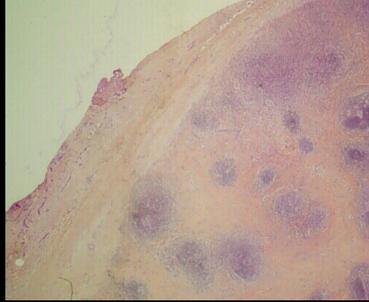
CD57

Zemin

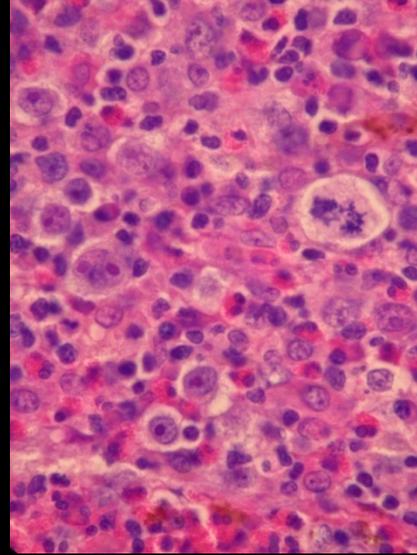
Klasik Hodgkin Lenfoma



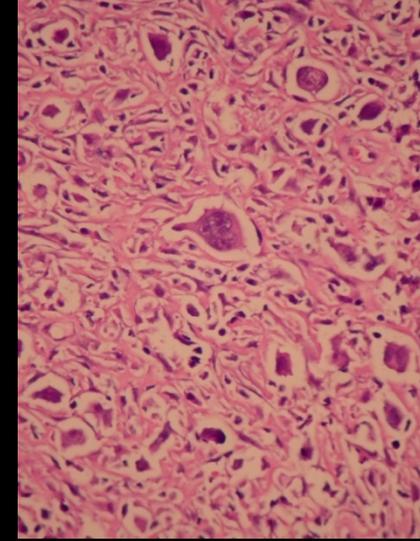
Lenfosit Zengin



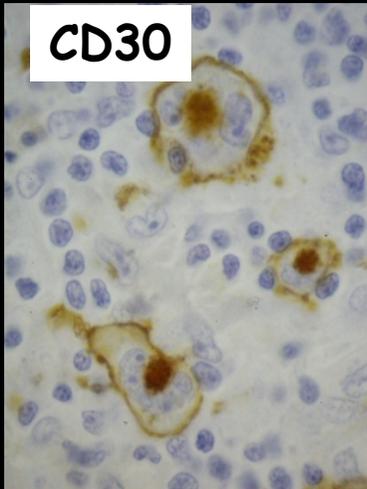
Nodüler Sklerozan



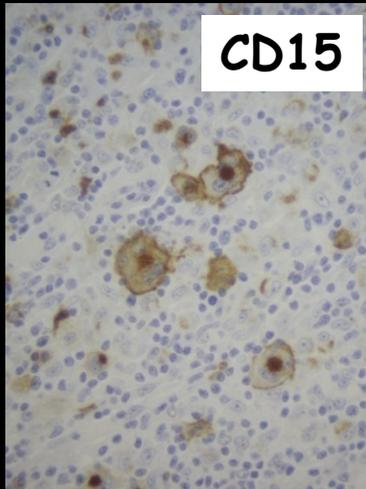
Karışık Hücreli



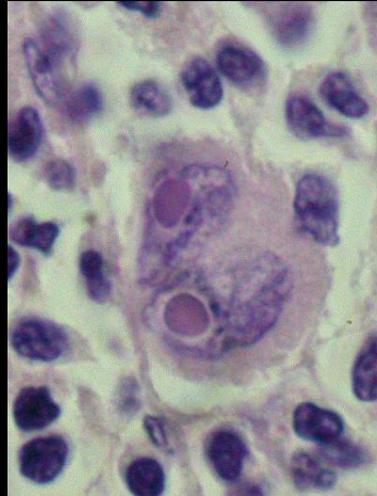
Lenfositten Fakir



CD30



CD15

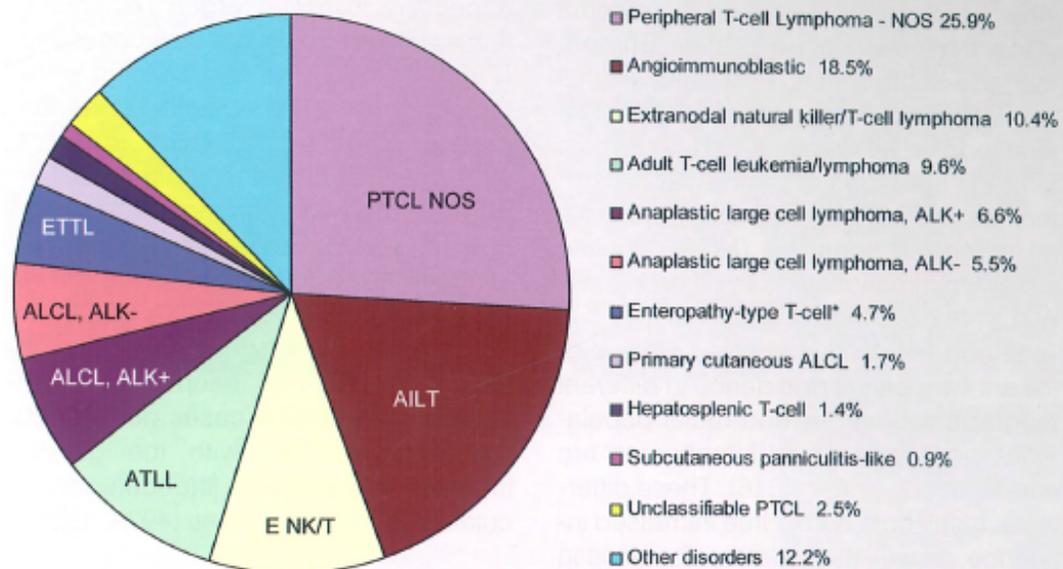


CD 20 -

CD 45 -

MATURE T-CELL AND NK-CELL NEOPLASMS

T-cell prolymphocytic leukaemia	9834/3
T-cell large granular lymphocytic leukaemia	9831/3
<i>Chronic lymphoproliferative disorder of NK-cells</i>	9831/3
Aggressive NK cell leukaemia	9948/3



Systemic EBV positive T-cell lymphoproliferative disease of childhood	9724/3
Hydroa vacciniforme-like lymphoma	9725/3
Adult T-cell leukaemia/lymphoma	9827/3
Extranodal NK/T cell lymphoma, nasal type	9719/3
Enteropathy-associated T-cell lymphoma	9717/3
Hepatosplenic T-cell lymphoma	9716/3
