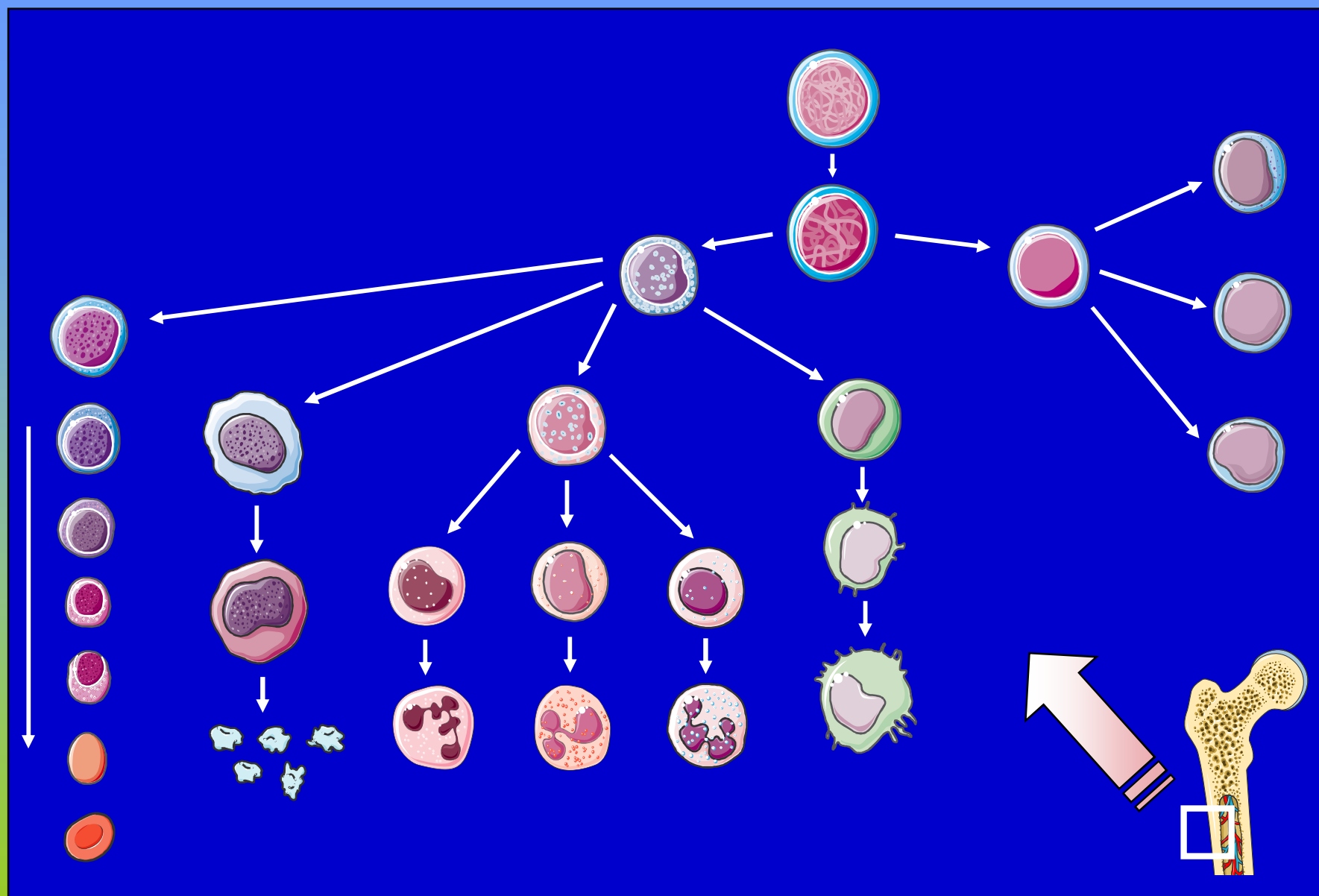
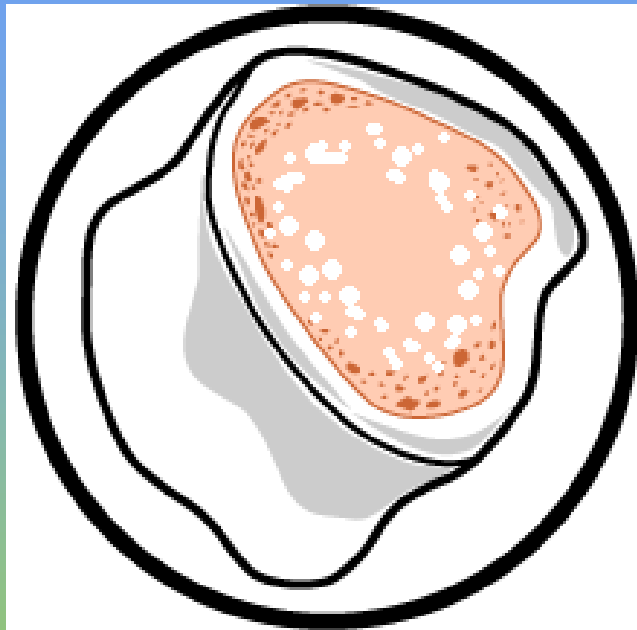


