

Neoplasias Hematológicas

Leucemias y Linfomas

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Fac Medicina UDP

CANCER

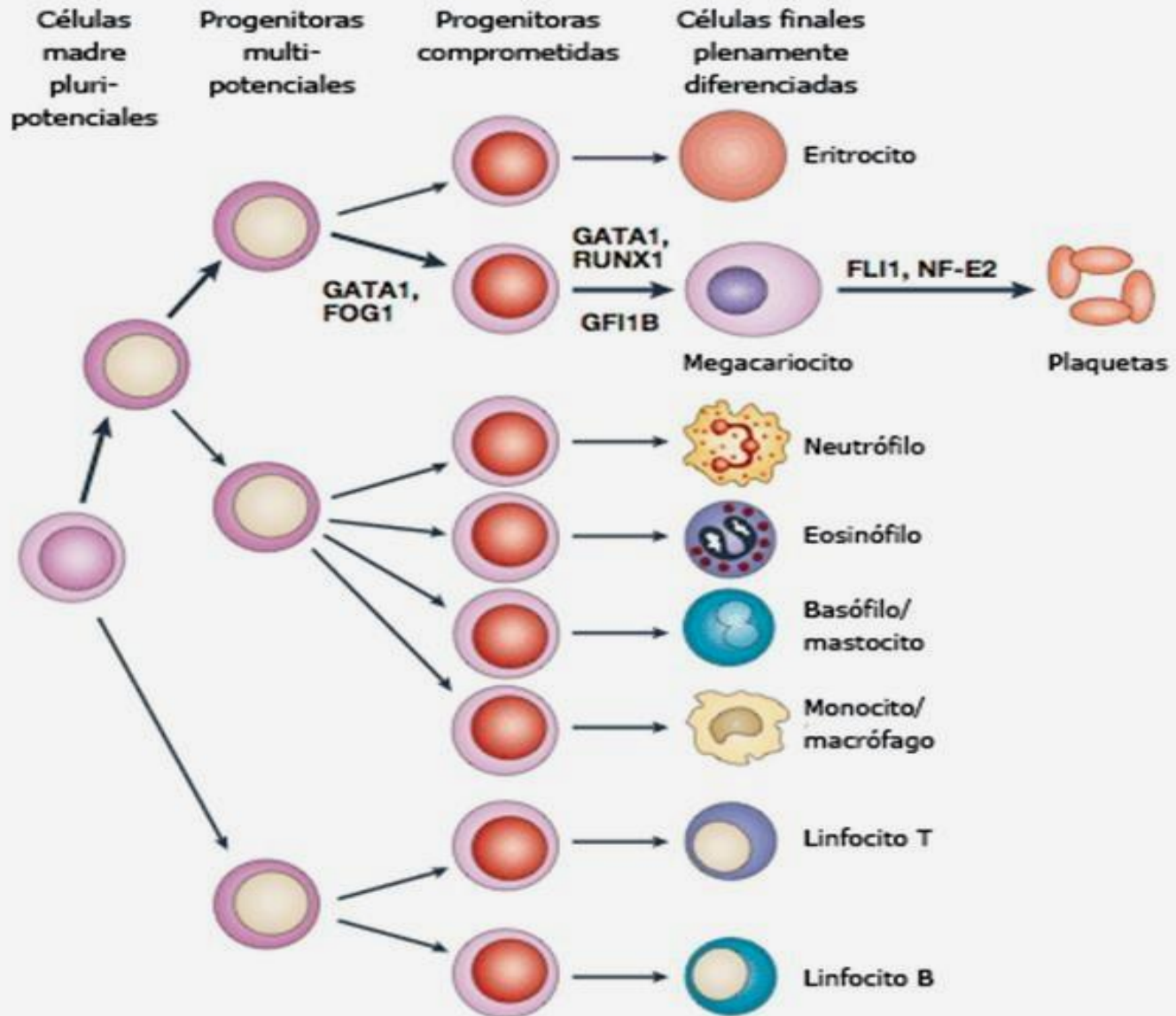
- Complejo conjunto de enfermedades
- Enfermedad multifactorial. Ocorre en etapas
- Afecta a células somáticas de nuestro organismo
- Se alteran controles de: Proliferación
Diferenciación
Posición
- Crecimiento de tumores primarios y metástasis



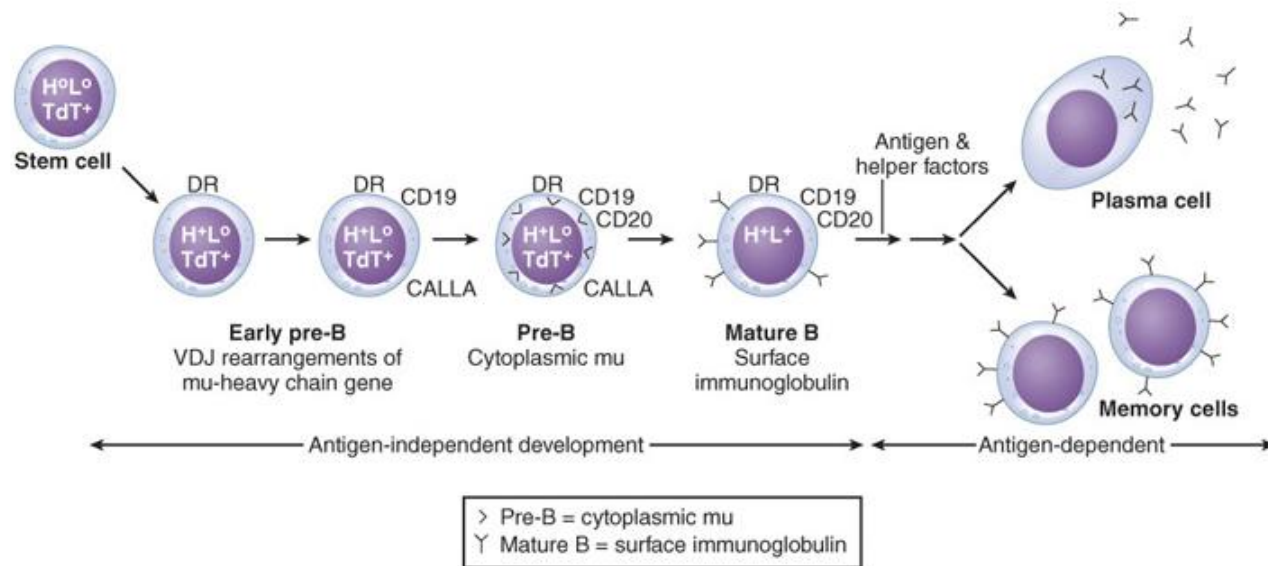
CANCER

- Afecta a células somáticas y material genético (DNA).
- Enfermedad genética. Se alteran ciertos genes.
Oncogenes y Genes supresores de tumor. Otros
- Células tumorales generan células tumorales.
- La proliferación de células tumorales genera tumores malignos.
- Tumores malignos : población **heterogenea** de células.
Aneuploidía y Heteroploidía

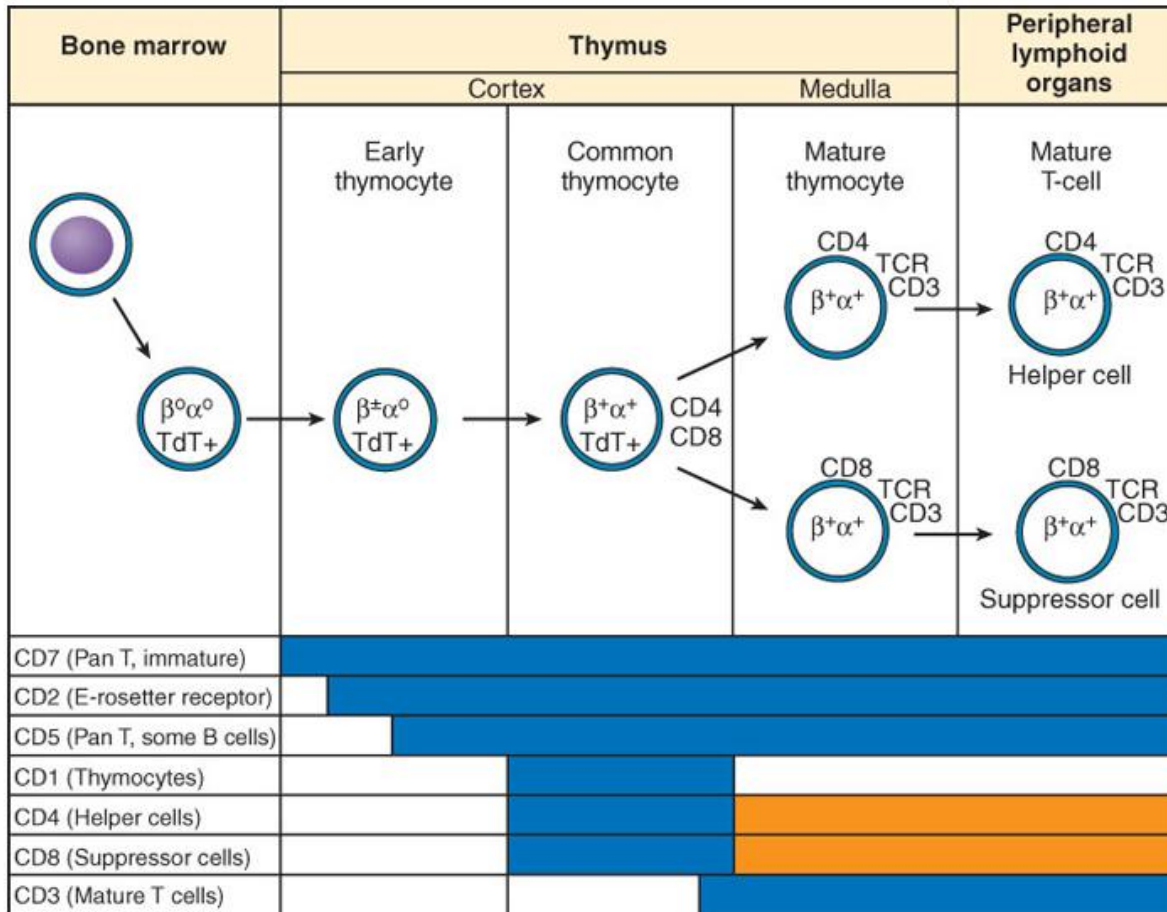
SISTEMA HEMATOPOYETICO

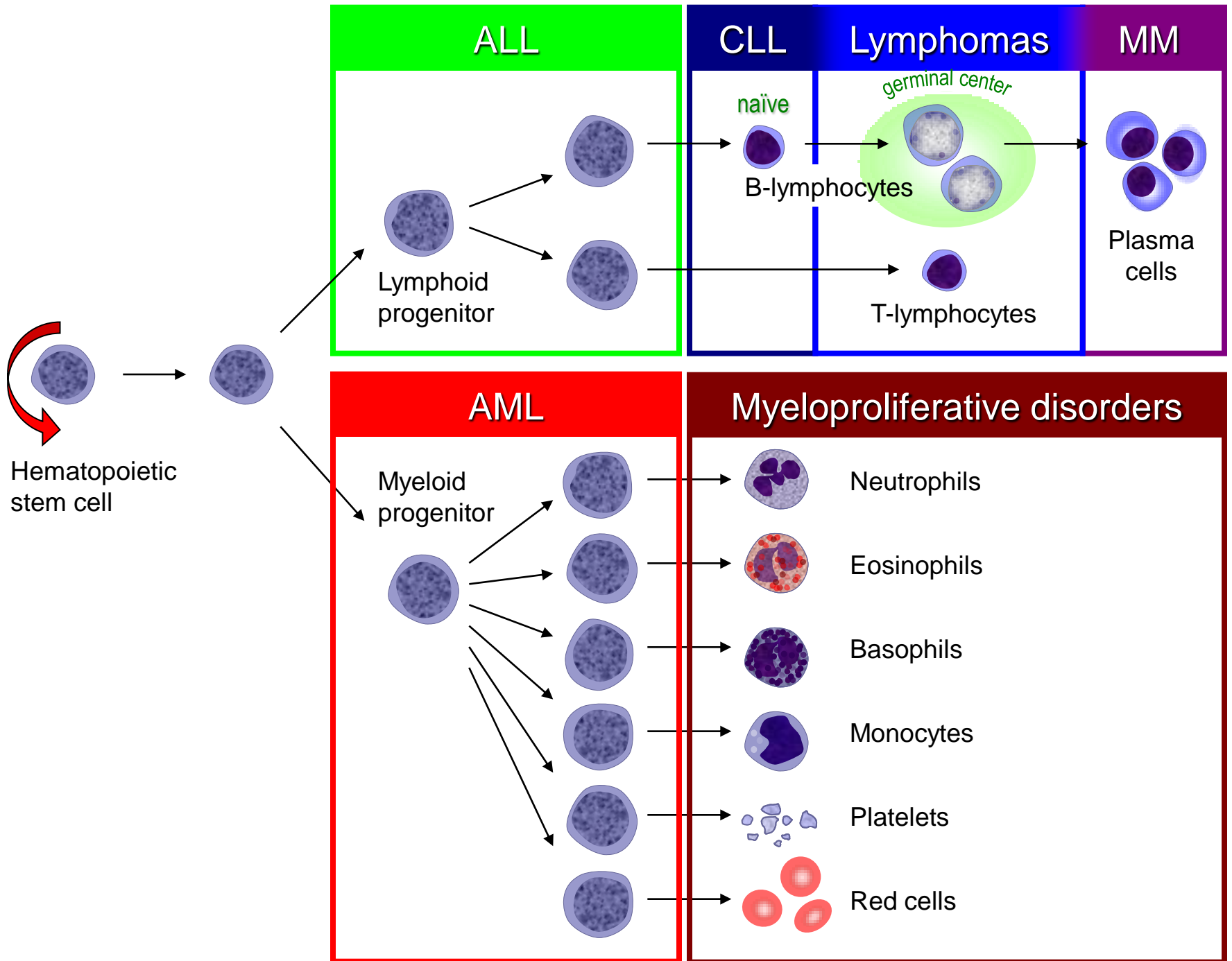


Diferenciación B



Diferenciación T





DNA

Transcripción

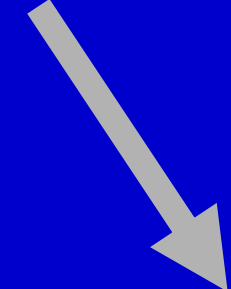
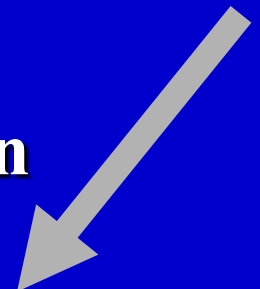
Replicación