Subcutaneous panniculitis-like T-cell lymphoma	9708/3
Mycosis fungoides	9700/3
Sézary syndrome	9701/3
Primary cutaneous CD30 positive T-cell lymphoproliferative disorders	
Lymphomatoid papulosis	9718/1
Primary cutaneous anaplastic large cell lymphoma	9718/3
Primary cutaneous gamma-delta T-cell lymphoma	9726/3
Primary cutaneous CD8 positive aggressive epidermotropic cytotoxic T-cell lymphoma	9709/3
Primary cutaneous CD4 positive small/medium T-cell lymphoma	9709/3
Peripheral T-cell lymphoma, NOS	9702/3
Angioimmunoblastic T-cell lymphoma	9705/3
Anaplastic large cell lymphoma, ALK positive	9714/3
Anaplastic large cell lymphoma, ALK negative	9702/3

Matür T Hücreli Lenfomalar

Lösemik Dissemine

T Prolenfositik Lösemi

T Large Granüler Lenfositik Lösemi

Agresif NK Hücreli Lösemi

Erişkin T Hücreli Lösemi-Lenfoma

Ekstranodal

Nazal T/NK Hücreli Lenfoma

Enteropati tipi T Hücreli Lenfoma

Hepatosplenik T hücreli Lenfoma

Subkutanöz Pannikülit Benzeri L.