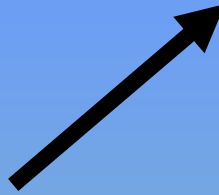
HEMATOPOYESIS

Dr Blaz Lesina
Otoño de 2009





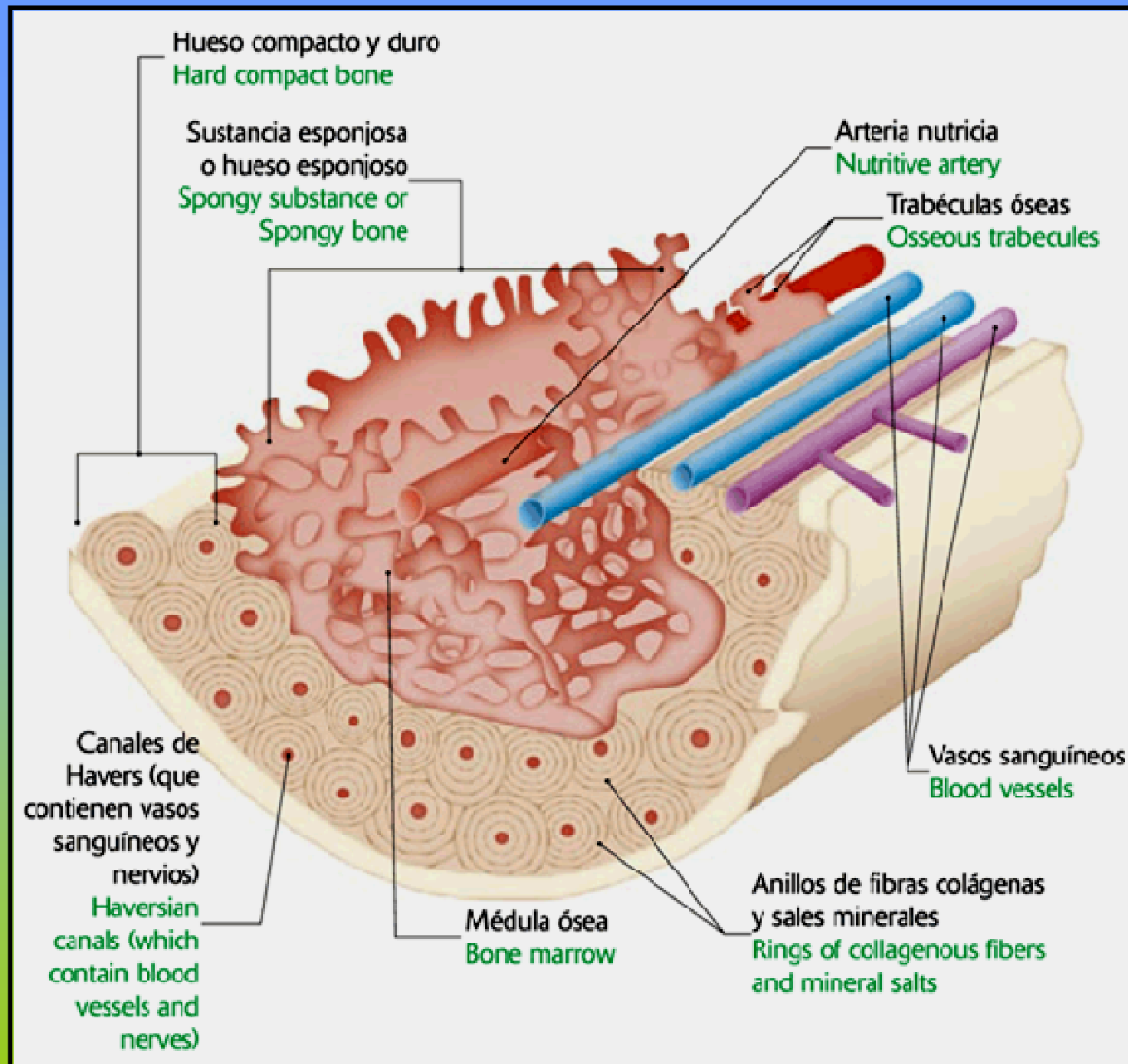
2.5 billones de Gr Kg/peso/día

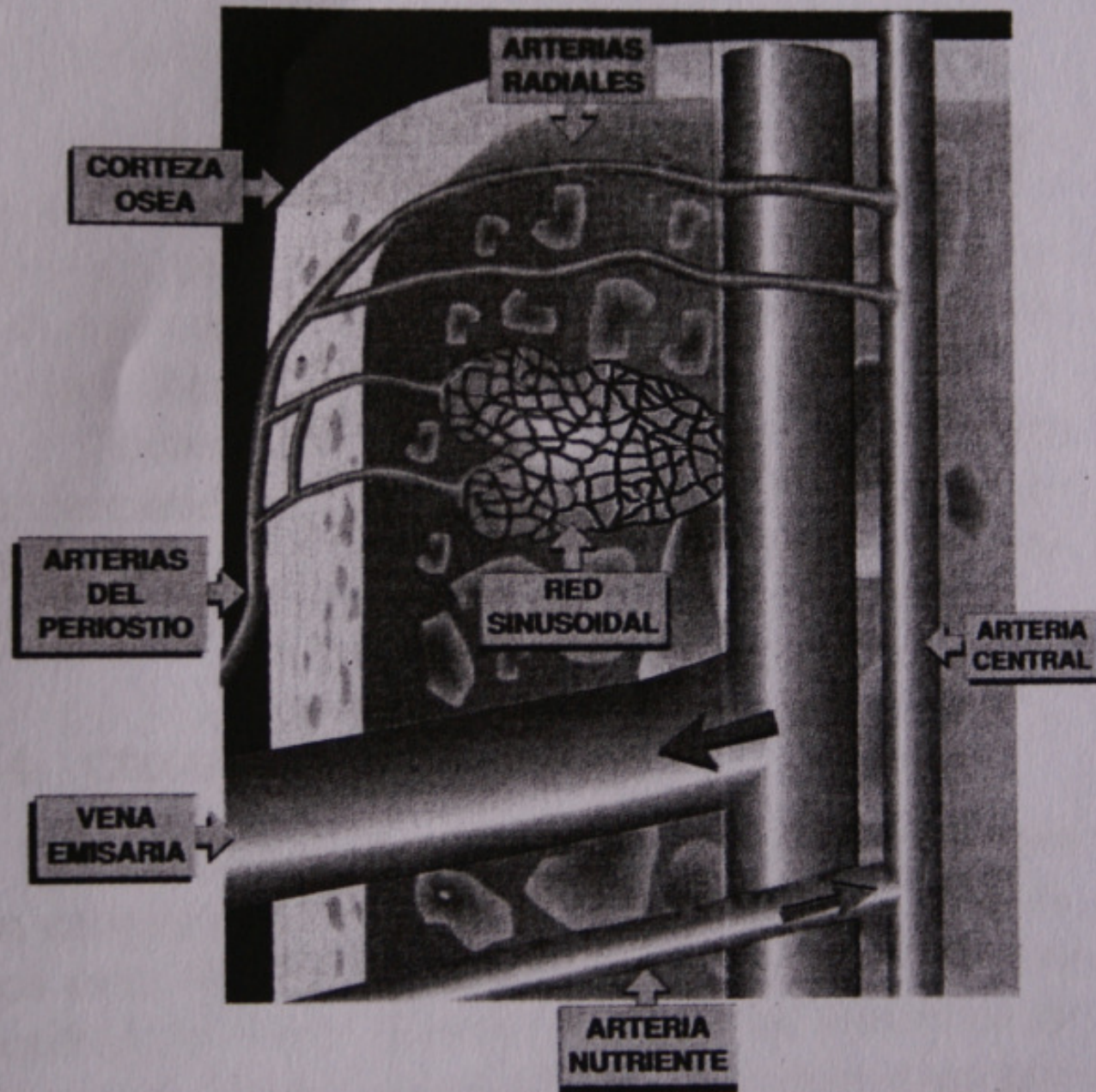


2.5 billones de Plq Kg/peso/día