mRNA

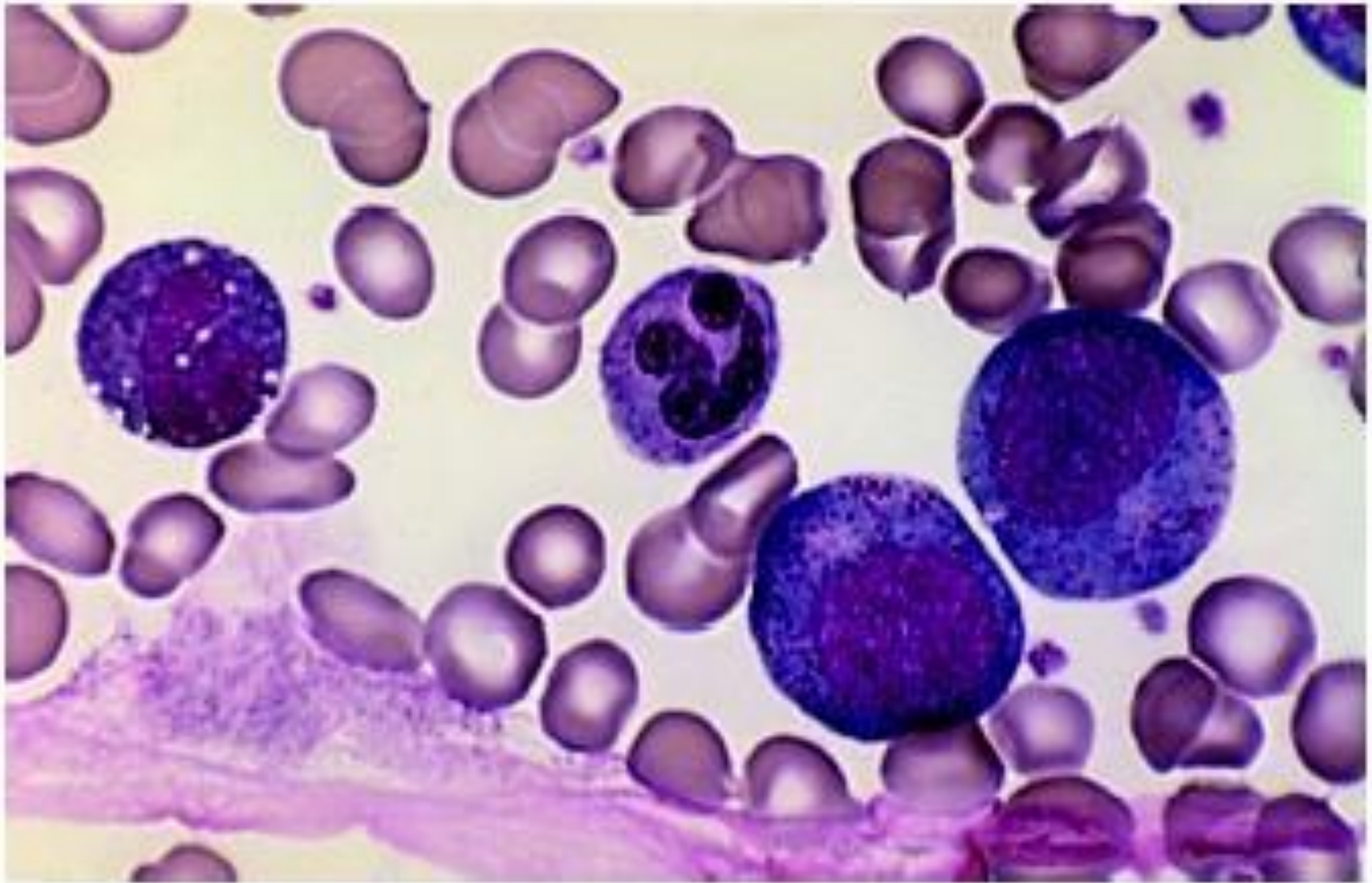
DNA

Traducción

Proteínas



LEUCEMIAS



Sintomatología

- Ganglios linfáticos inflamados (cuello y axilas, sin dolor)
- Fiebres o sudores nocturnos
- Infecciones frecuentes
- Debilidad o cansancio
- Sangrado y facilidad para magullarse (sangrado de
- Encías, manchas de color morado en la piel o pequeños puntos rojos bajo la piel)
- Hinchazón o molestia en el abdomen (Hepato Esplenomegalia)
- Pérdida de peso por razones desconocidas
- Dolor en los huesos o articulaciones

LEUCEMIAS

<p>AGUDAS (Todas edades)</p>	<p>Mieloides AML (adultos)</p>	<p>Linfoides ALL (niños)</p>
<p>CRONICAS (Adultos)</p>	<p>Mieloide CML (30-50años)</p>	<p>Linfoides CLL (>40 años)</p>

LEUCEMIAS

	AGUDA	CRONICA
Aparición	Repentina	Insidiosa
Curso	6 meses	2-6 años
Células	> 30% blastos	≈ diferenciadas
Anemia	prominente	leve
Trombocitopenia	prominente	leve
Recuento Leucocitos	variable	elevado
Linfoadenopatía	leve	prominente
Esplenomegalia	leve	prominente

DIFERENCIACION MIELOIDE

mieloblasto

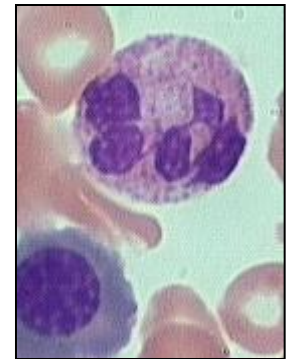
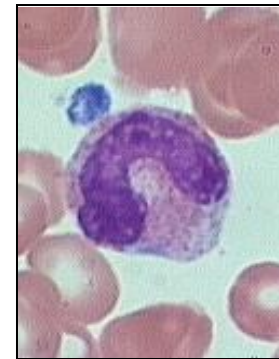
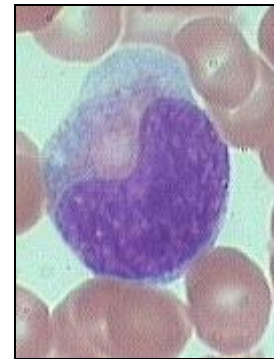
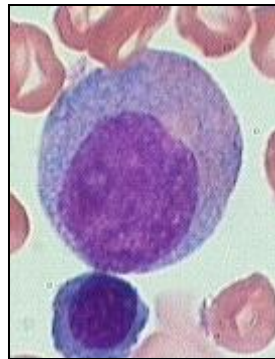
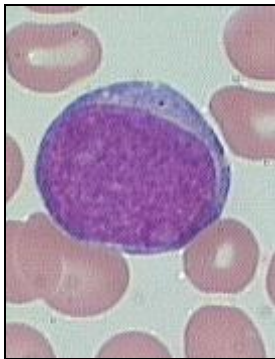
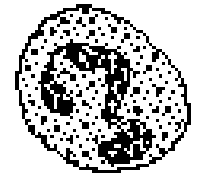
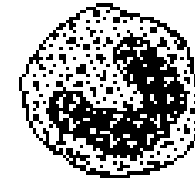
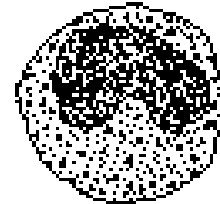
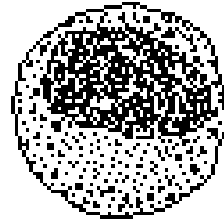
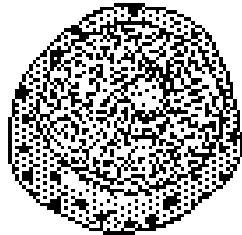
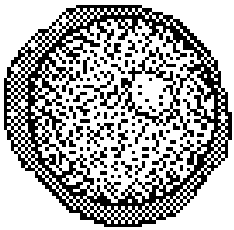
promielocito

mielocito

metamielocito

banda

neutrofilo



MADURATION

Leucemias y Translocaciones Cromosomicas

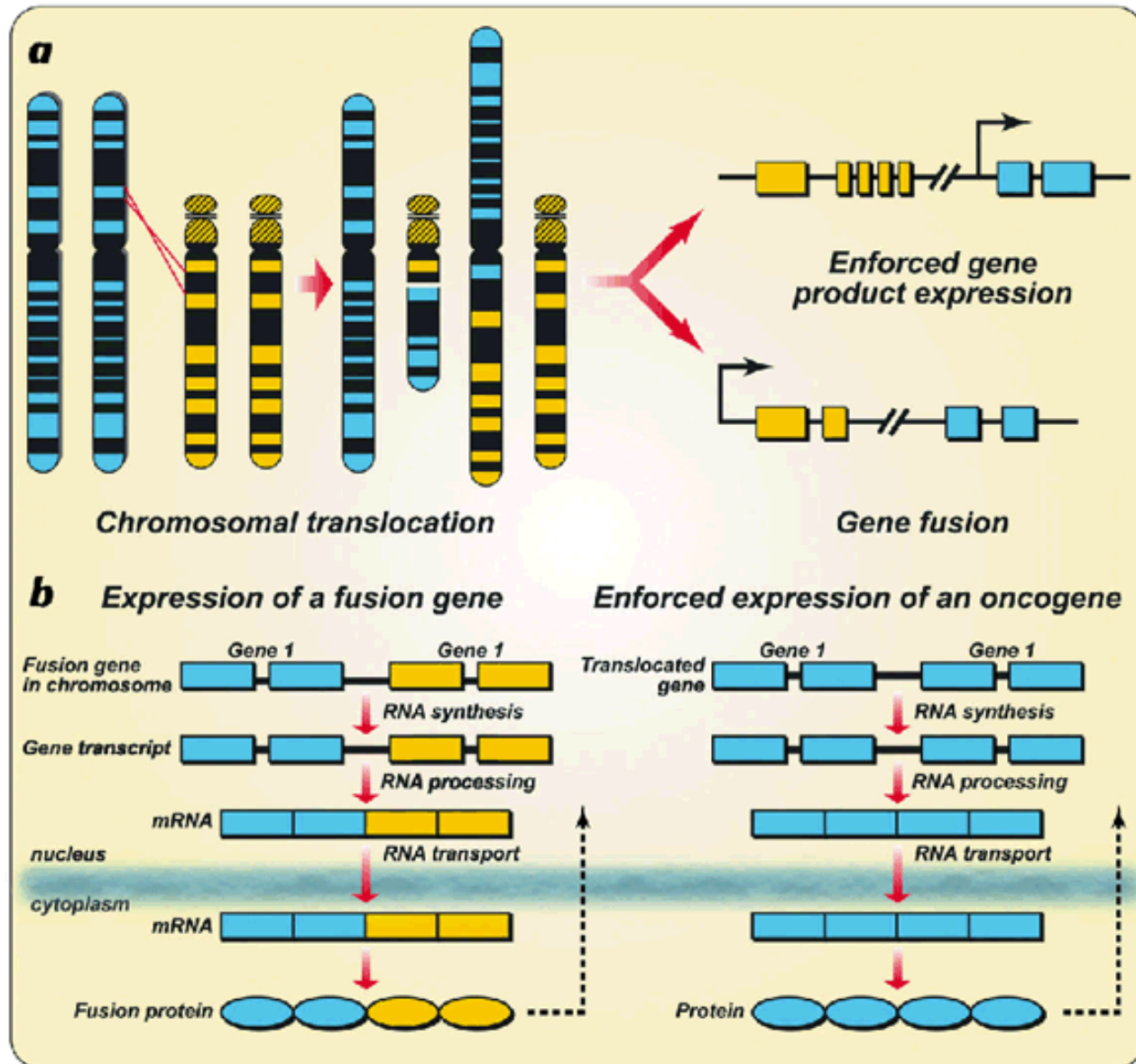


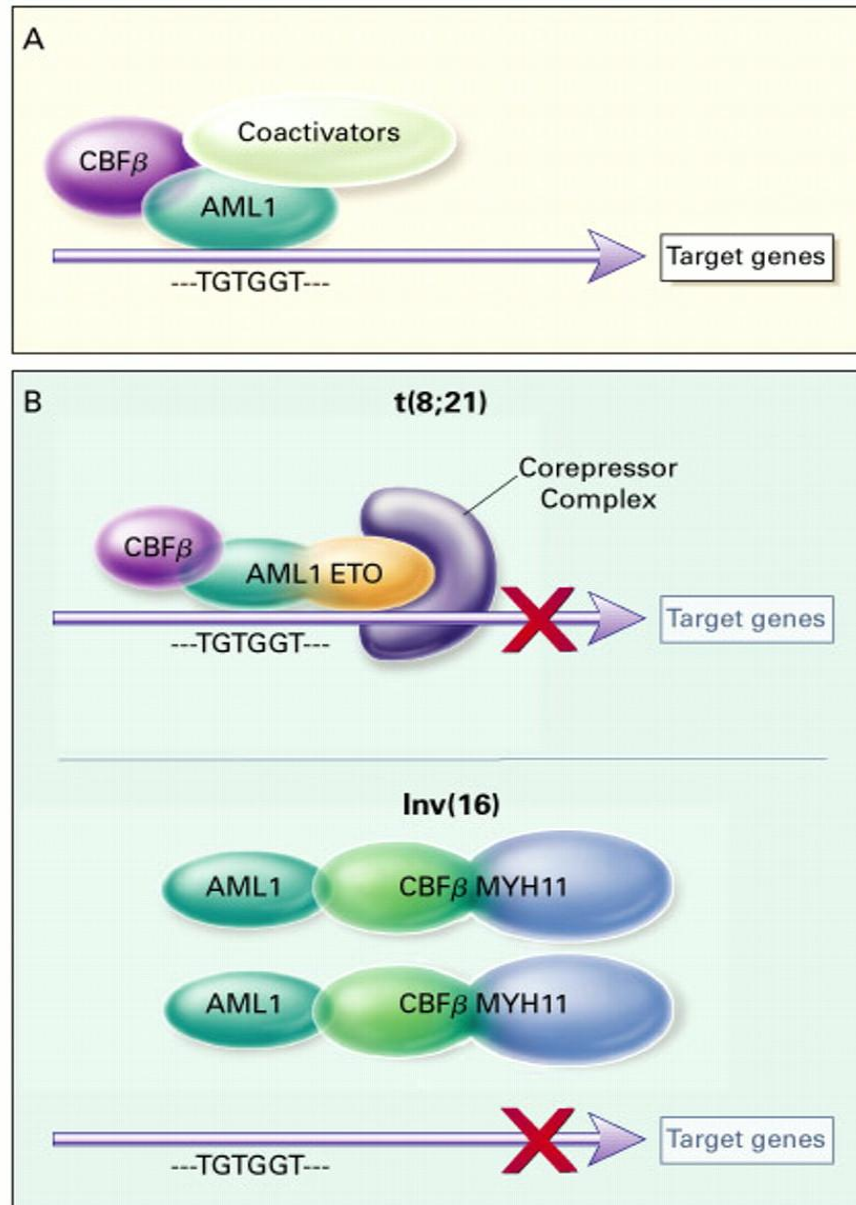
TABLE 1. THE FRENCH-AMERICAN-BRITISH (FAB) CLASSIFICATION OF AML AND ASSOCIATED GENETIC ABNORMALITIES.

FAB SUBTYPE	COMMON NAME (% OF CASES)	RESULTS OF STAINING			ASSOCIATED TRANSLOCATIONS AND REARRANGEMENTS (% OF CASES)	GENES INVOLVED
		MYELOPER- OXIDASE	SUDAN BLACK	NONSPECIFIC ESTERASE		
M0	Acute myeloblastic leukemia with minimal differentiation (3%)	-	-	-*	inv(3q26) and t(3;3) (1%)	<i>EVII</i>
M1	Acute myeloblastic leukemia without maturation (15-20%)	+	+	-		
M2	Acute myeloblastic leukemia with maturation (25-30%)	+	+	-	t(8;21) (40%), t(6;9) (1%)	<i>AML1-ETO, DEK-CAN</i>
M3	Acute promyelocytic leukemia (5-10%)	+	+	-	t(15;17) (98%), t(11;17) (1%), t(5;17) (1%)	<i>PML-RARα, PLZF-RARα, NPM RARα</i>
M4	Acute myelomonocytic leukemia (20%)	+	+	+	11q23 (20%), inv(3q26) and t(3;3) (3%), t(6;9) (1%)	<i>MLL, DEK-CAN, EVII</i>
M4Eo	Acute myelomonocytic leukemia with abnormal eosinophils (5-10%)	+	+	+	inv(16), t(16;16) (80%)	<i>CBFβ-MYH11</i>
M5	Acute monocytic leukemia (2-9%)	-	-	+	11q23 (20%), t(8;16) (2%)	<i>MLL, MOZ-CBP</i>
M6	Erythroleukemia (3-5%)	+	+	-		
M7	Acute megakaryocytic leukemia (3-12%)	-	-	+†	t(1;22) (5%)	Unknown