Nodal

Periferik T Hücreli Lenfoma

Anjiyoimmunoblastik Tip T Hücreli L

Anaplastik Büyük Hücreli Lenfoma
(ALCL)

Deri

1. Blastik NK Hücreli lenfoma
2. Mycosis Fungoides / Sezary Sendromu
3. Primer Deri Anaplastik Büyük Hücreli Lenfoma

Matür T Hücreli Lenfomalar

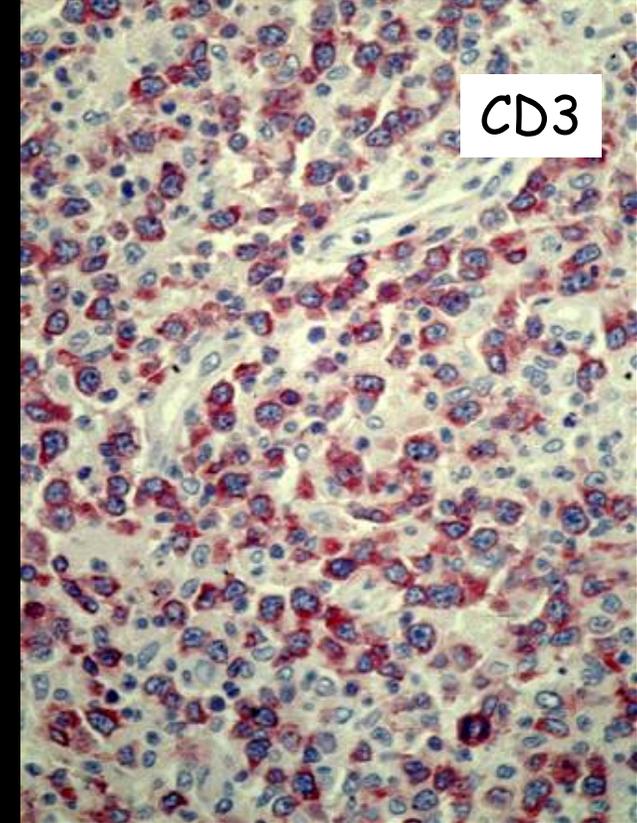
HISTOLOJİ :

- LN T Hücre zonu tutulumu
- Damar artışı
- Polimorfik hücrelerin varlığı (Zeminde çok sayıda histiyosit, Eozinofil Lökosit, plazma hücre varlığı)
- Neoplastik Hücrelerde pleomorfizm

FENOTİP:

- CD3E, CD20 -
- CD1 -, tdt -

GENOTİP : TCR genlerinde clonal rearranjman



Matür T Hücreli Lenfomalar

Genetik Anomaliler

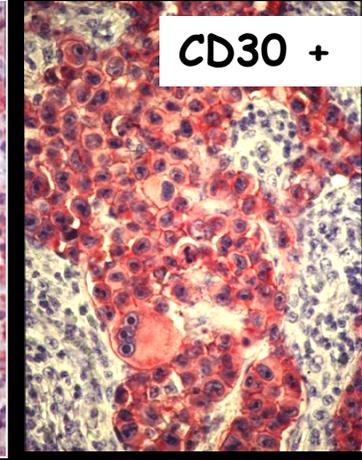
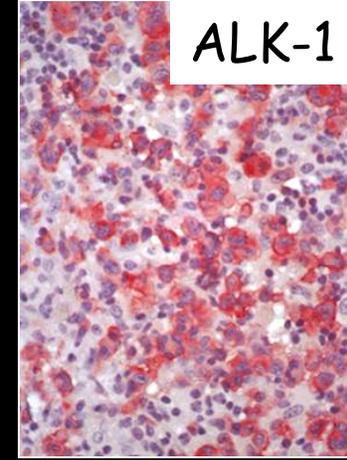
- T-Lenfoblastik del 1p32 (25%) <-----> *TAL1*
- T-Prolenfositik inv14q(q11-q32) <-----> *TCL1*
t(X;14)(q28;q11) <----> *MTCP1*
- ALCL (sistemik) t(2;5) t(2;?) <-----> *ALK(2p23)*
- Anjiyoimmunoblastik ? trisomy 3, trisomy 5 (?)
- NK/T, nasal -tip del(6)(q21-q25) (?)
- Enteropati-tipi +9q (9q33) (?)
- Hepatosplenik tip iso 7q (?)