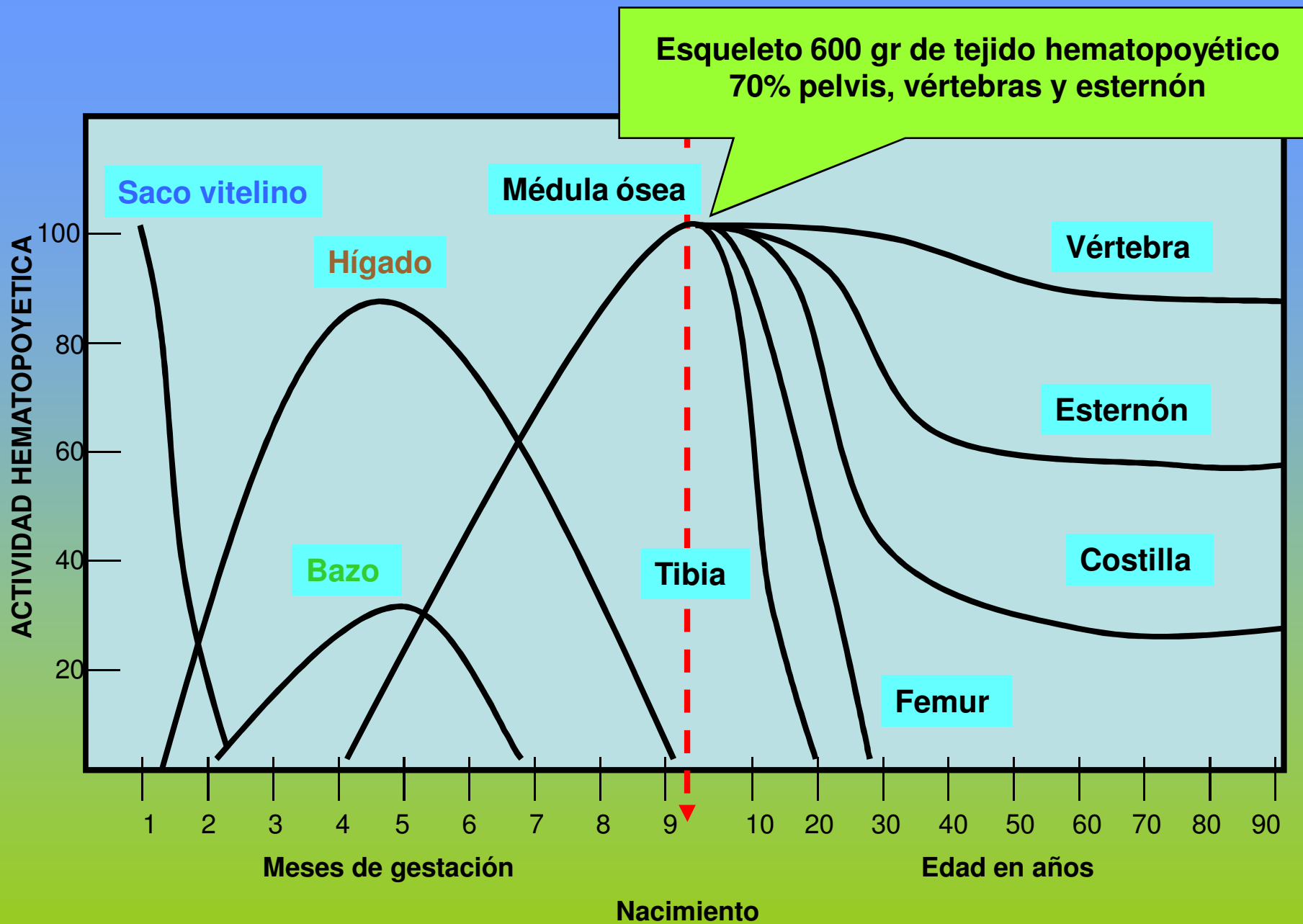


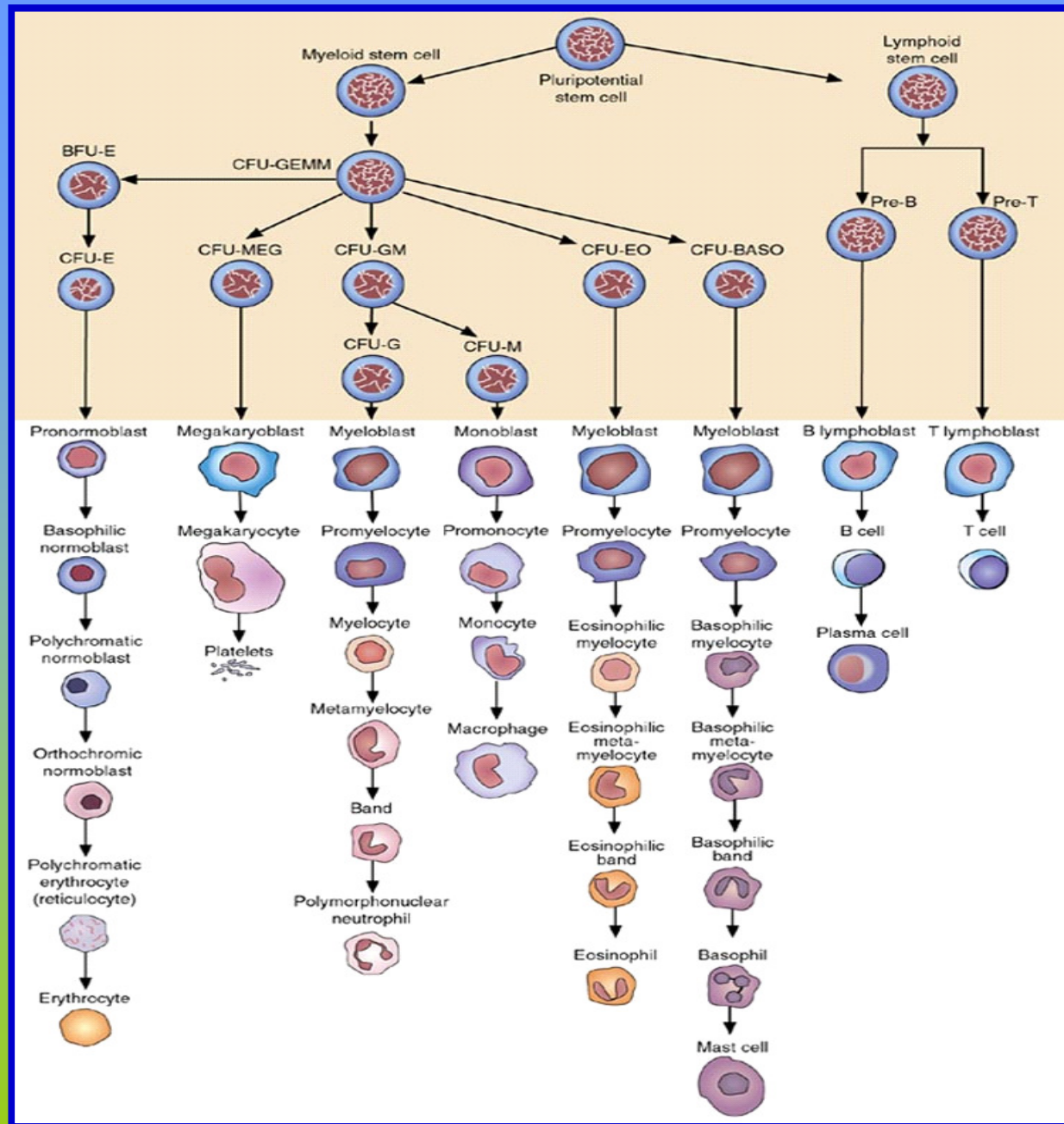
1 billon de Gran Kg/peso/día





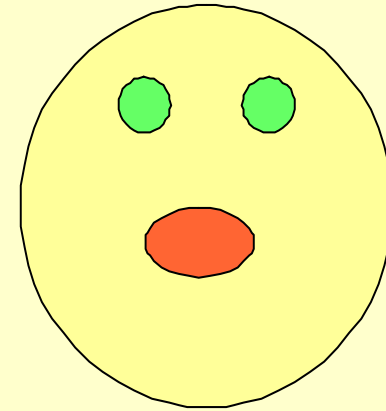
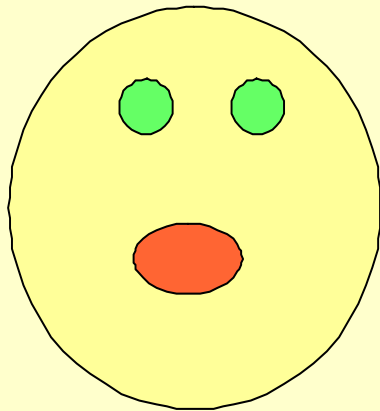
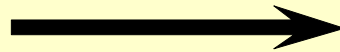