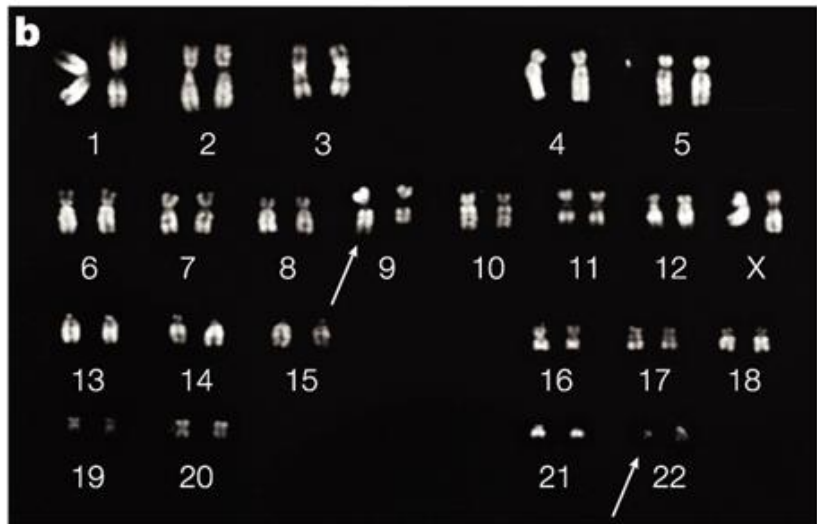
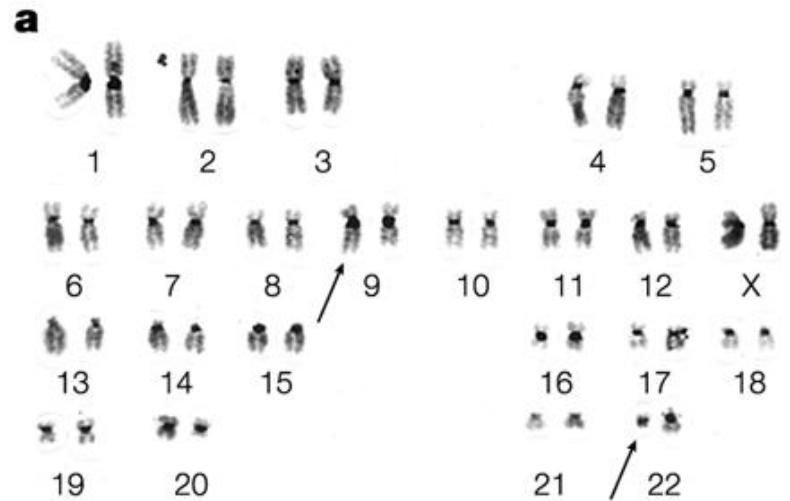
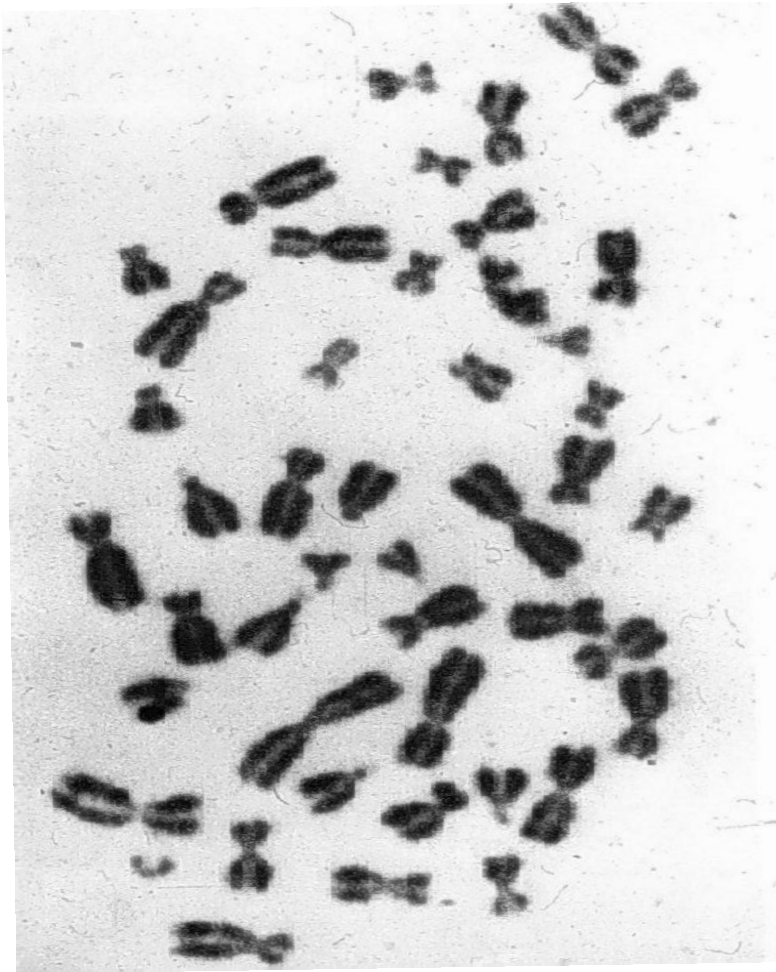
*Cells are positive for myeloid antigen (e.g., CD13 and CD33).

†Cells are positive for α -naphthylacetate and platelet glycoprotein IIb/IIIa or factor VIII-related antigen and negative for naphthylbutyrate.

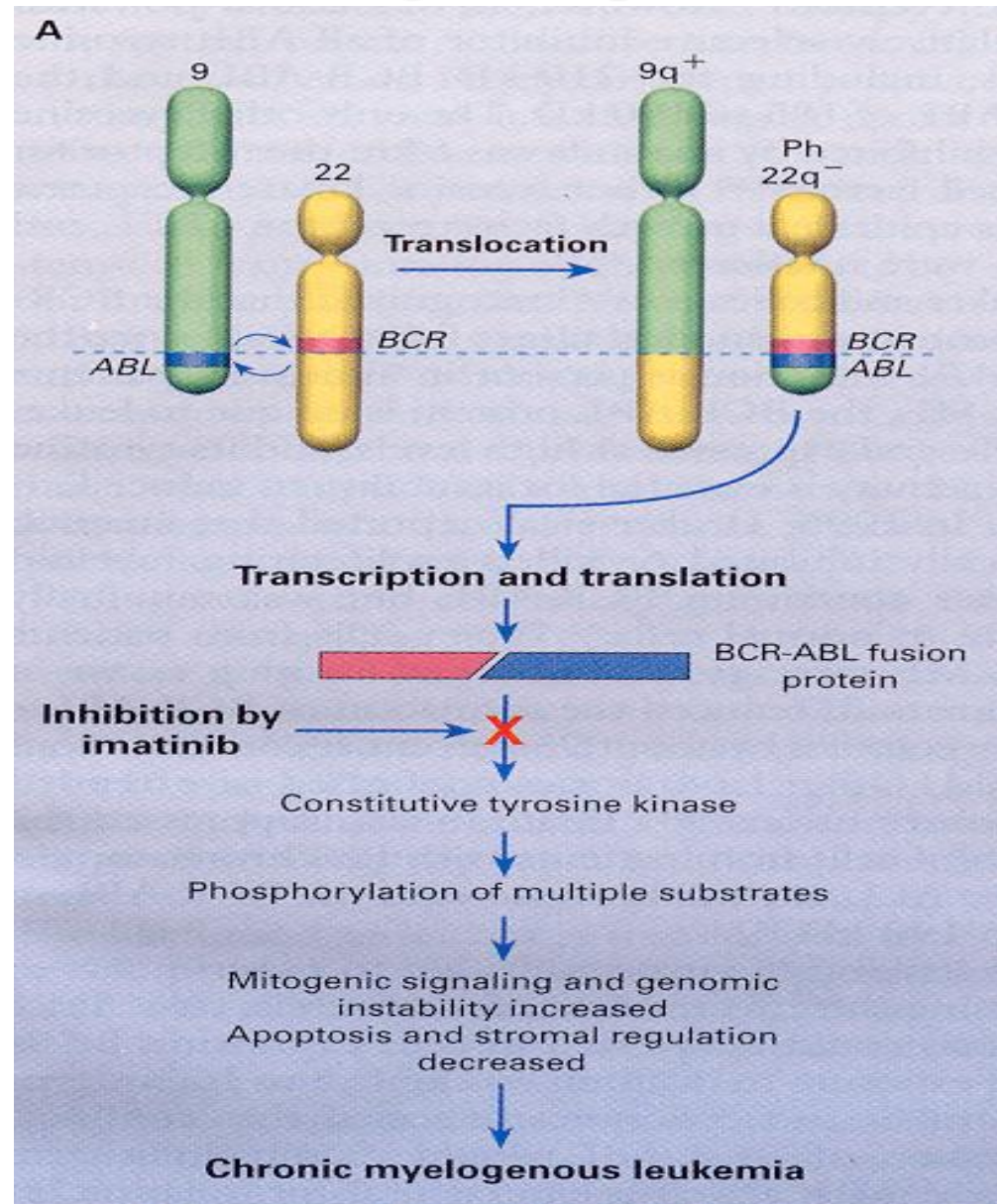
TRANSLOCACIONES Y REPRESION DE GENES



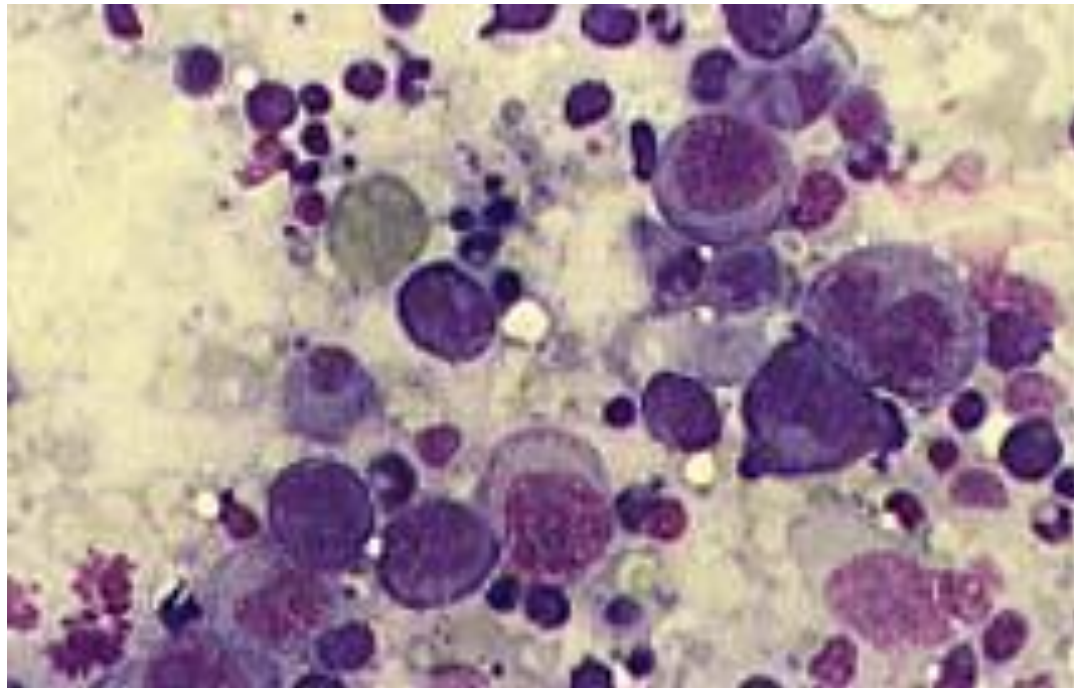
CML Cromosoma Phi y Translocacion 9/22



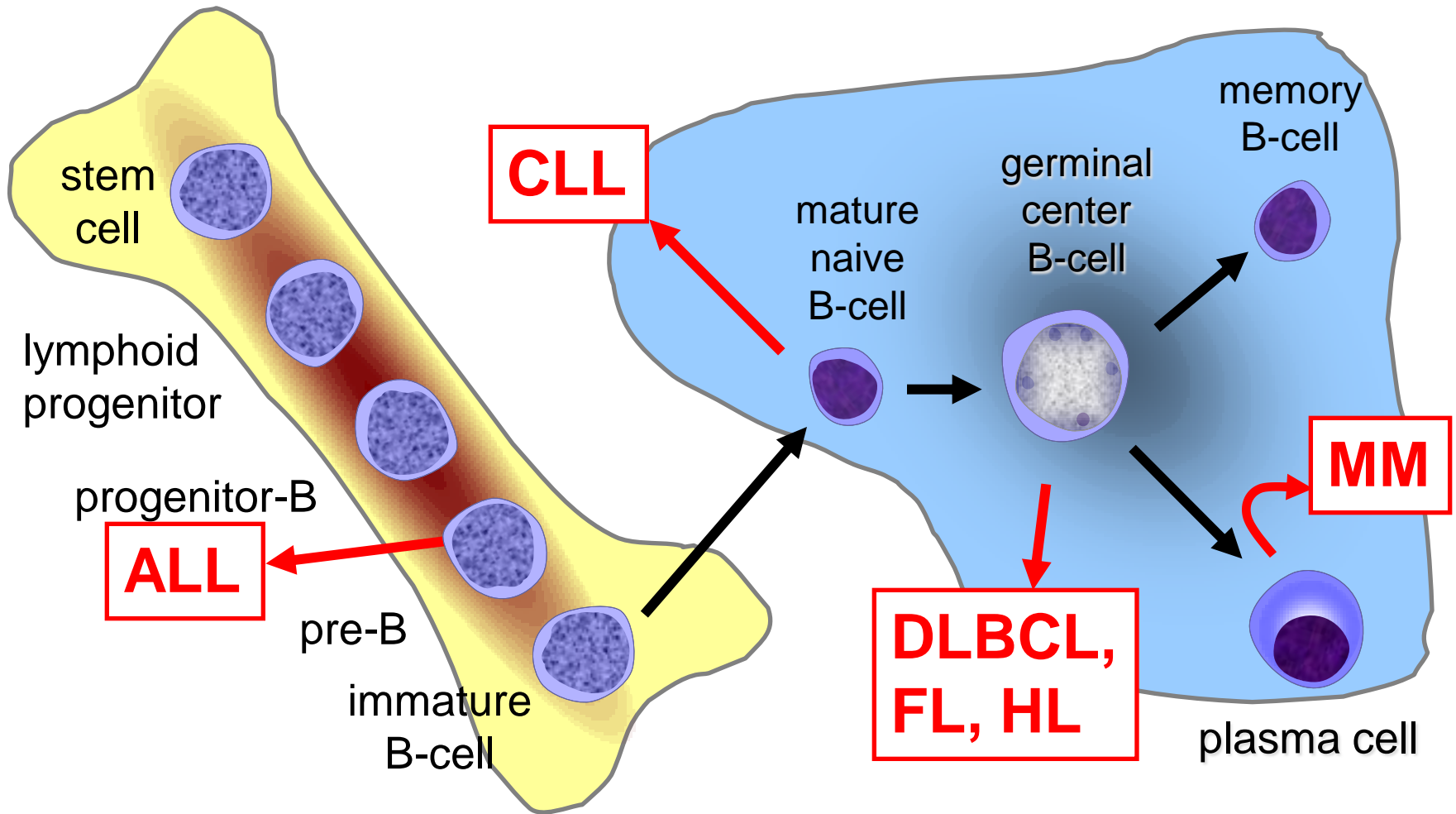
Activación oncogen abl por translocación