Anaplastik Büyük Hücreli Lenfoma

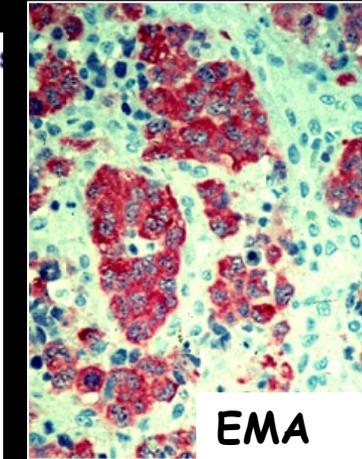
İmmunfenotip

- CD30 +
- EMA + (sıklıkla)
- CD3 + (heterojen)/ CD3 -
- Active sitotoksik profil:
(TIA-1, Perf, GrB +)
- ALK + : 50-80 %

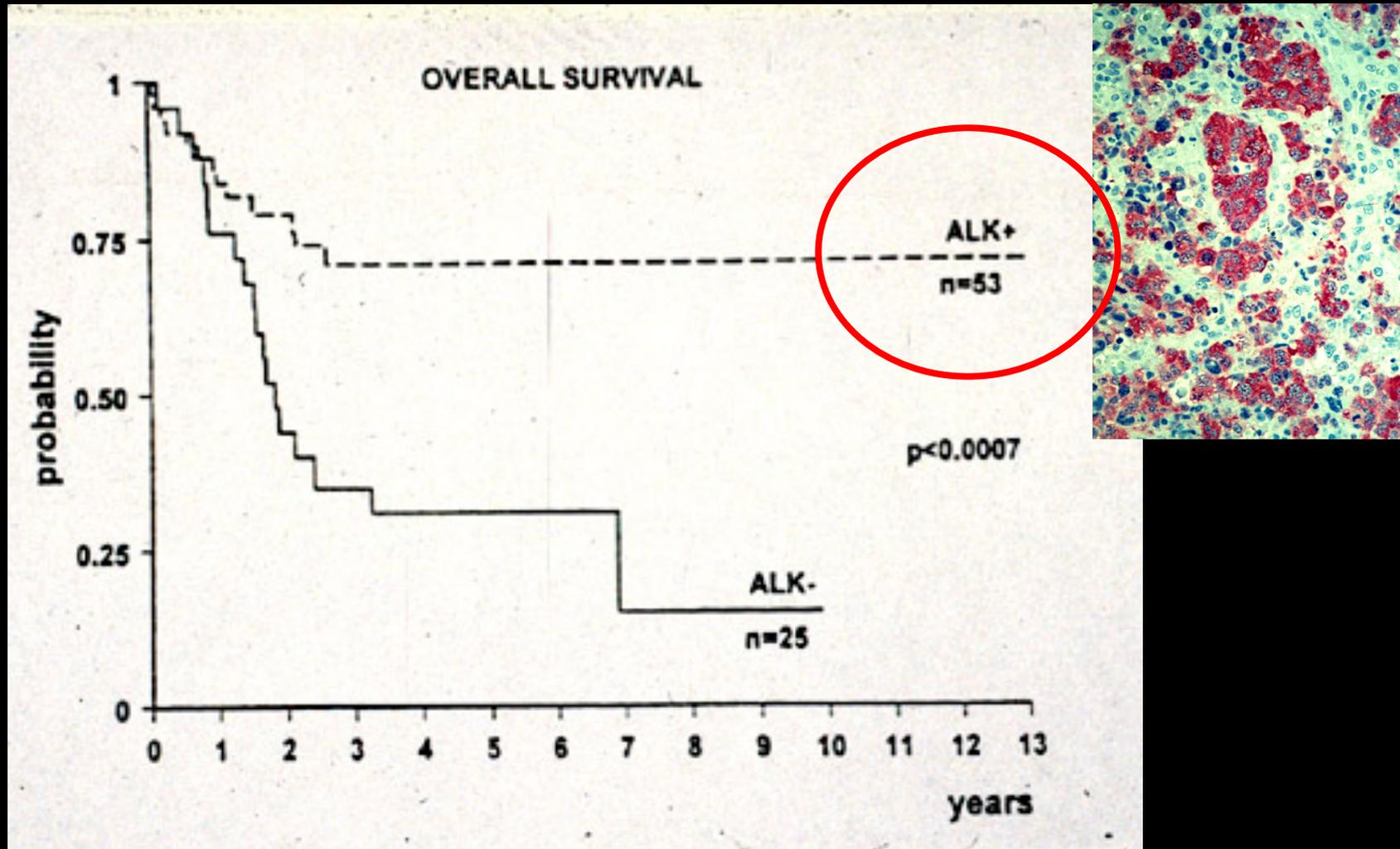
(*) CD15 ve EBV negatif

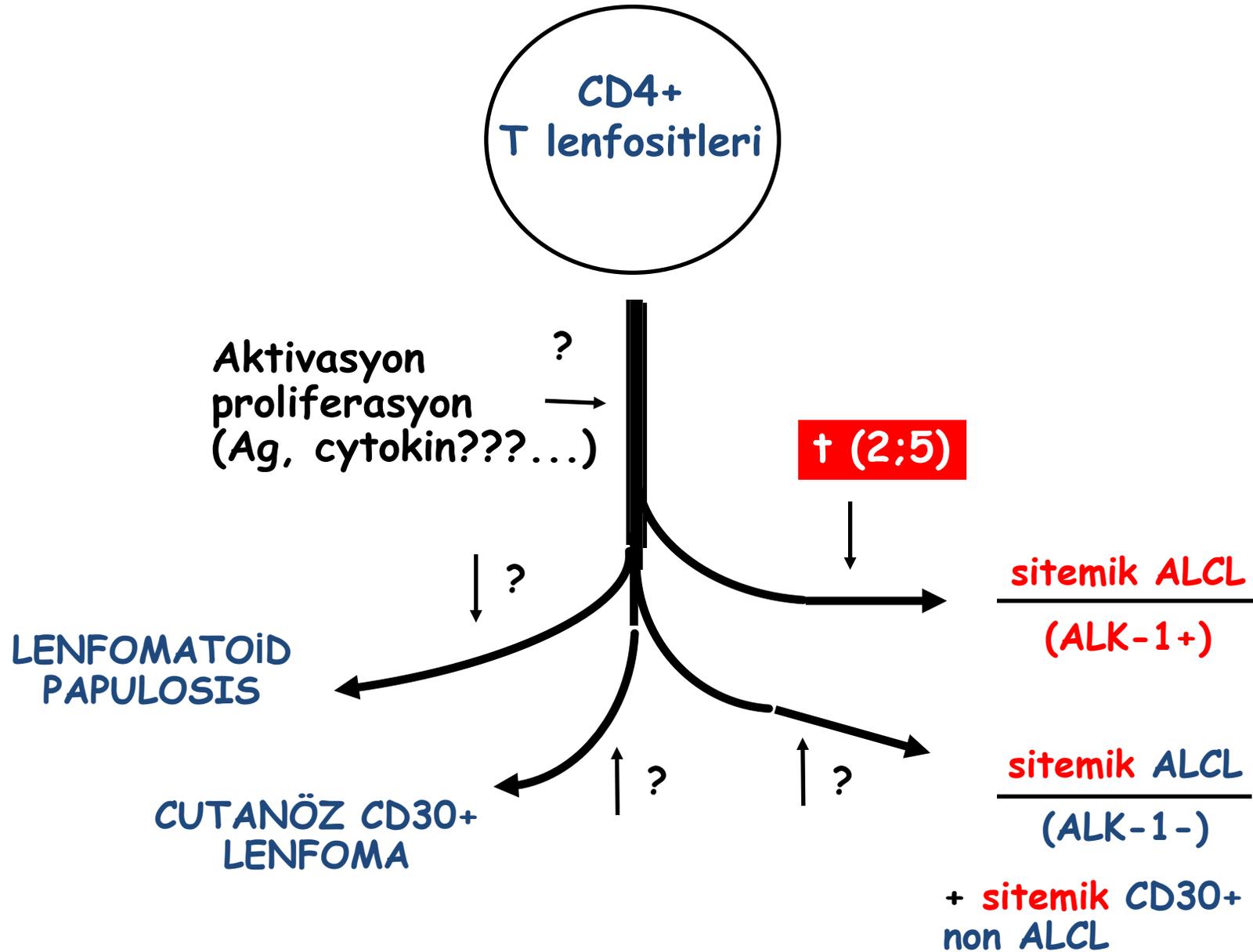


Frequency	Genetic Alteration	Fusion Proteins
72.5%	t(2;5)	Nucleophosmin (80 kd) fused with ALK (TKD)
17.5%	t(1;2)	Tropomyosin 3 (104 kd) fused with ALK (TKD)
2.5%	t(2;3)	Ttk Fusion Gene* (97 kd) fused with ALK (TKD)
2.5%	inv(2)	AT1C (Pur H gene)** (96 kd) fused with ALK (TKD)
2.5%	t(2;22)	Clathrin Heavy Chain (250 kd) fused with ALK (TKD)