Routes a stem cell can take

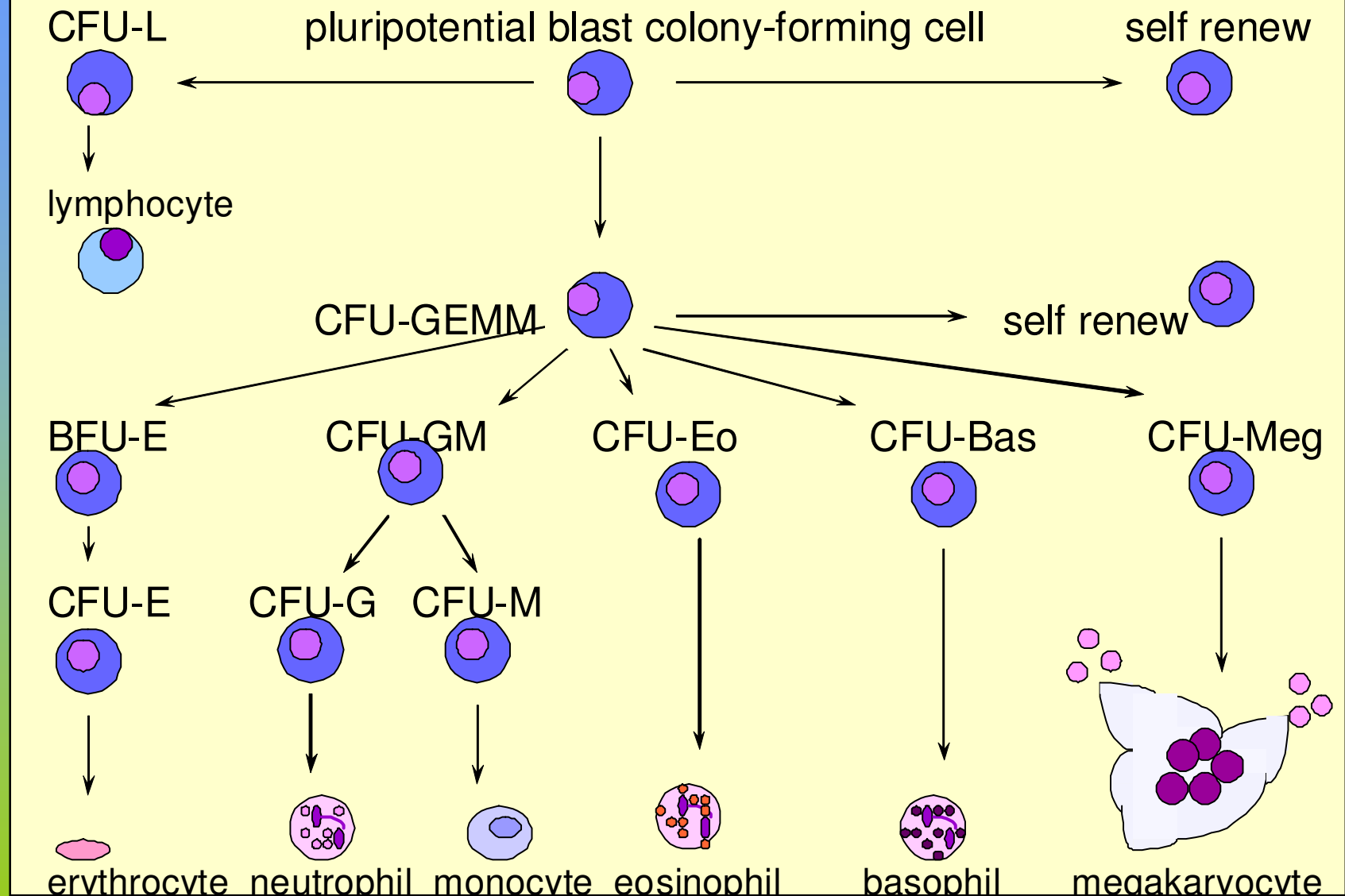
self-renew



differentiate



Hematopoietic Cell Differentiation

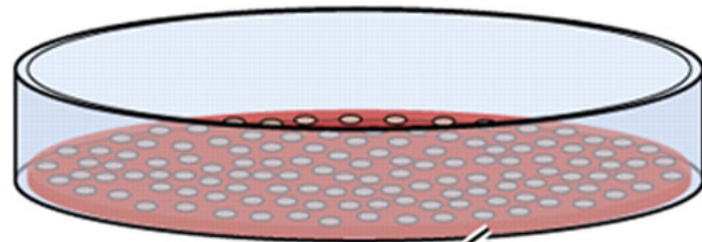


Plasticidad

Célula troncal	Tejido convencional	Tejido no convencional	Referencias
Hematopoyética	Células de la sangre	Nervioso epitelial hepático músculo esquelético y cardiaco	Petersen 1999, Krause 2001
Neuronal	Nervioso	Sangre músculo	Bjornson 1999, Galli 2000
Muscular	Muscular	Nervioso sangre	Gussoni 1999, Jackson 1999
Mesenquimática	Óseo, cartílago adiposo músculo nervioso pulmón estroma hematopoyético renal		Koppen 1999, Ito 2001