LINFOMAS



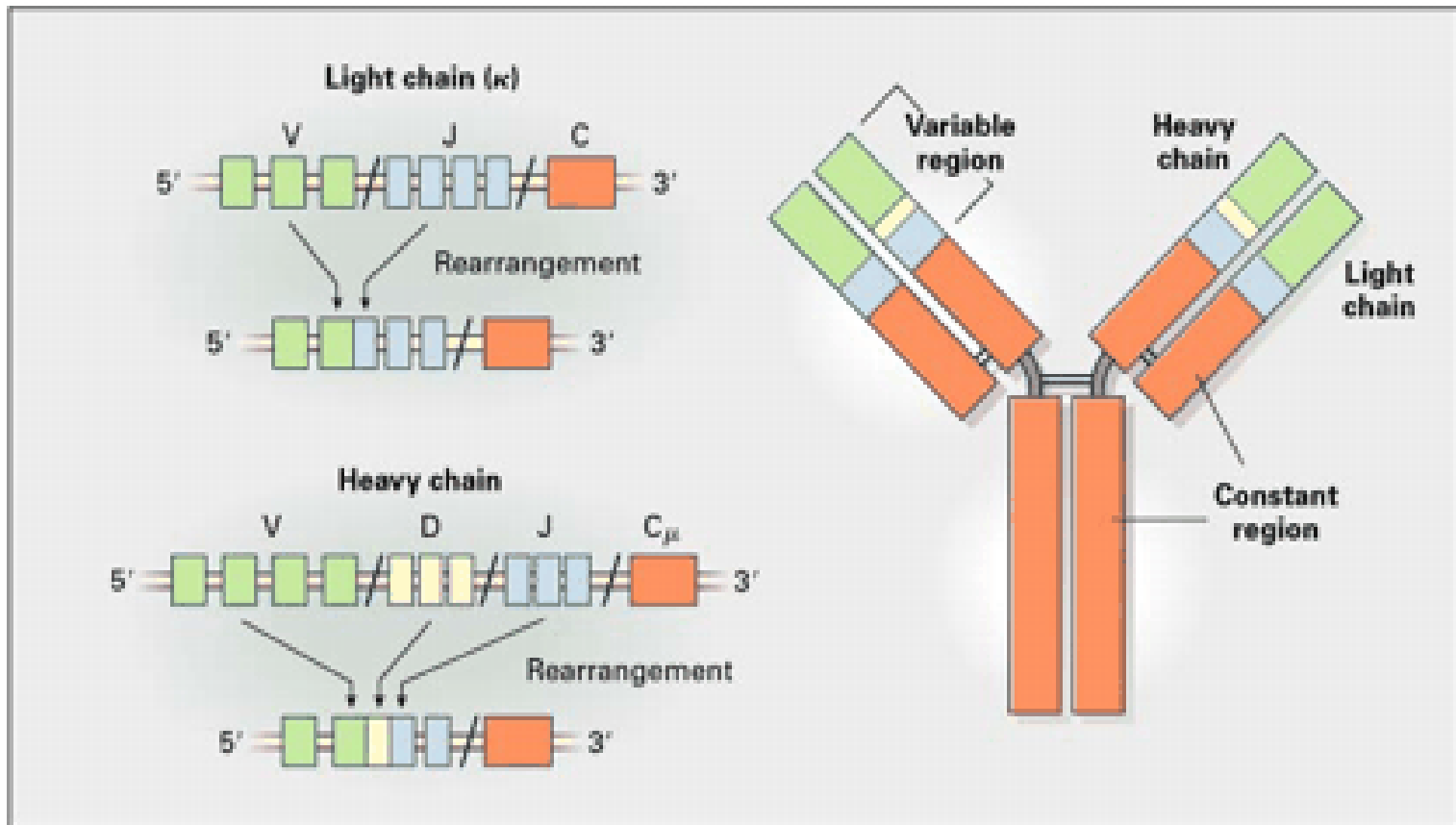
DESARROLLO CELULAS B

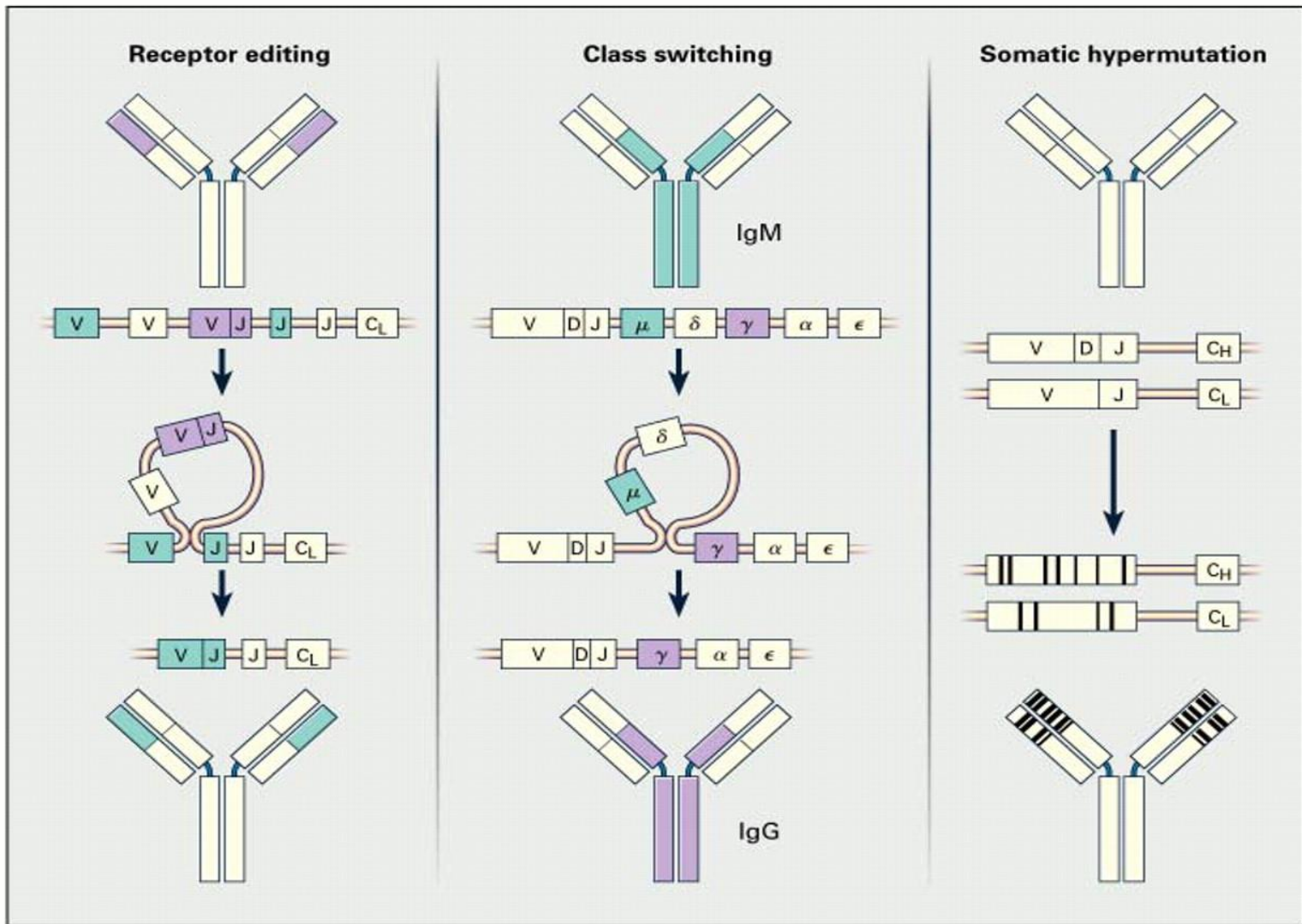


Médula Osea

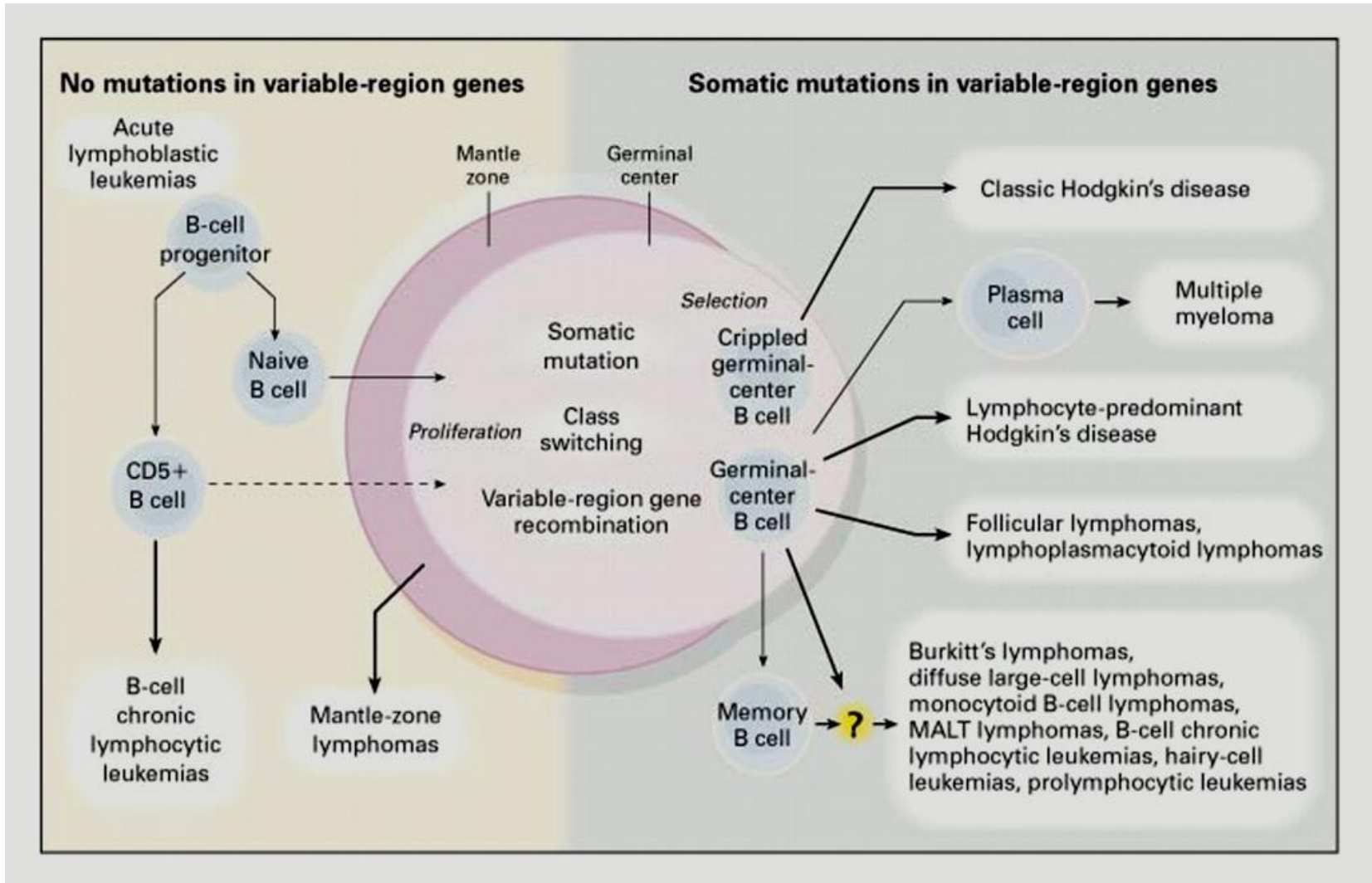
Tejido Linfoide

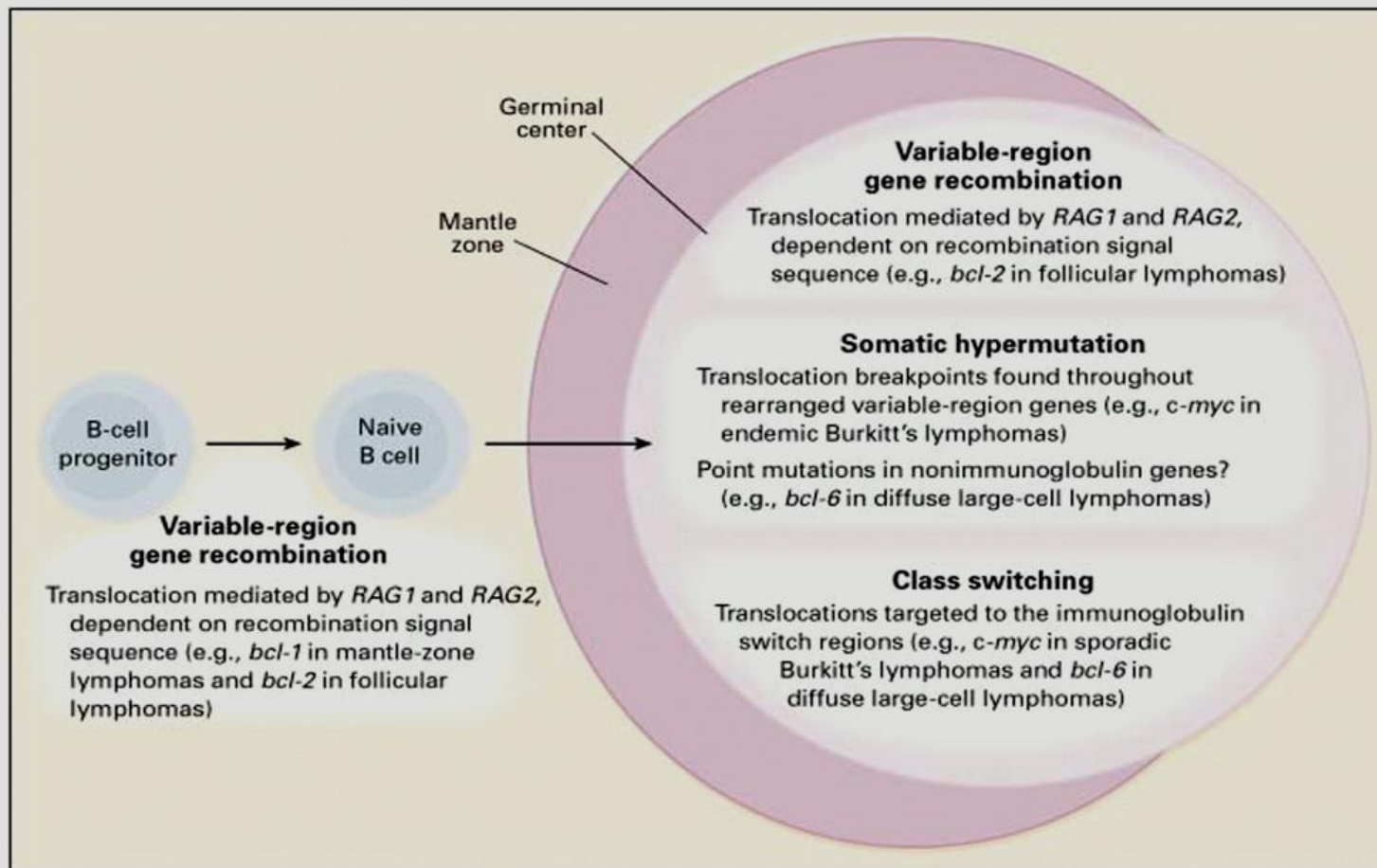
GENES Igs Y ORIGEN DE LINFOMAS

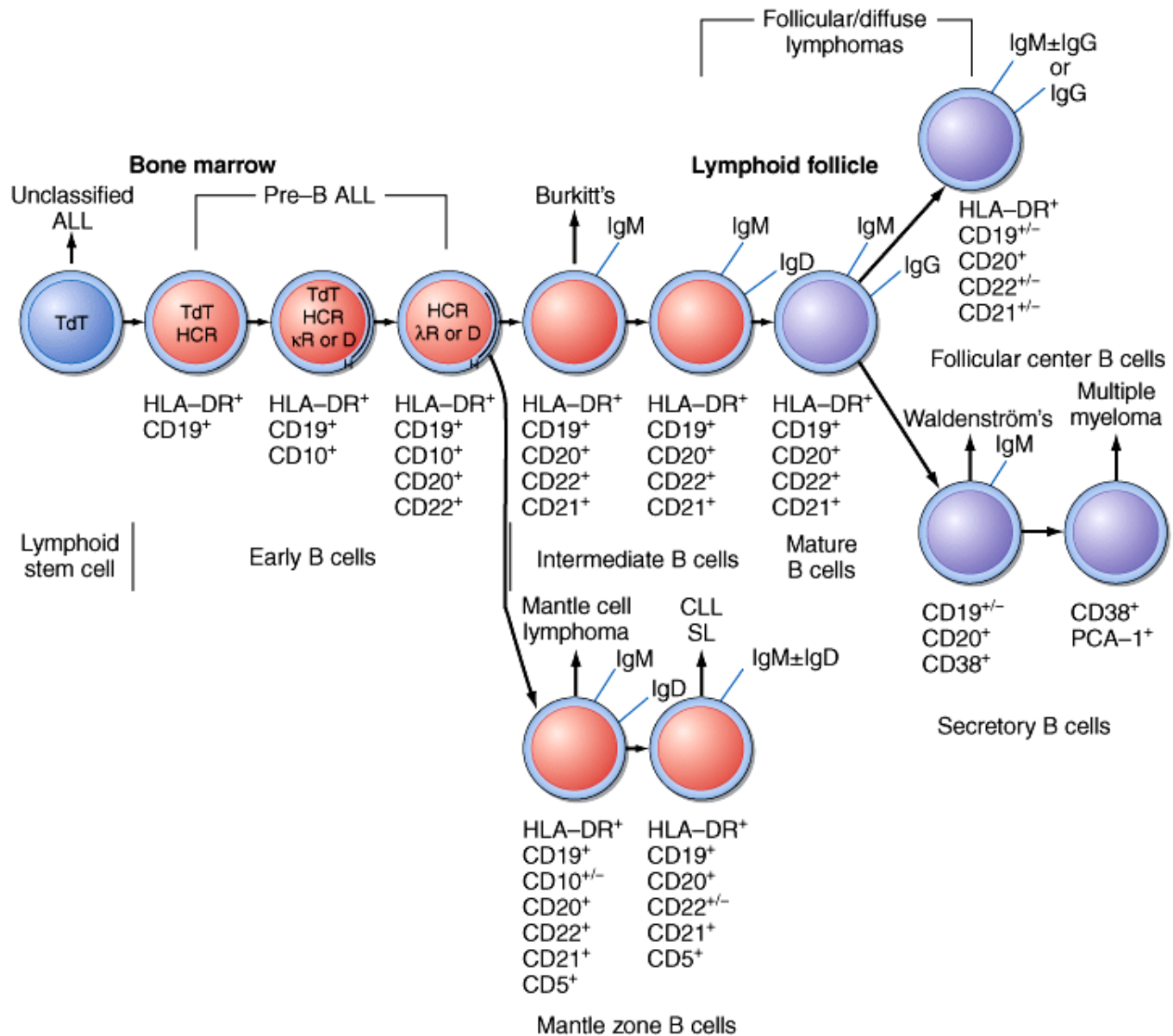




ORIGEN DE LINFOMAS