Anaplastik Büyük Hücreli Lenfoma

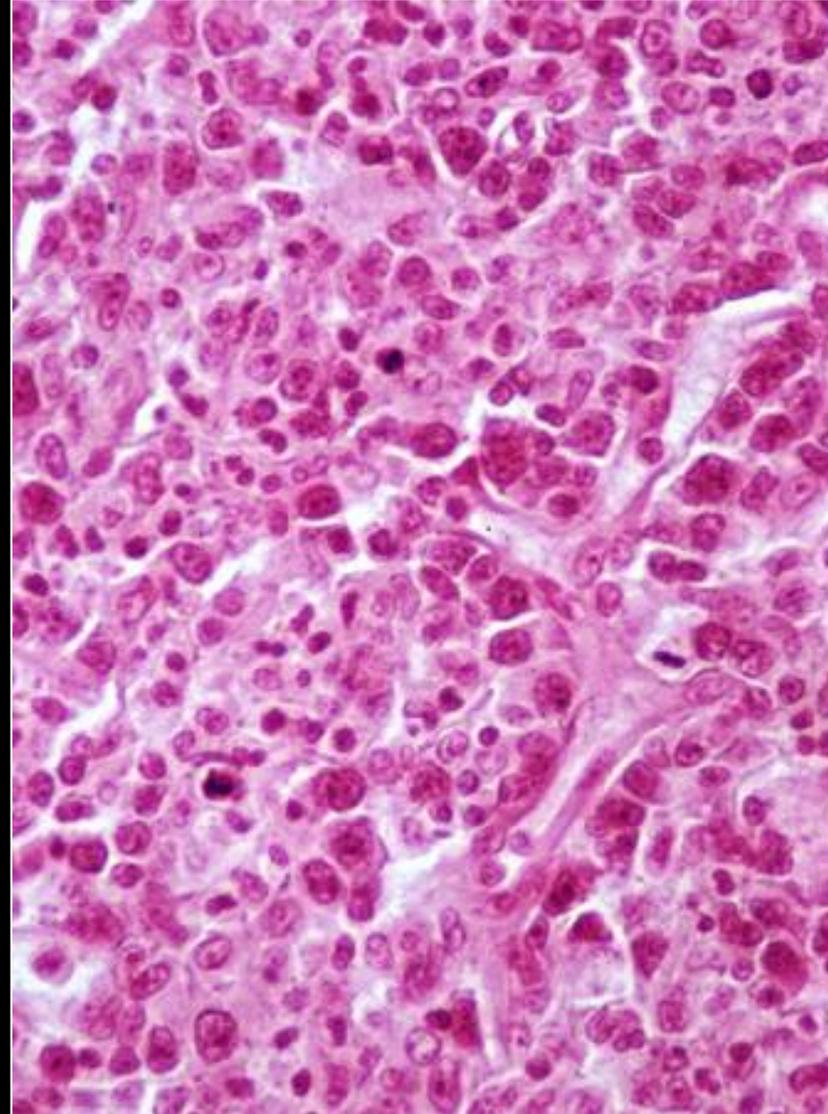




PERİFERİK T-HÜCRELİ LENFOMA (PTCL), UNSPECIFIED

HİSTOLOJİK TİPLER

- Pleomorfik tip
- Lymphoepithelioid (Lennert's) lenfoma
- T-zone lenfoma



Angioimmunoblastic Tip T Hücreli Lymphoma

immunhistokimya

- orta boyutlu T (CD3 +) hücreler
- FDC network (CD23, CD21)
- B-blastlar (EBV +)

GENETİK

- TCR g R (80%), IgH R (20-40%)
- Trizomi 3 (40%)

Klinik

- B-symptoms
- Multiple LAP
- Splenomegali, Deri döküntüsü
- Hipergamma globulinemi,
- anemi (+/- Coombs +)
- Kötü prognoz

Patogenez (?) :

- Hücre kökeni $\alpha\beta$ CD4 + (CD10+) T hücreleri
- IL6