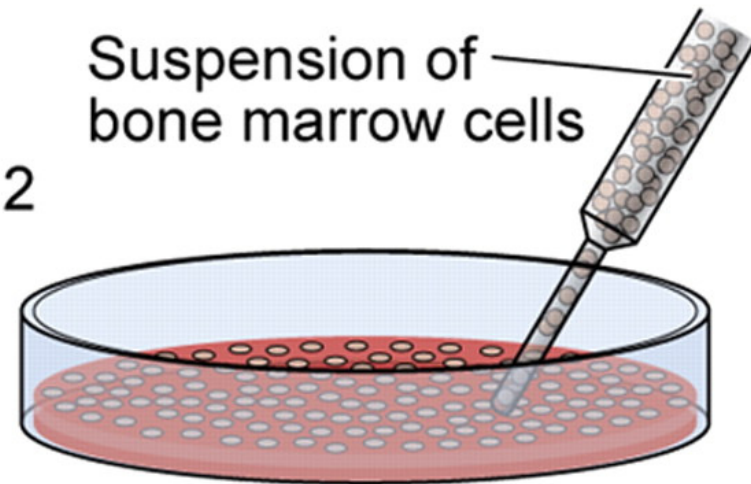
Bone marrow colony assay system

1



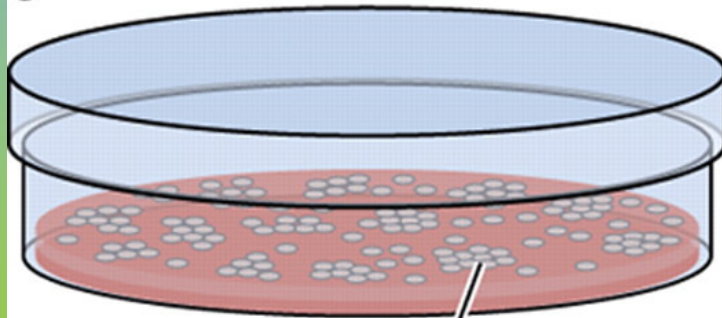
"Feeder" layer

2



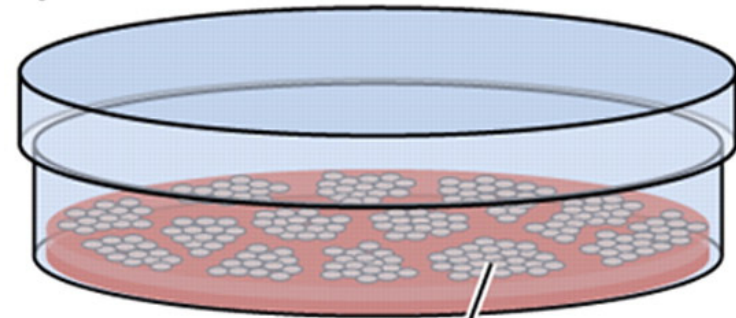
Suspension of
bone marrow cells

3



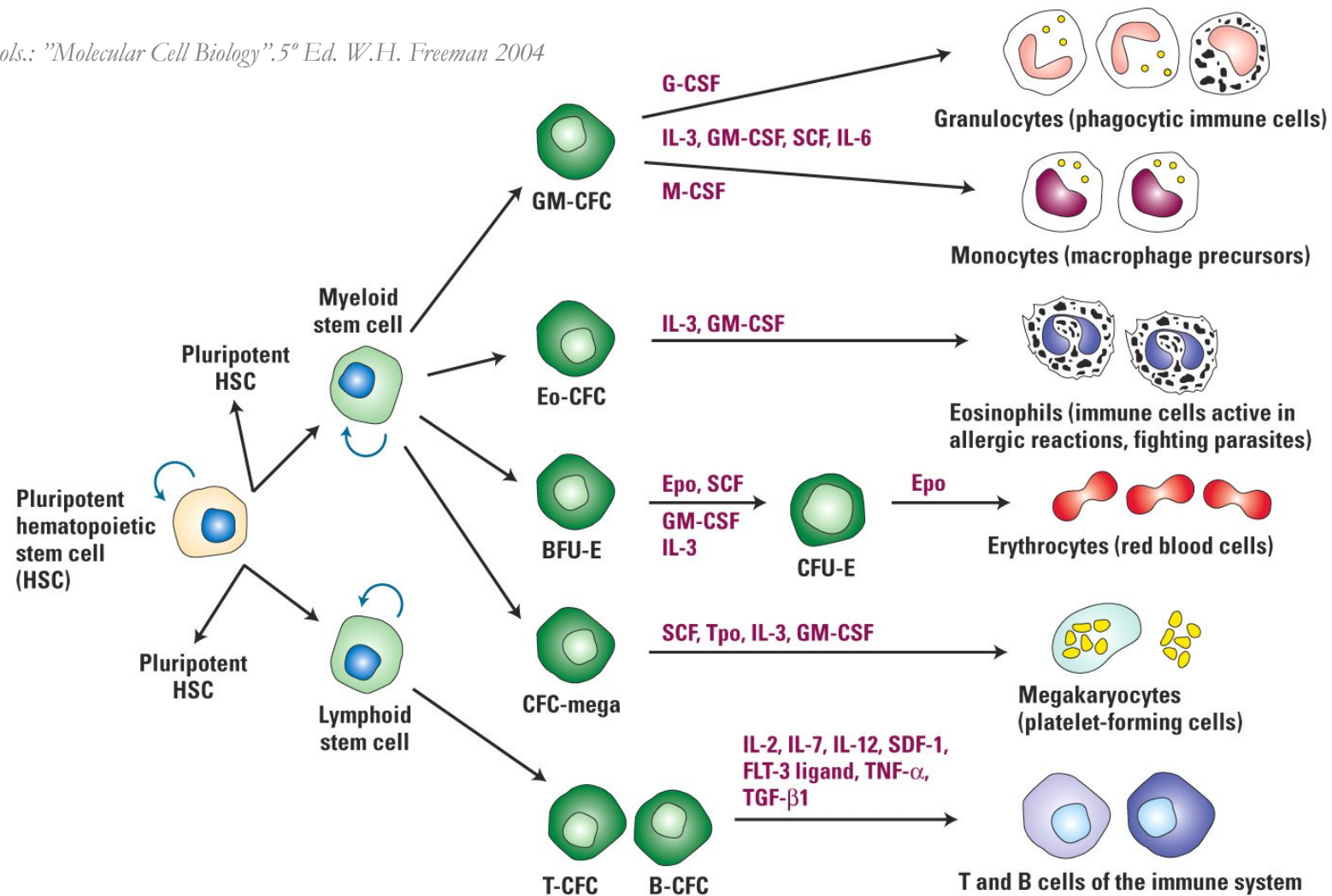
Forming colony

4



Mature colony

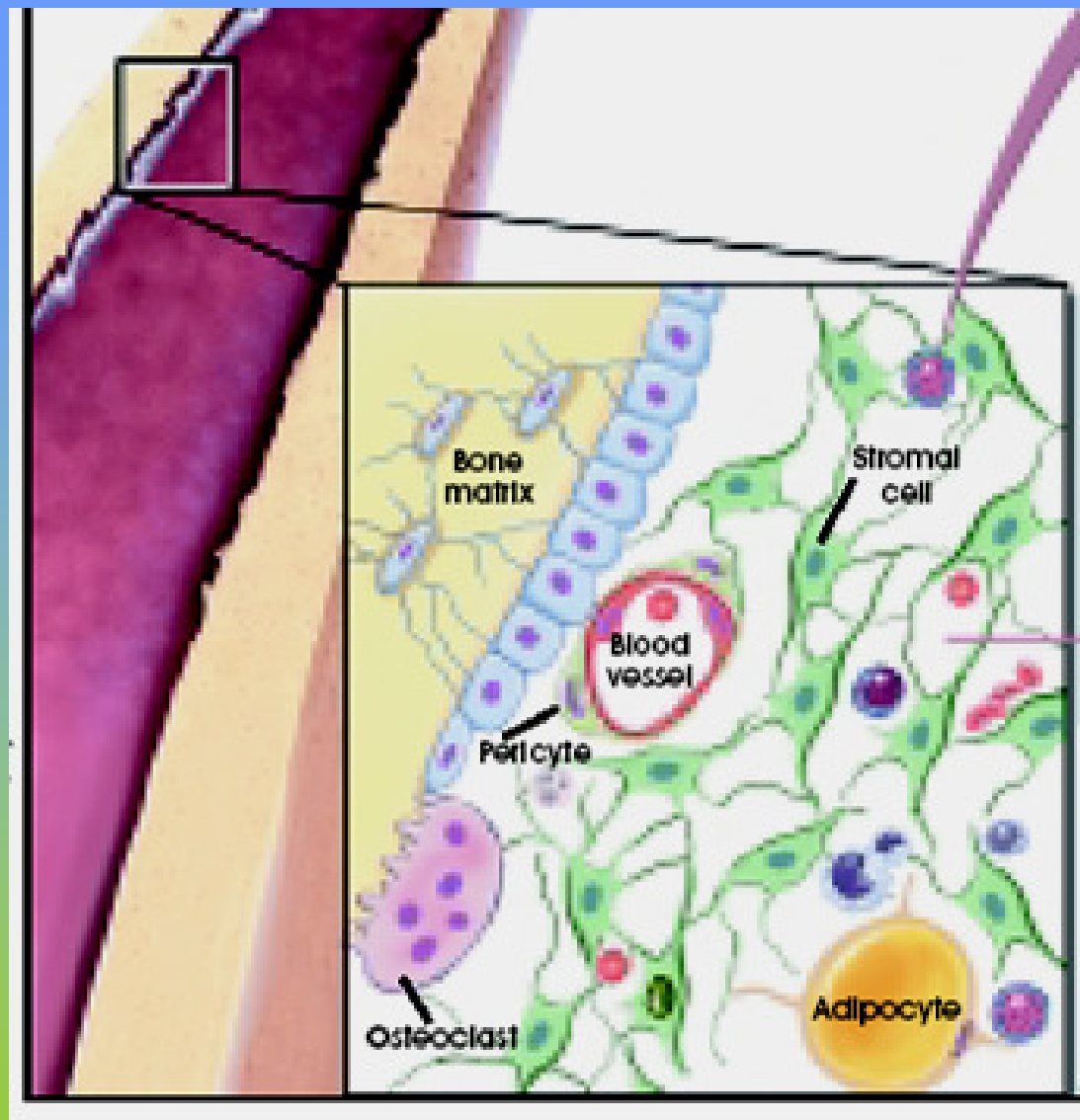
Lodish y cols.: "Molecular Cell Biology". 5° Ed. W.H. Freeman 2004