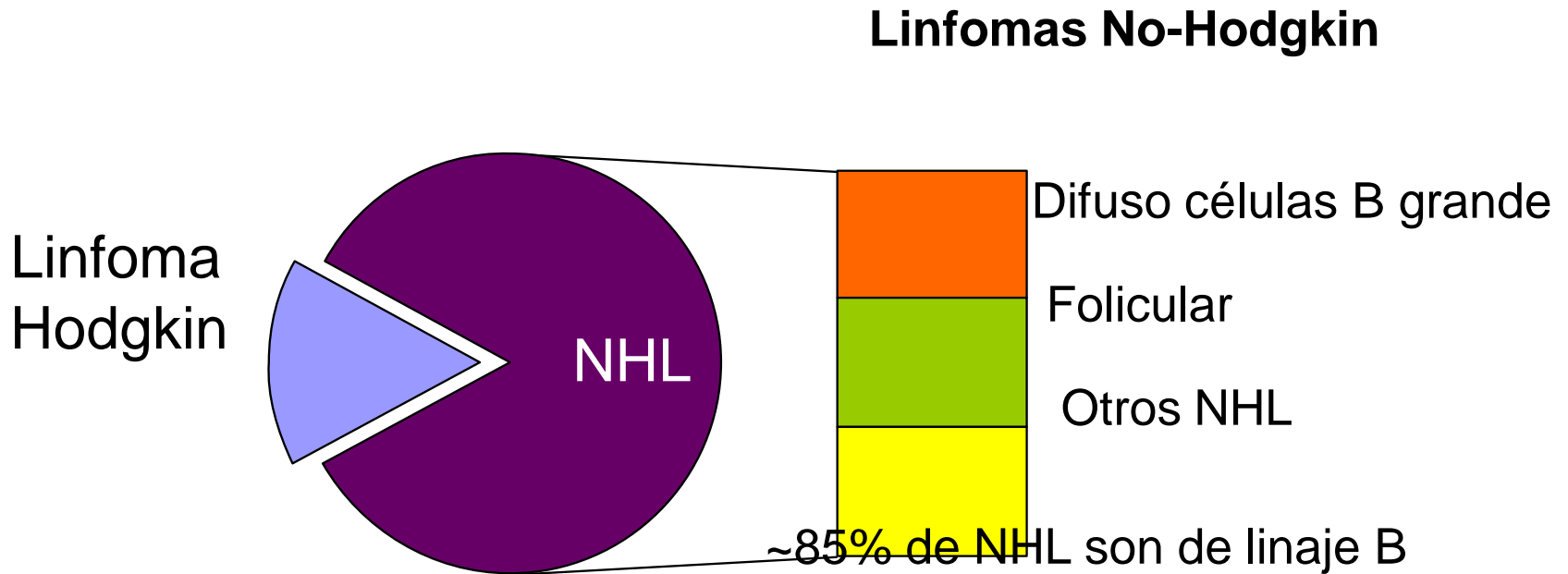




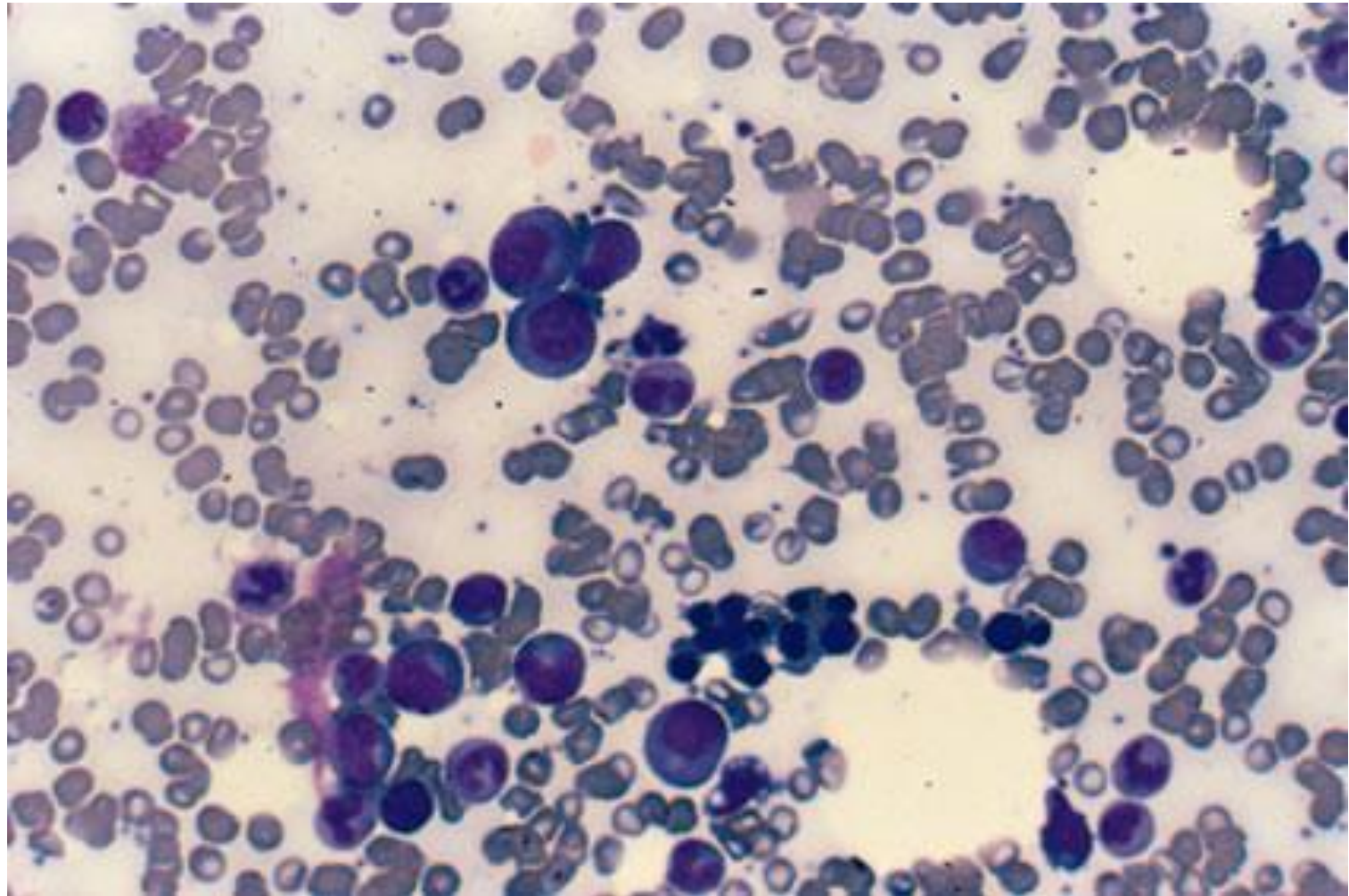
Antigen-independent differentiation

Antigen-driven differentiation

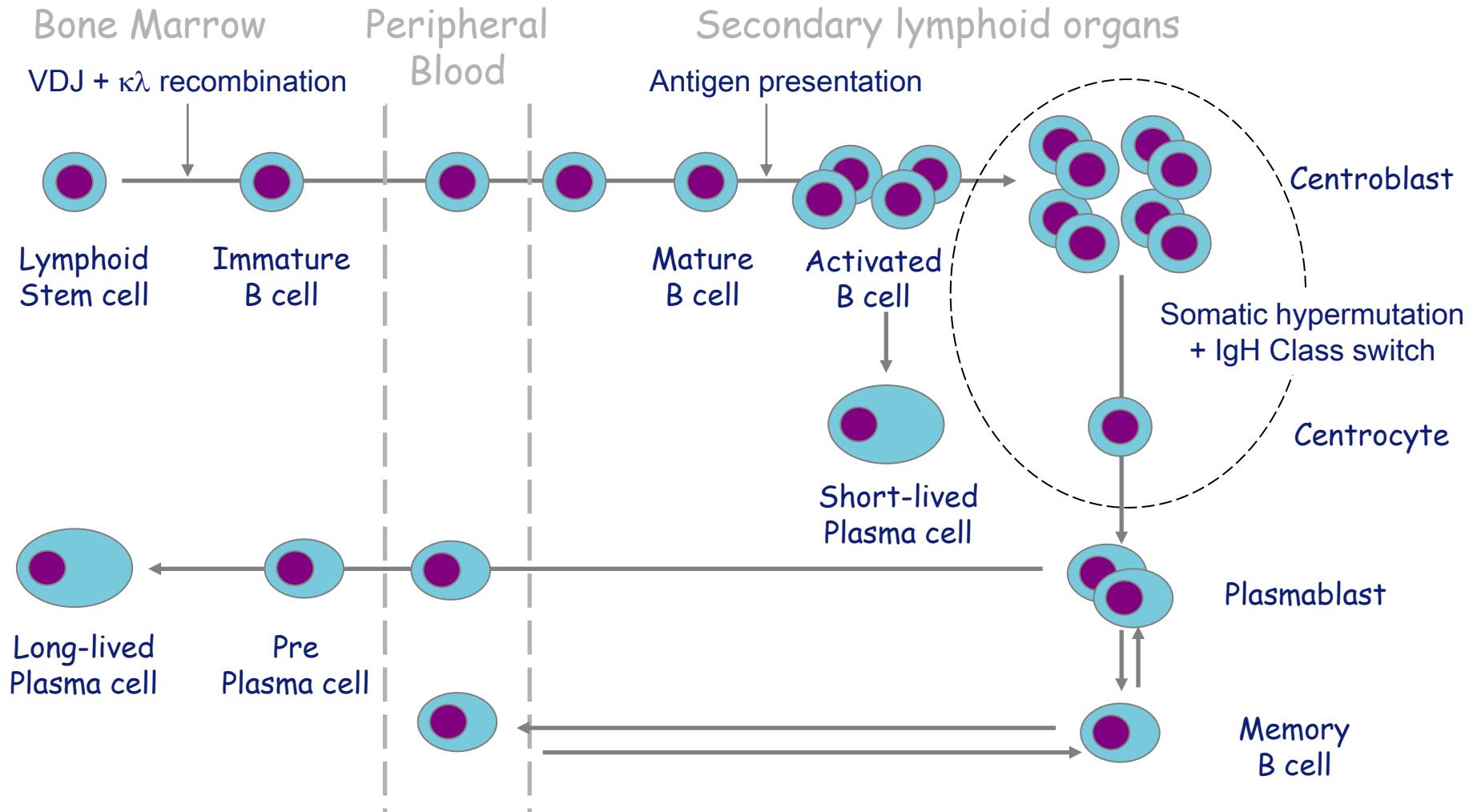
Frecuencia relativa de Linfomas

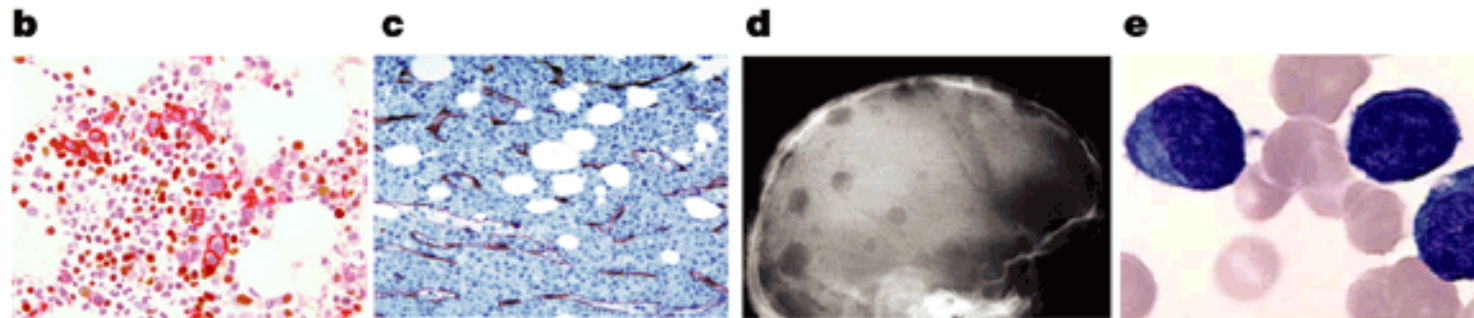
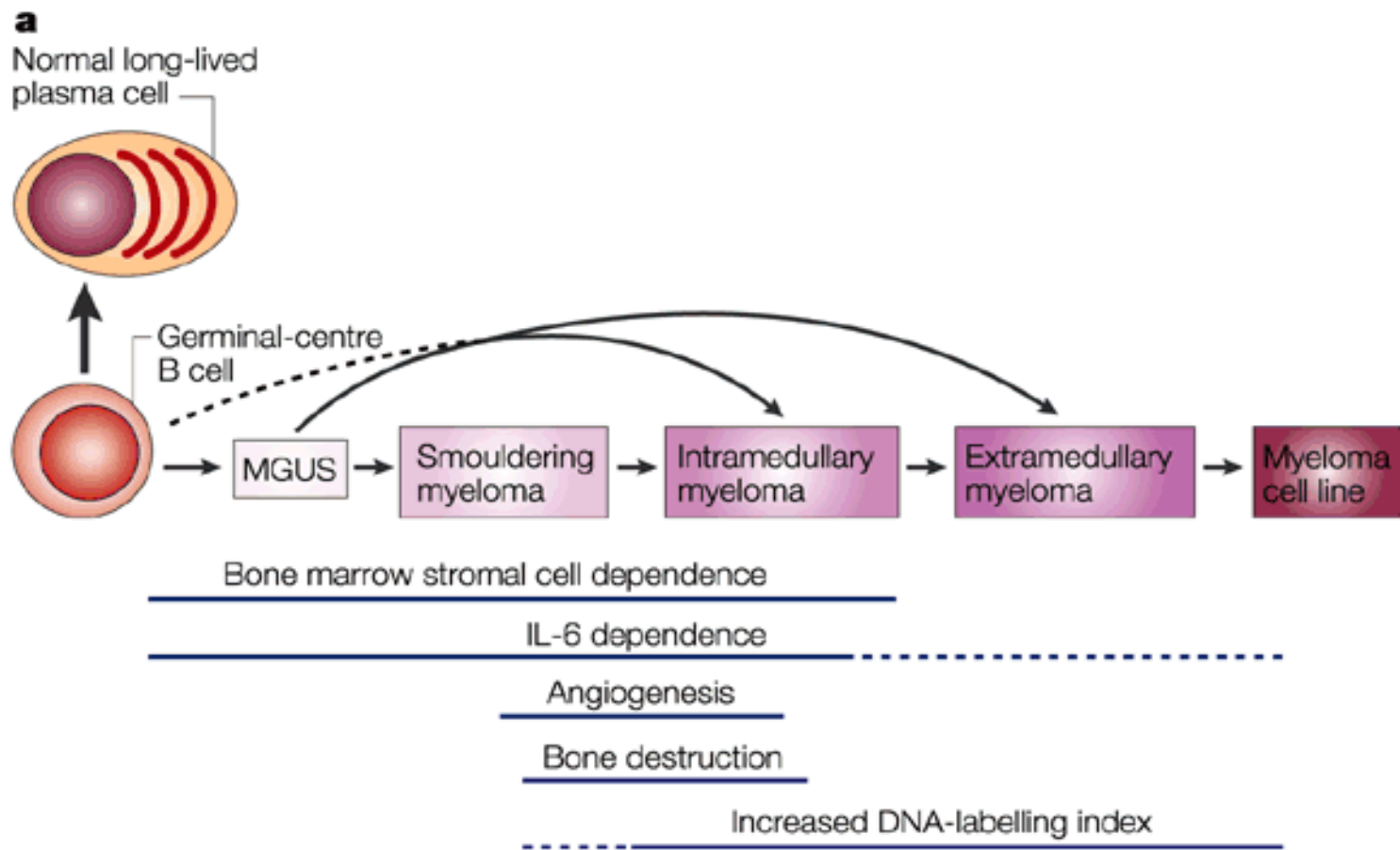


MIELOMA

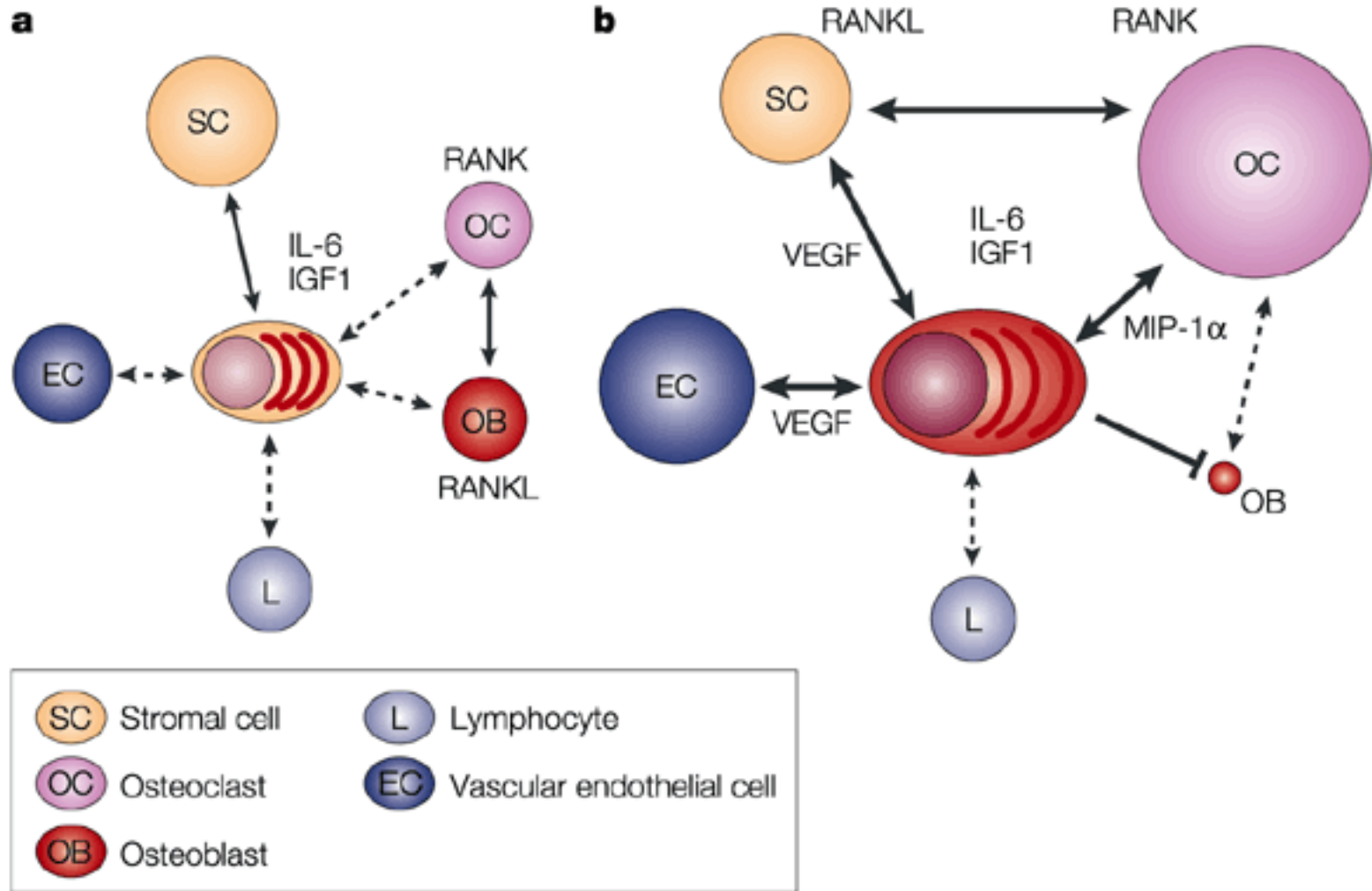


MIELOMA MULTIPLE

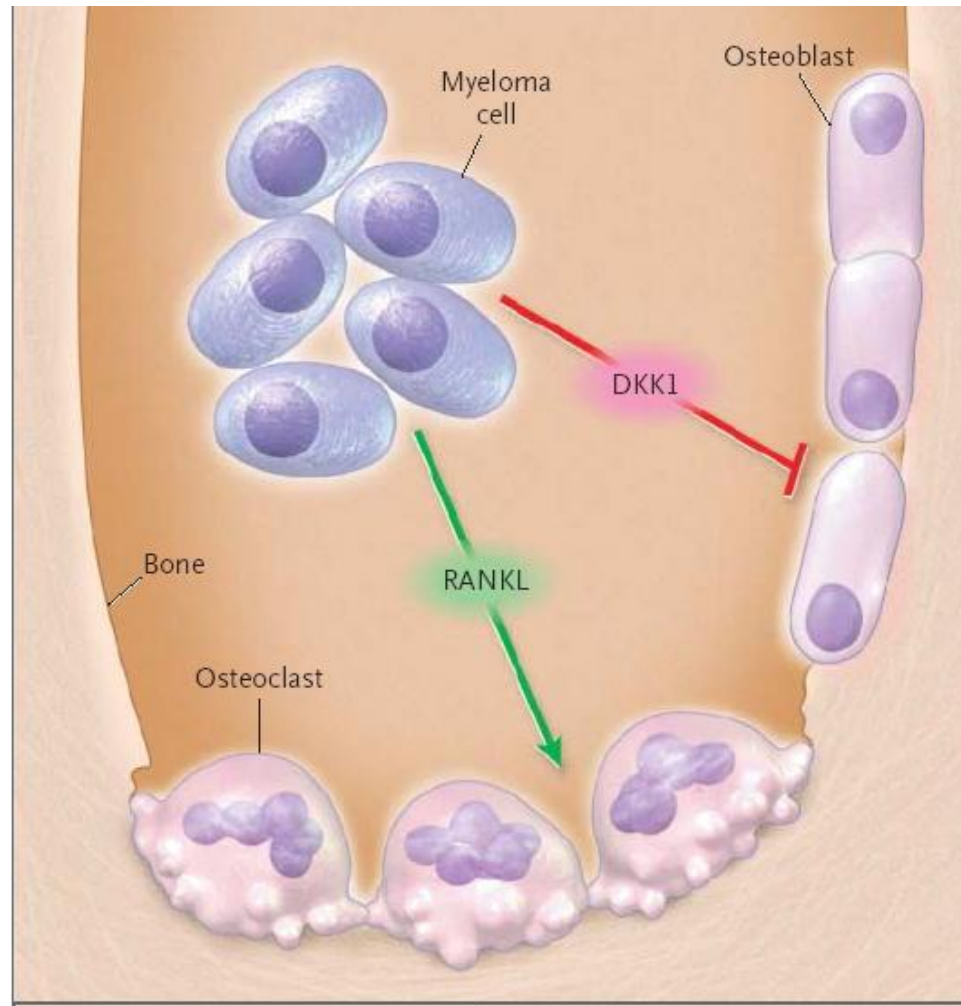


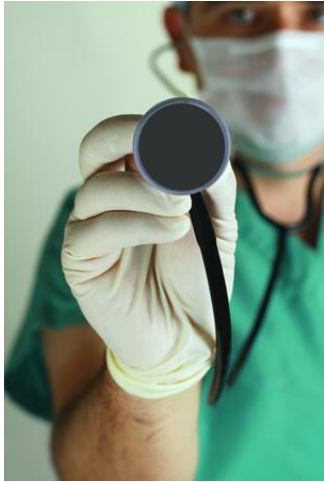


INTERACCIONES CELULARES Y MOLECULARES EN MM



METASTASIS OSEAS EN MIELOMA MULTIPLE





Clínica

Imágenes

Biopsia

Laboratorio

Informe



Informe



**Diagnóstico
Pronóstico
Tratamiento**

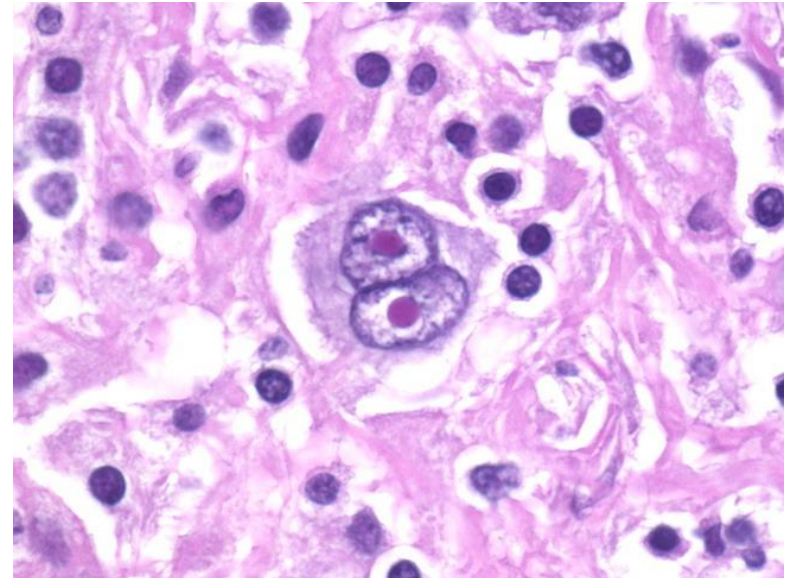
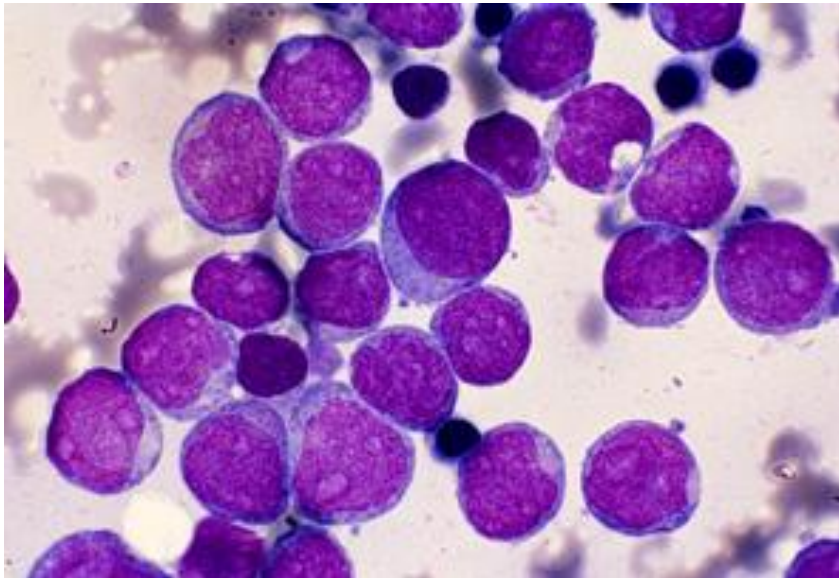


METODOS DIAGNOSTICO

- **Imágenes:** Ecografía, TAC, MRI, Pet/CT
- **Patología:** Citología. IHQ
- **Hematología:** Citología, Citometría de flujo
- **Diagnósticos Moleculares:** BioMarcadores.
(FISH, PCR y Microarrays)

DIAGNOSTICOS ONCOHEMATOLOGIA

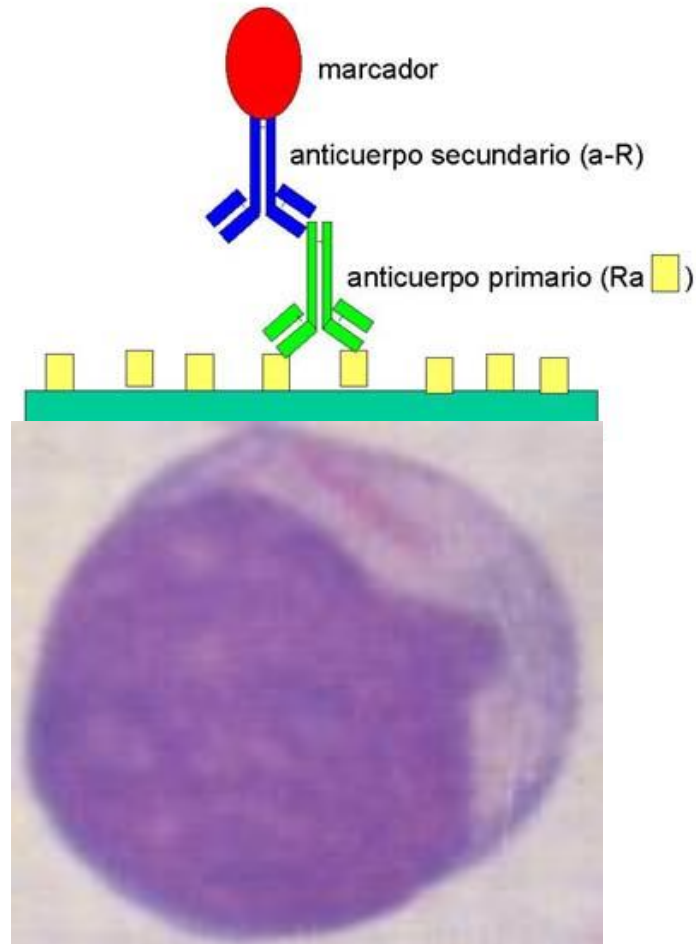
CITOLOGIA . Leucemias y Linfomas



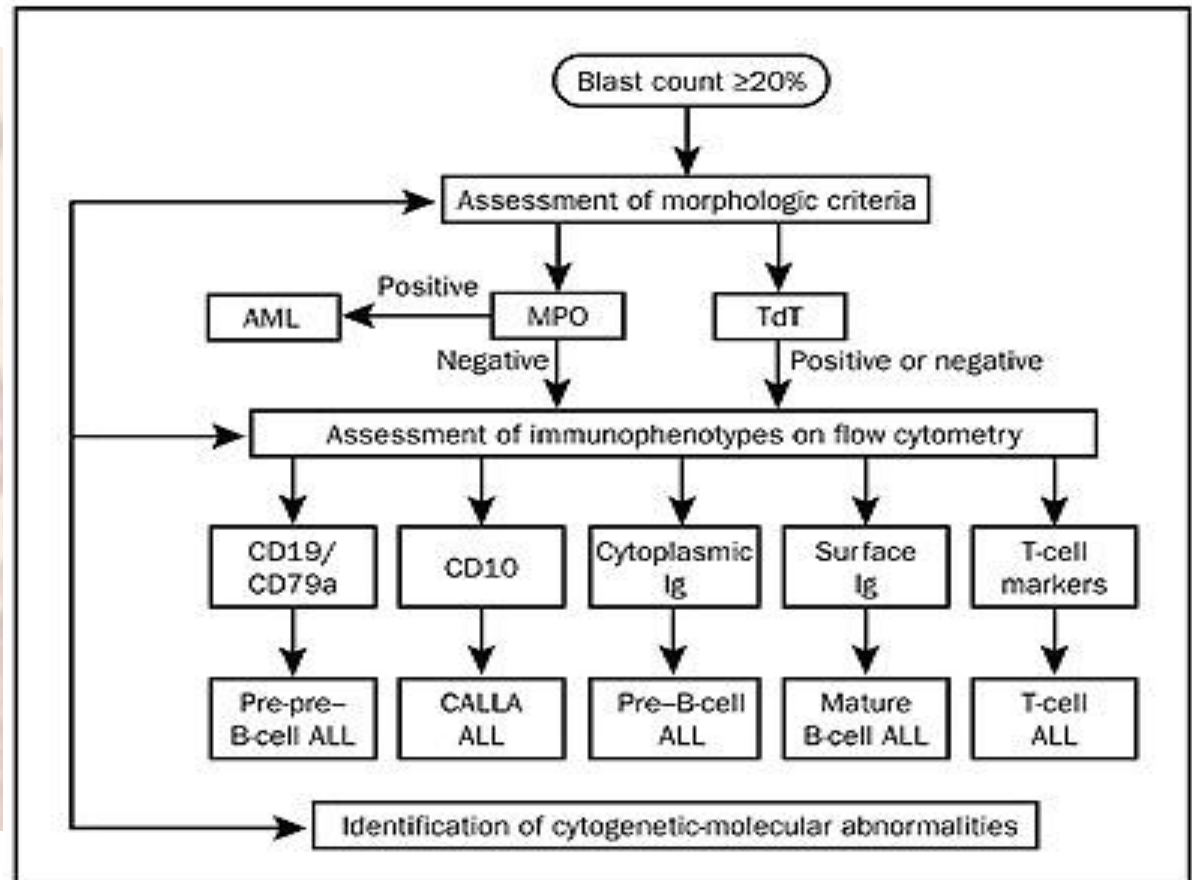
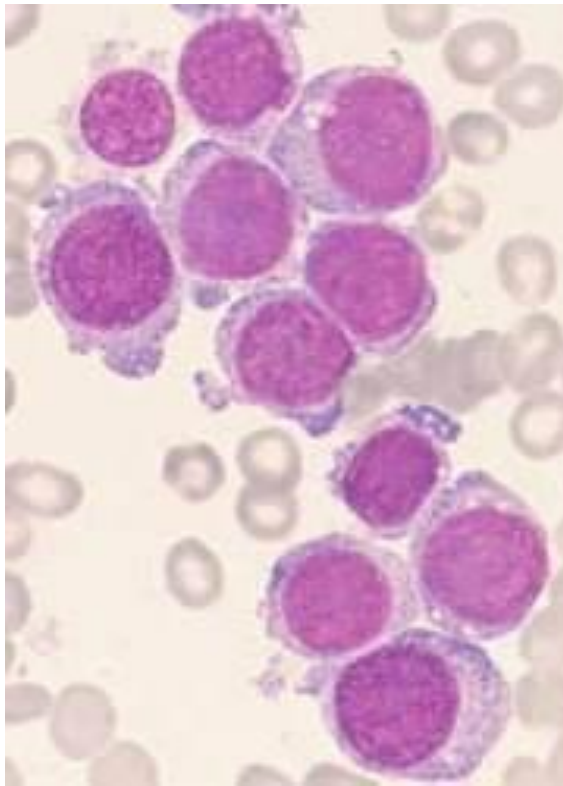
Leucemia Mieloide Aguda Linfoma Hodgkin