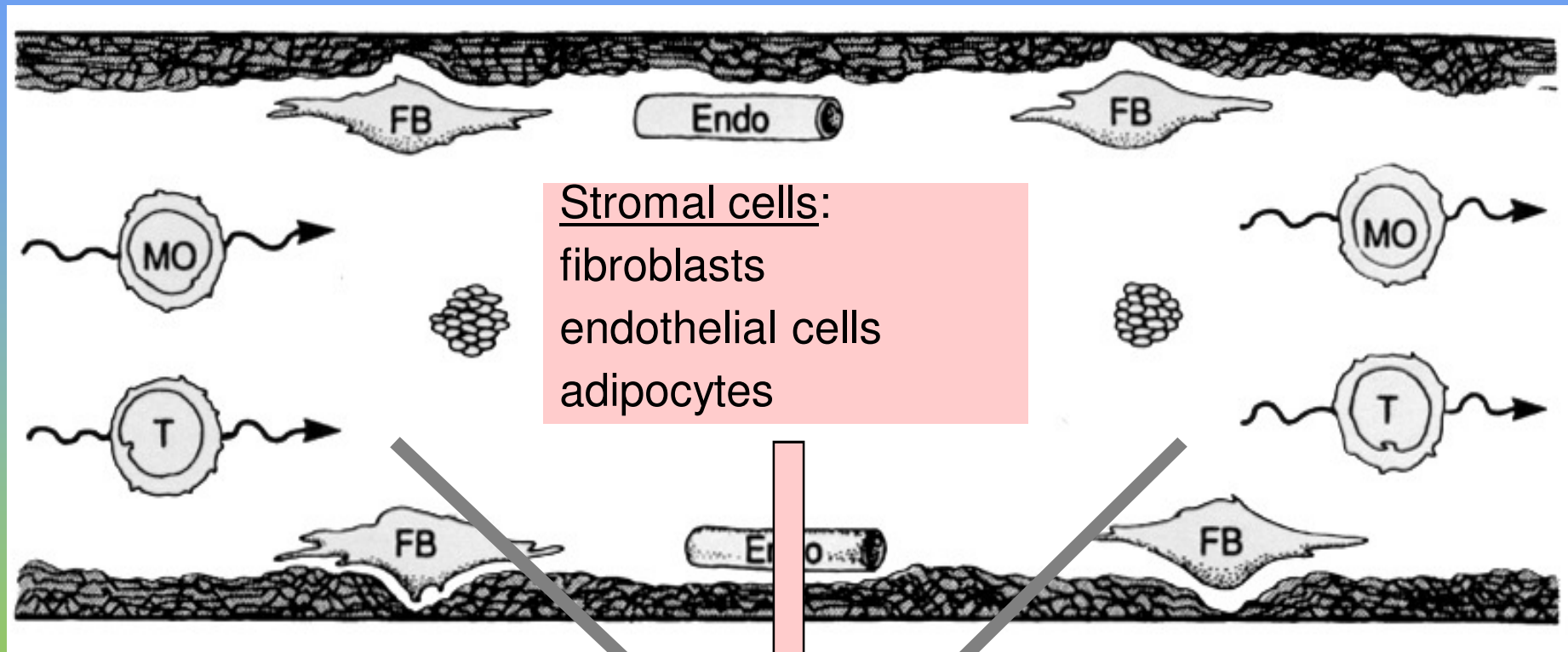
CD34⁺,
CD38⁻,
c-kit⁺ (CD117)

CD34⁺,
CD38⁻,
c-kit⁺

CD38⁺,
CD3,
CD4,
CD8,.....