INMUNO CITO/HISTOQUIMICA

- Detecta antígenos (proteínas) en células o tejidos



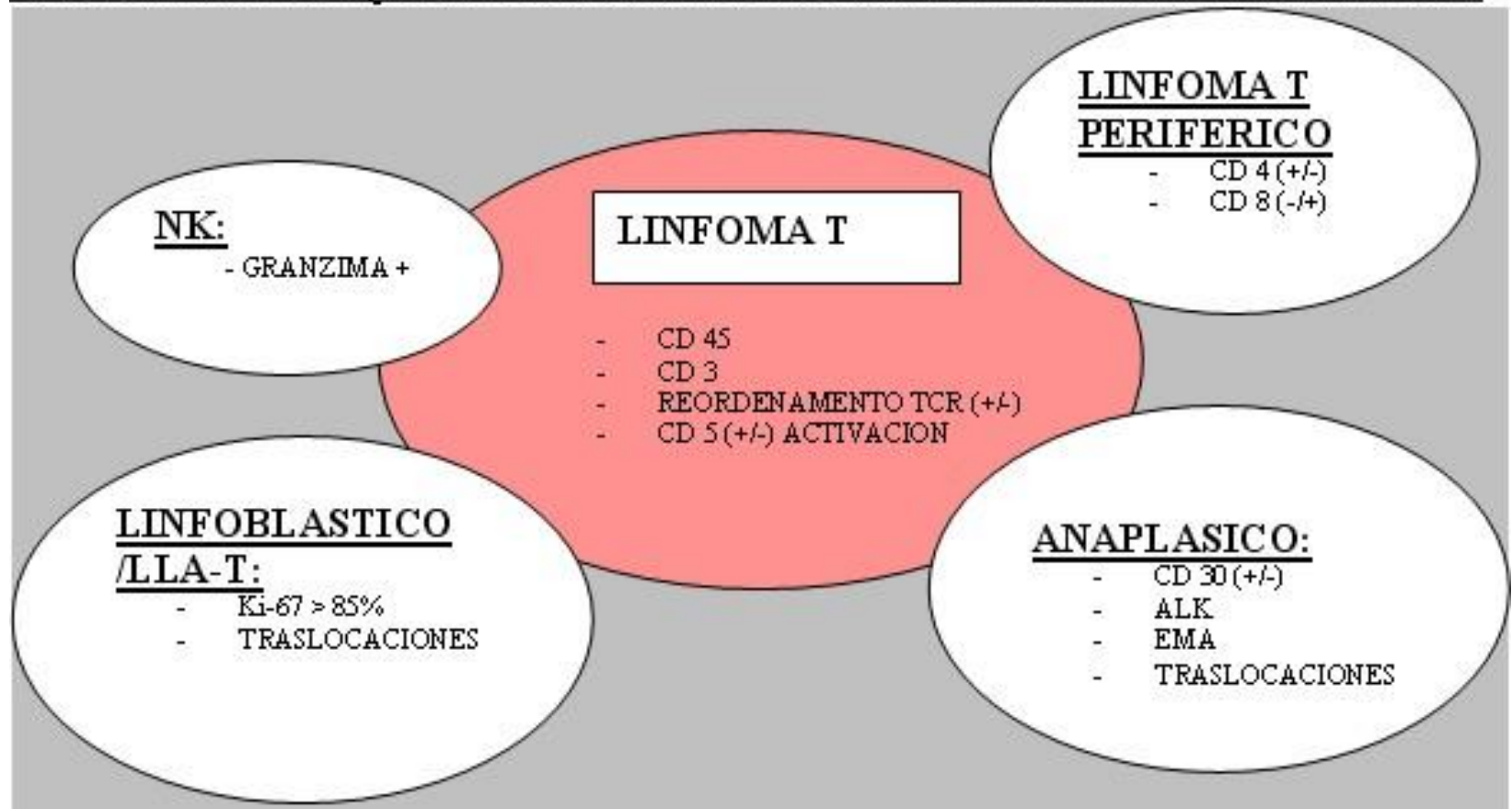
DIAGNOSTICO DE LEUCEMIAS Y LINFOMAS



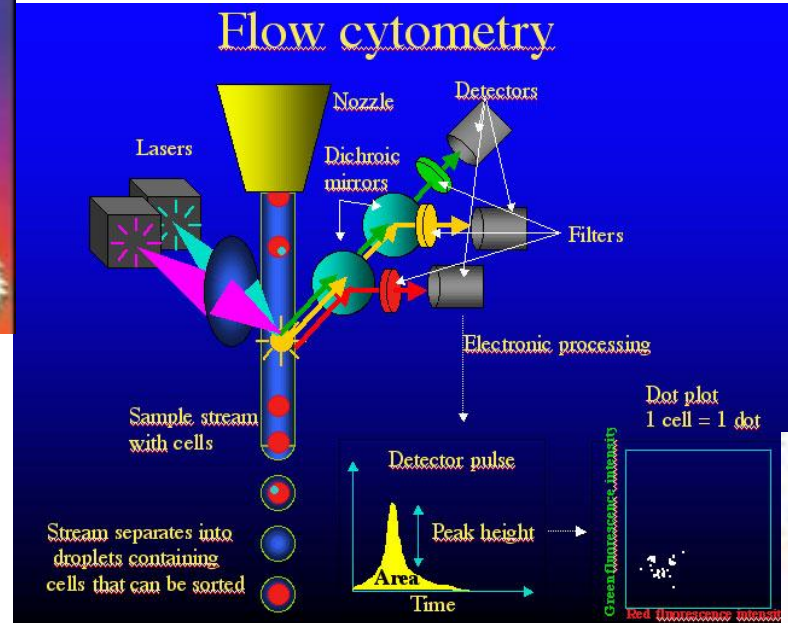
ONCOHEMATOLOGIA

Esquema 4

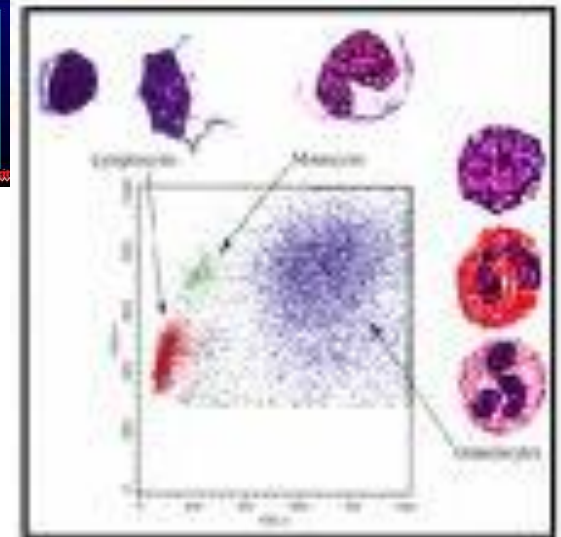
PERFIL INMUNOHISTOQUIMICO MAS IMPORTANTE PARA EL DIAGNOSTICO DE LOS LINFOMAS T

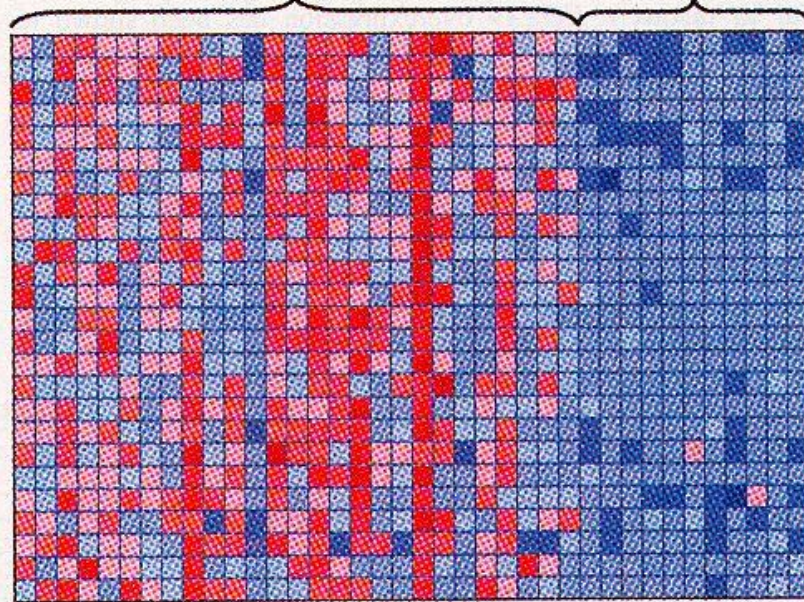


CITOMETRIA DE FLUJO

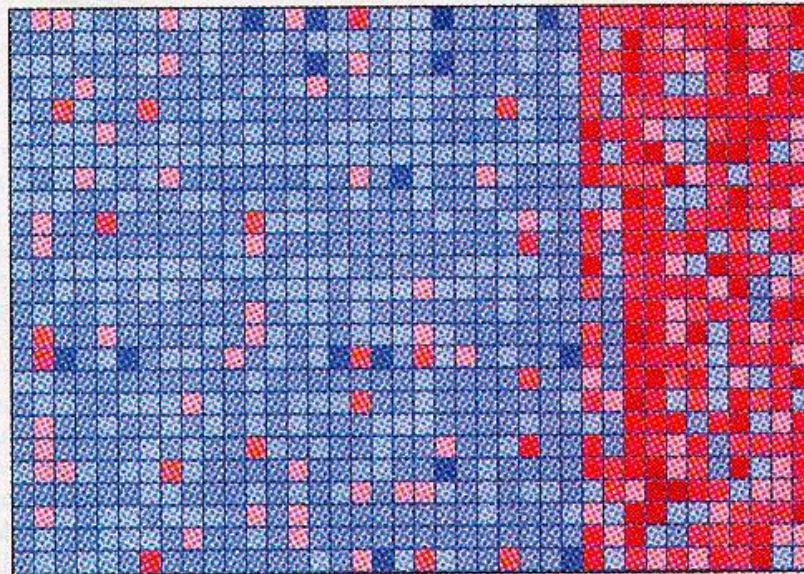


CD: Cluster differentiation
Immunofenotipo

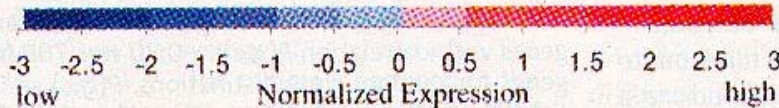


B**ALL****AML**

C-myb (U22376)
 Proteasome iota (X59417)
 MB-1 (U05259)
 Cyclin D3 (M92287)
 Myosin light chain (M31211)
 RbAp48 (X74262)
 SNF2 (D26156)
 HkrT-1 (S50223)
 E2A (M31523)
 Inducible protein (L47738)
 Dynein light chain (U32944)
 Topoisomerase II β (Z15115)
 IRF2 (X15949)
 TFIIIE β (X63469)
 Acyl-Coenzyme A dehydrogenase (M91432)
 SNF2 (U29175)
 (Ca²⁺)-ATPase (Z69881)
 SRP9 (U20998)
 MCM3 (D38073)
 Deoxyhypusine synthase (U26266)
 Op 18 (M31303)
 Rabaptin-5 (Y08612)
 Heterochromatin protein p25 (U35451)
 IL-7 receptor (M29696)
 Adenosine deaminase (M13792)

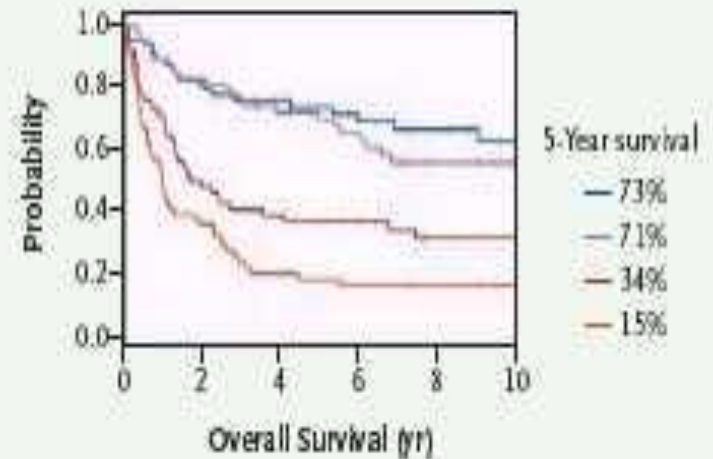
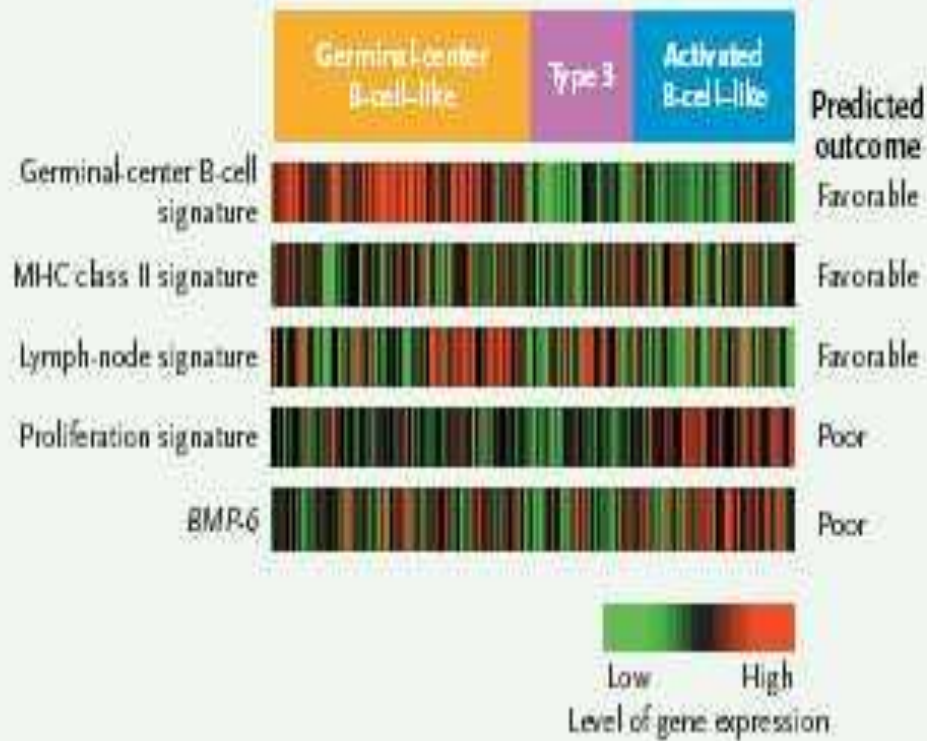


Fumarylacetoacetate (M55150)
 Zyxin (X95735)
 LTC₄ synthase (U50136)
 LYN (M16038)
 HoxA9 (U82759)
 CD33 (M23197)
 Adipsin (M84526)
 Leptin receptor (Y12670)
 Cystatin C (M27891)
 Proteoglycan 1 (X17042)
 IL-8 precursor (Y00787)
 Azurocidin (M96326)
 p62 (U46751)
 Cyp3 (M80254)
 MCL1 (L08246)
 ATPase (M62762)
 IL-8 (M28130)
 Cathepsin D (M63138)
 Lectin (M57710)
 MAD-3 (M69043)
 CD11c (M81695)
 Ebp72 (X85116)
 Lysozyme (M19045)
 Properdin (M83652)
 Catalase (X04085)

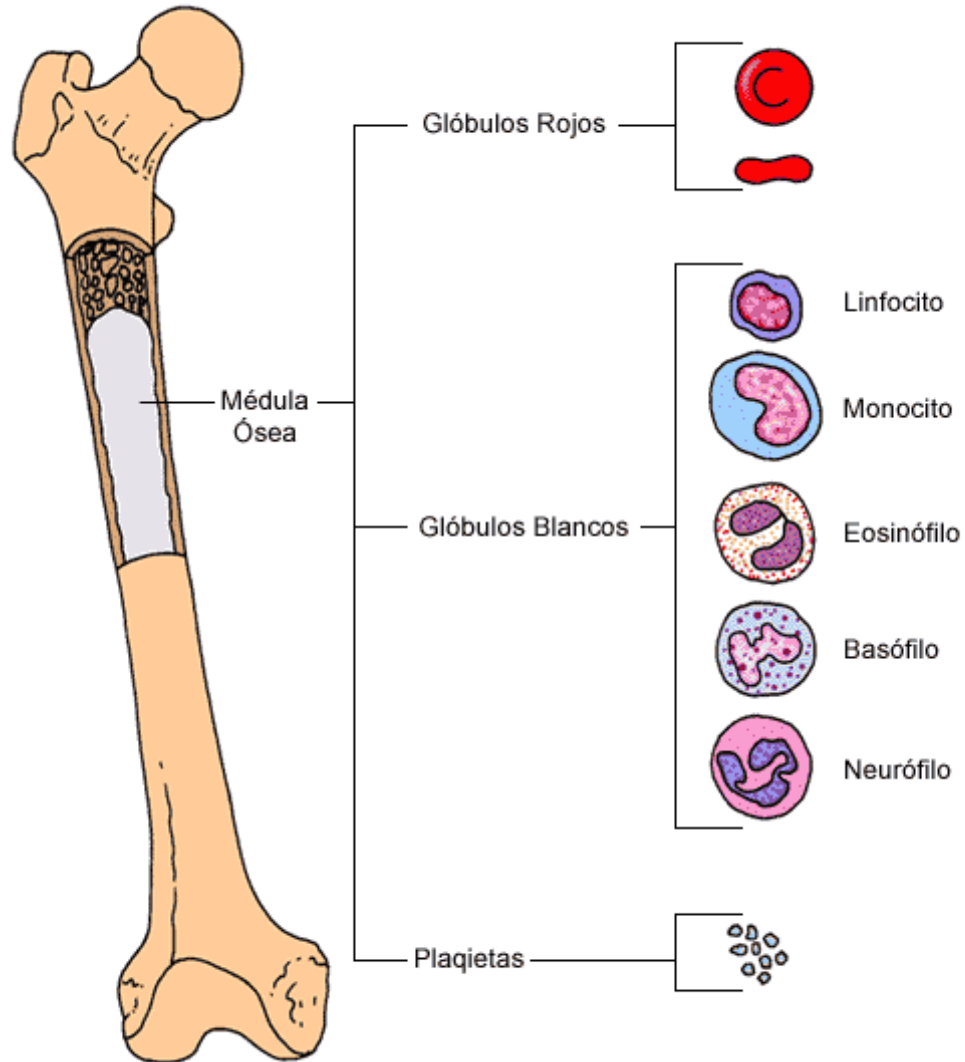


EXPRESSION GENES Y PRONOSTICO

B Diffuse Large-B-Cell Lymphoma-Biopsy Specimens



MEDULA OSEA



Acute leukemias

- There are four general types of therapy
 - Chemotherapy – usually a combination of drugs is used
 - Bone marrow transplant
 - Radiotherapy
 - Immunotherapy – stimulate the patients own immune system to mount a response against the malignant cells
 - Monoclonal antibodies – examples include Rituxin

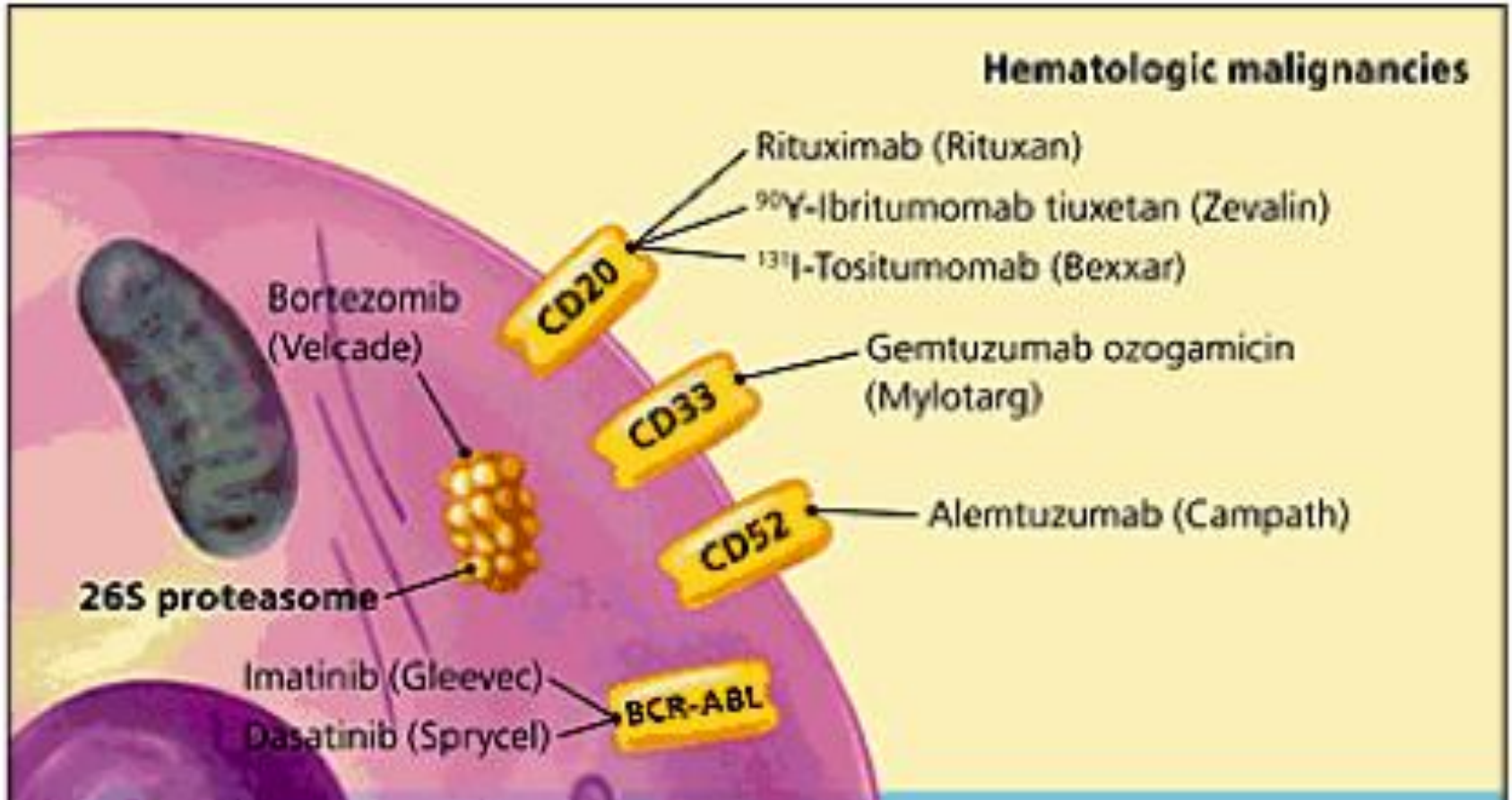
Treatment

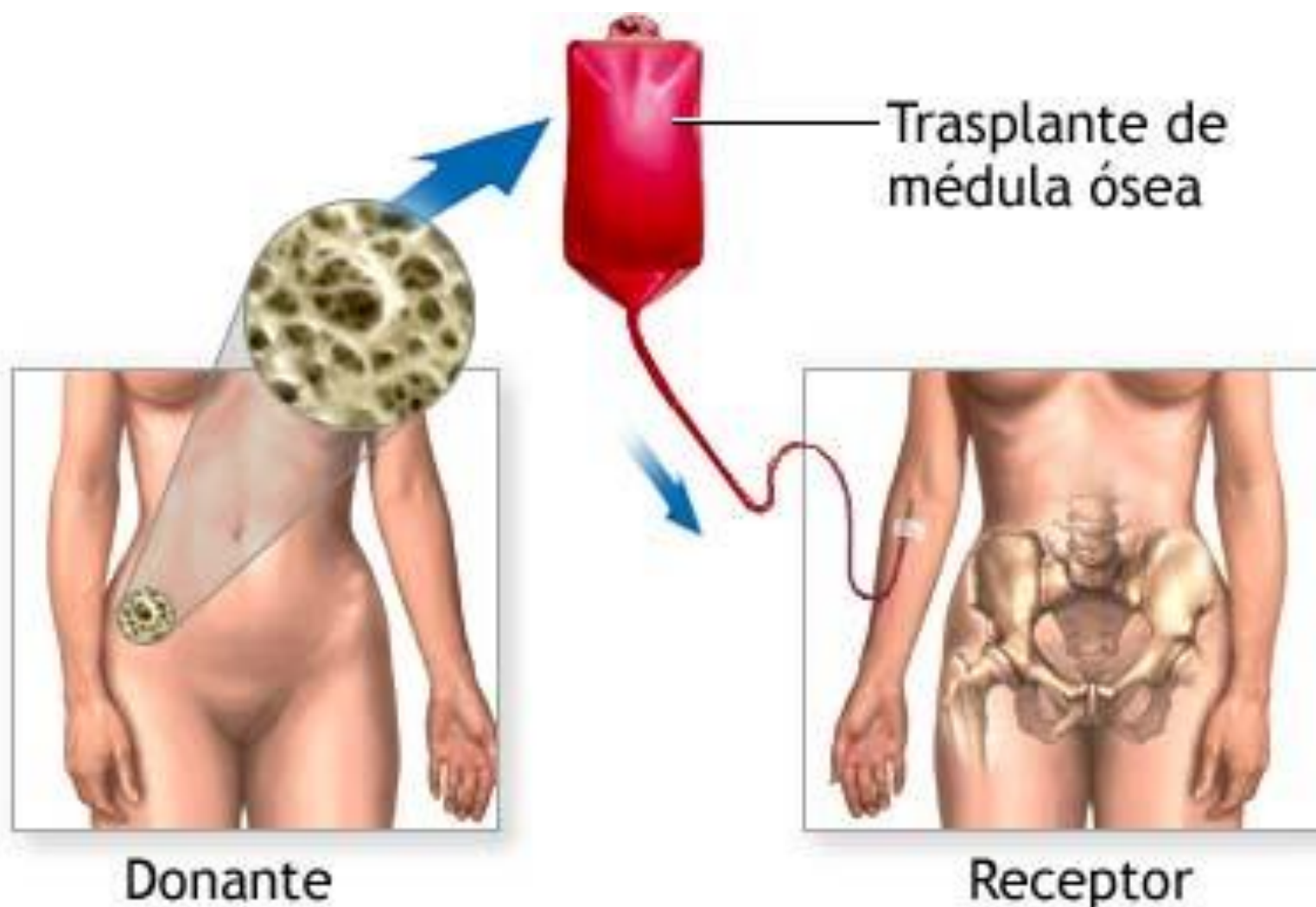
- Chlorambucil, CVP, CHOP
- Fludarabine
- Rituximab
- Campath (alemtuzamab)
- Bendamustine
- Treat early vs. wait?
- Allogeneic SCT

Terapias Mieloma Múltiple

- Terapia Primaria:
- Melphalan/prednisone (MP)
- Vincristine/doxorubicin/dexamethasone (VAD)
- Dexamethasone
- Thalidomide, Lenalidomide
- Doxil
- Bortezomib
- Transplantation: Auto (1 or 2?) vs. Allo

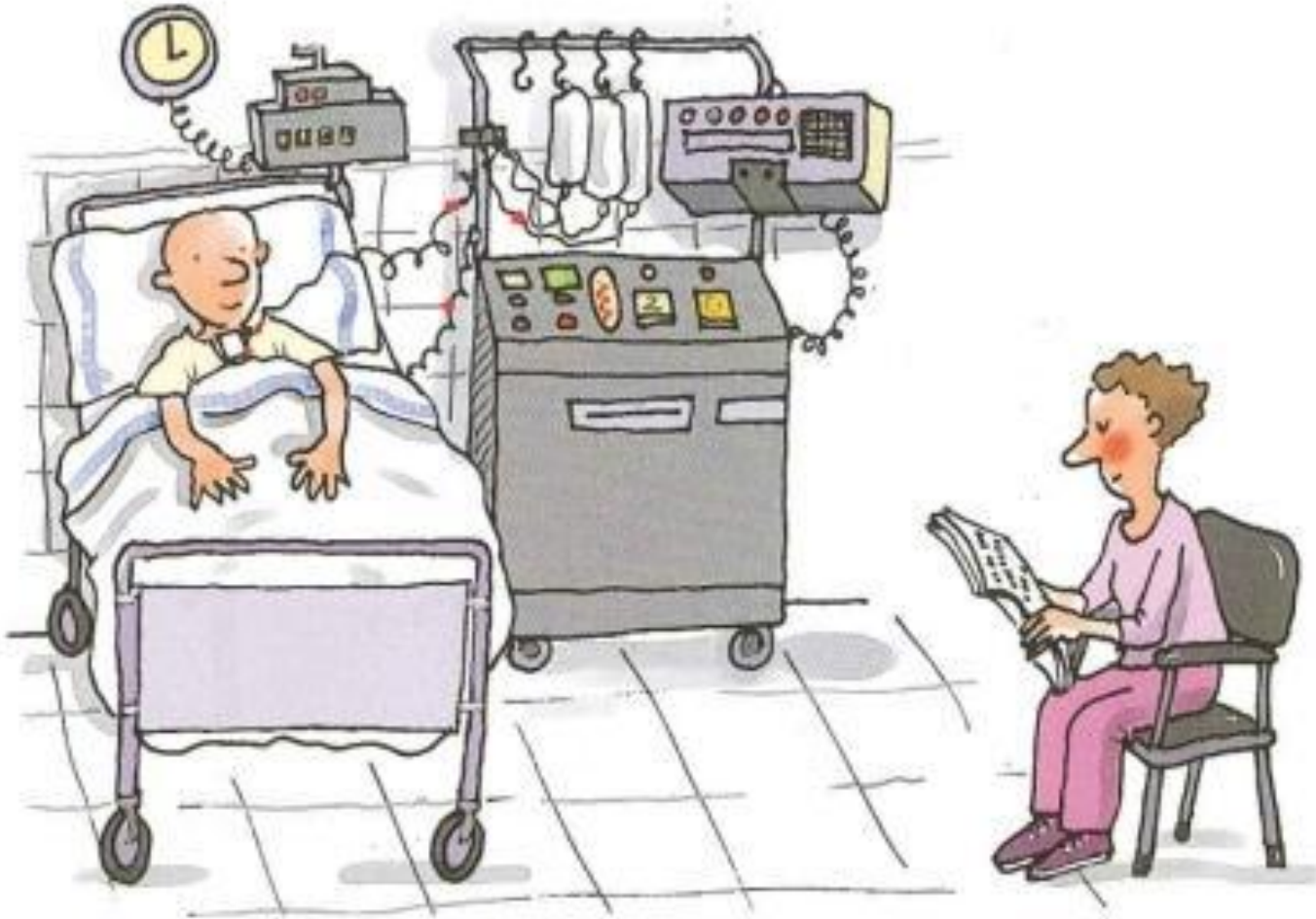
Terapias Moleculares





Las células de la médula ósea del donante pueblan la médula ósea del receptor

UNIDAD DE TRANSPLANTE



TERAPIAS CELULARES Y GENICAS