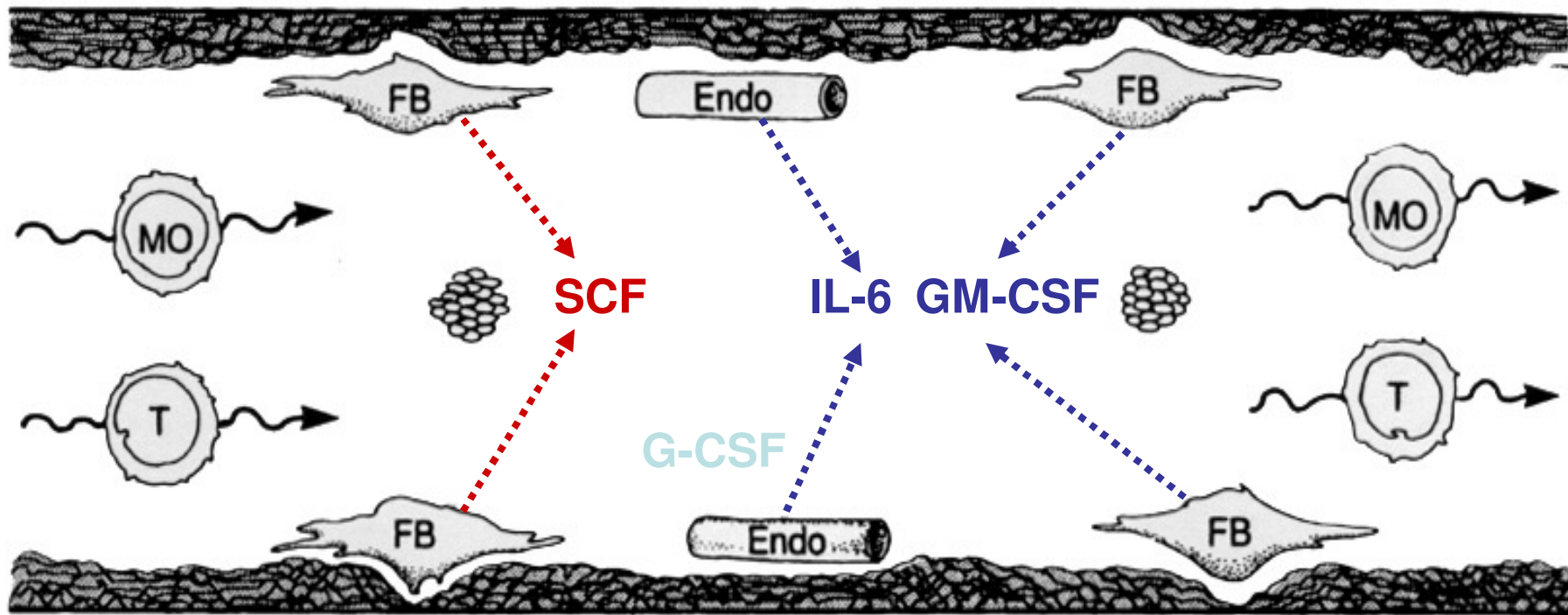


Hematopoietic Microenvironment



Growth Factors

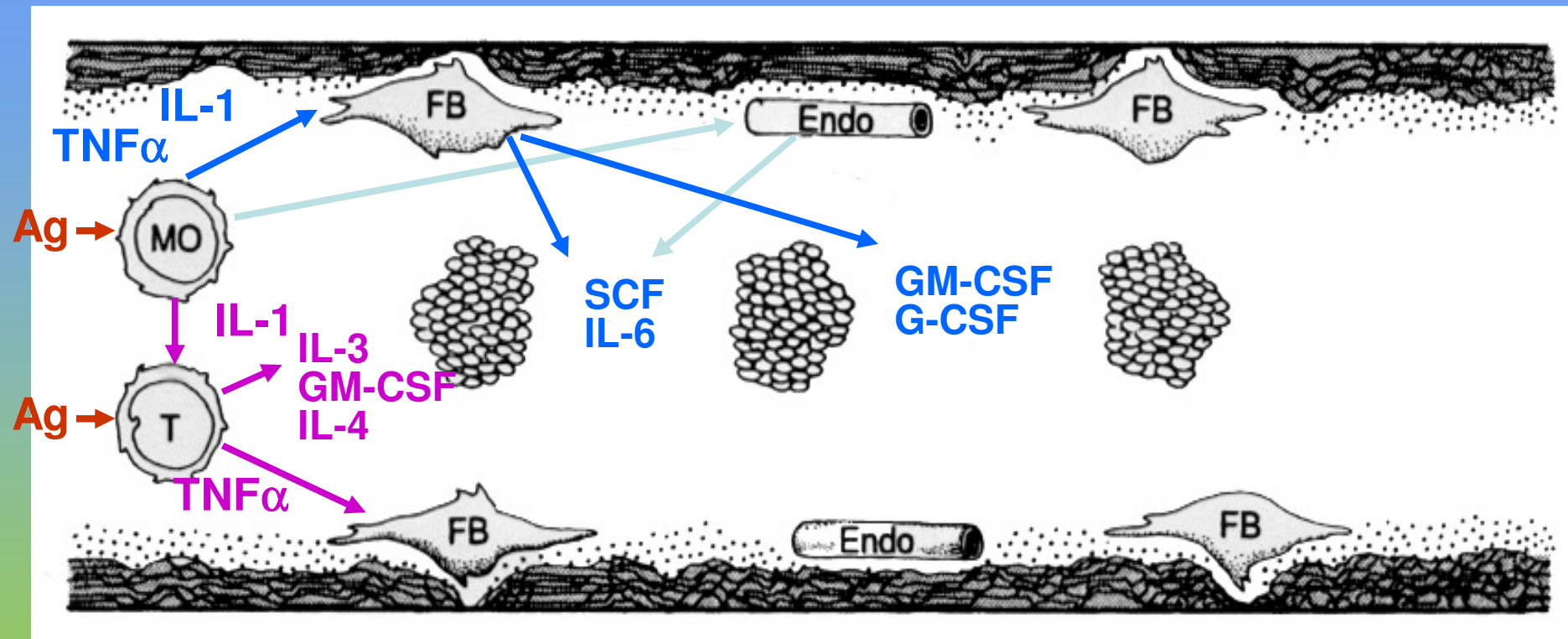
Basal Hematopoiesis

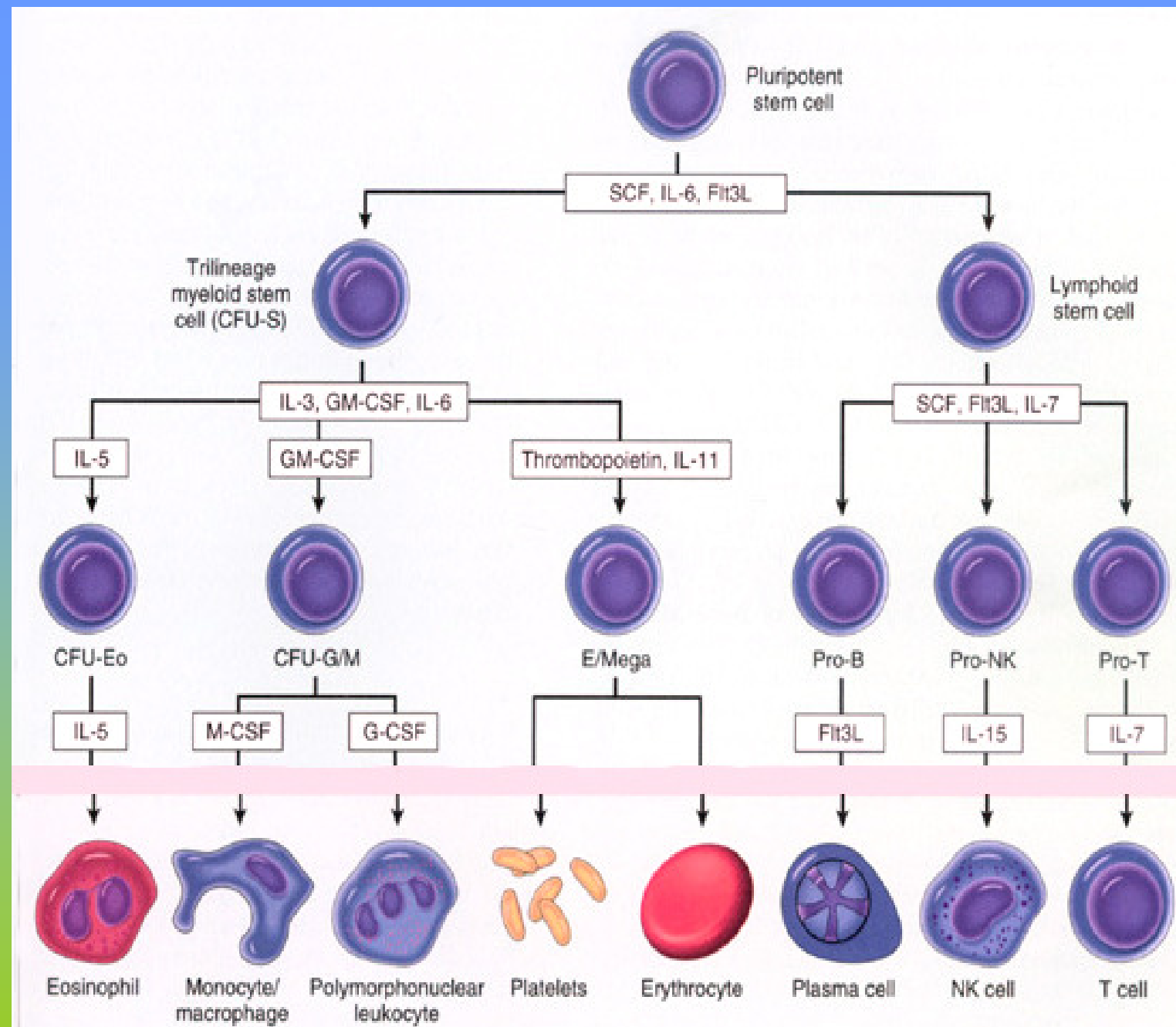


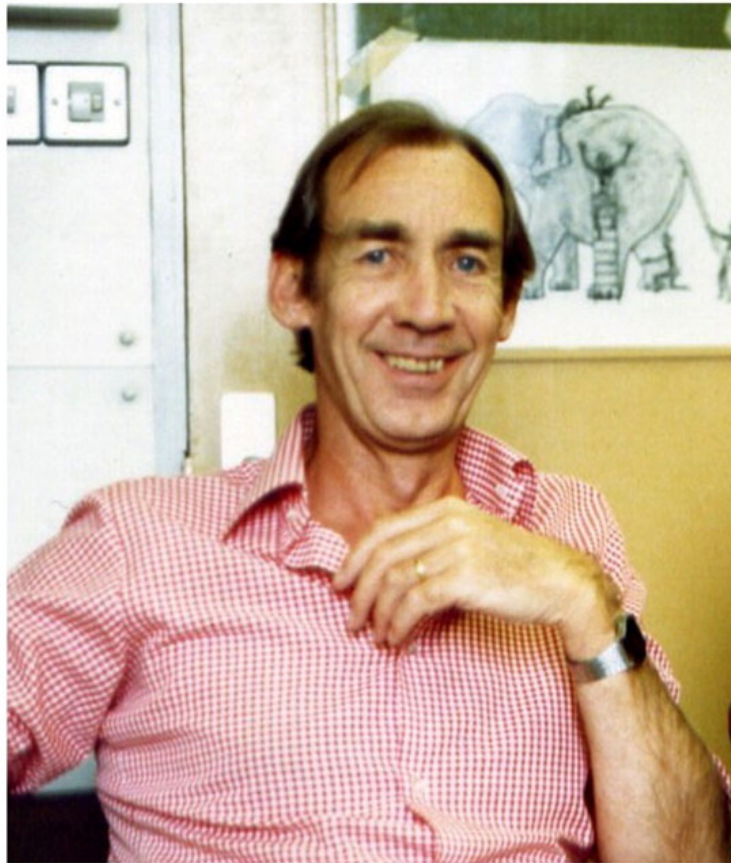
SCF: stem cell factor

GM-CSF: granulocyte-macrophage colony-stimulating factor

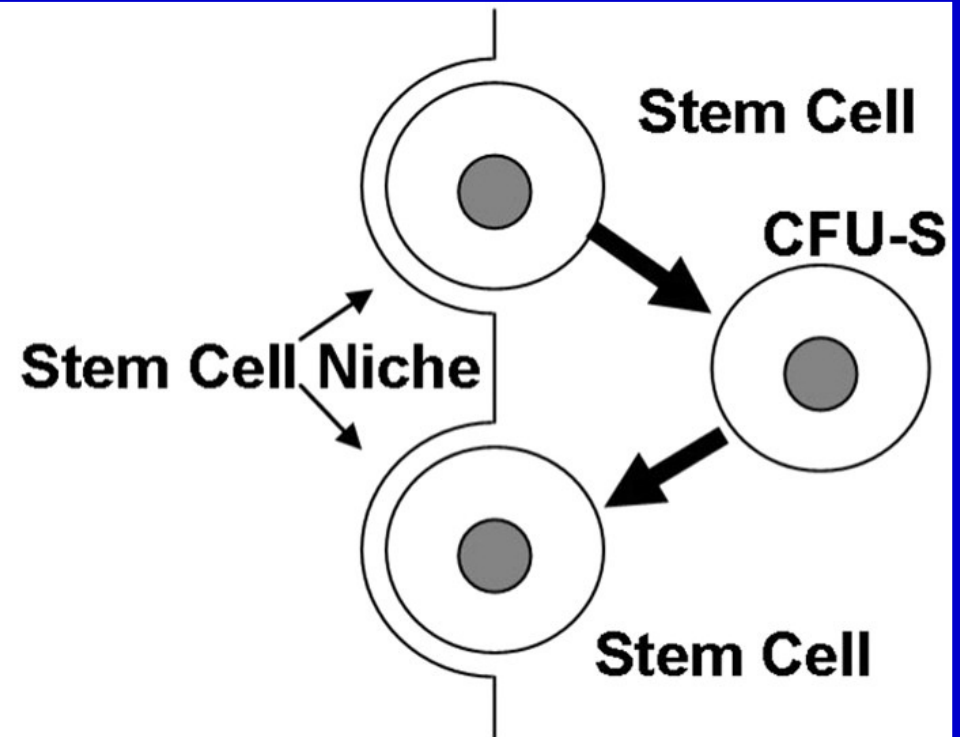
G-CSF: granulocyte colony-stimulating factor







R. Schofield



Papayannopoulou, T. et al. Blood 2008;111:3923-3930

5 fundamentos (1978)

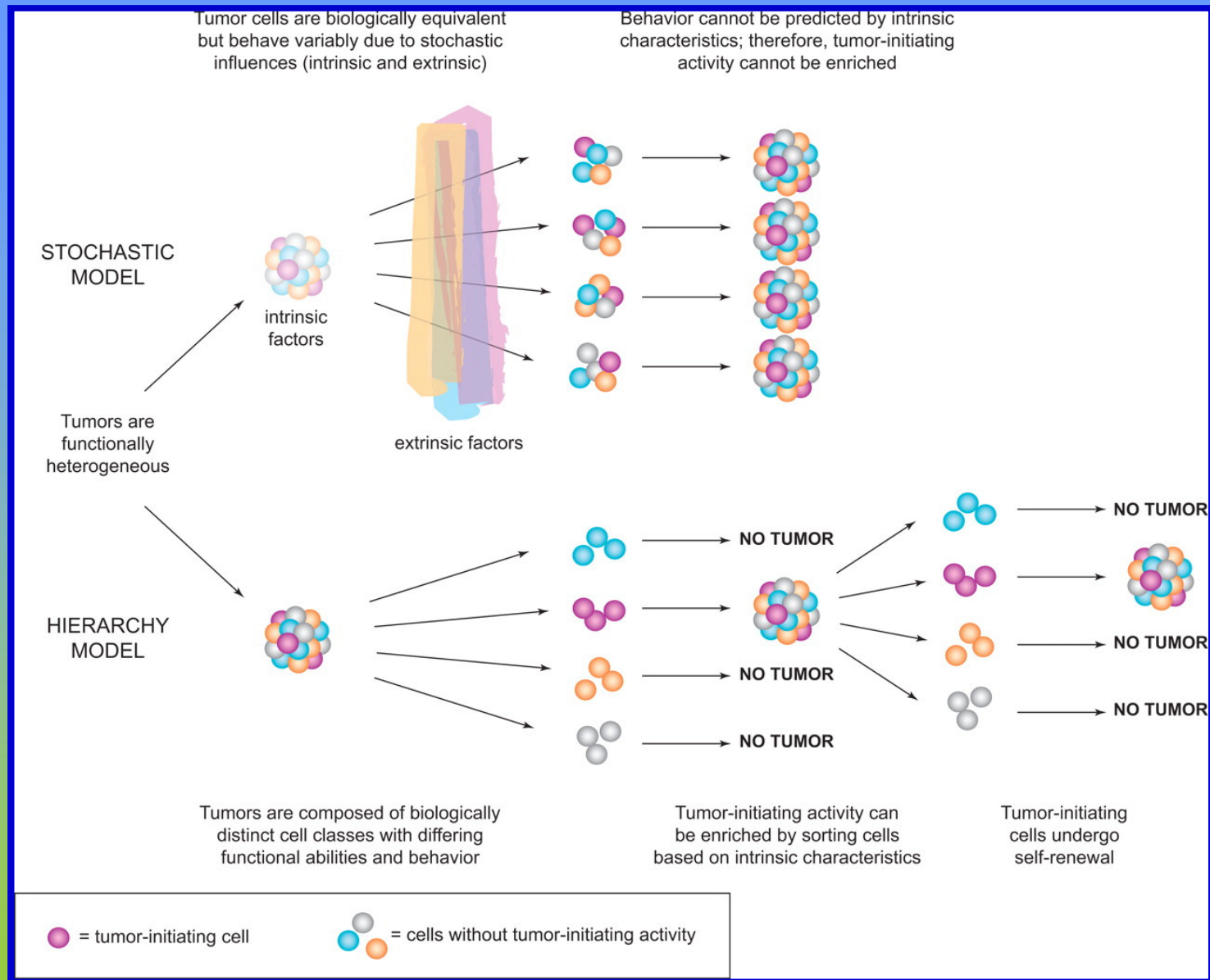
- ▶ Sitio anatómico definido
- ▶ Lugar donde sostenerse y reproducirse
- ▶ Lugar donde se inhibe la diferenciación
- ▶ Espacio limitado que limita el n de cél
- ▶ Lugar donde cél mas maduras puedan revertirse a stem cell

Genes involucrados en la decisión de linaje

▶ HOX

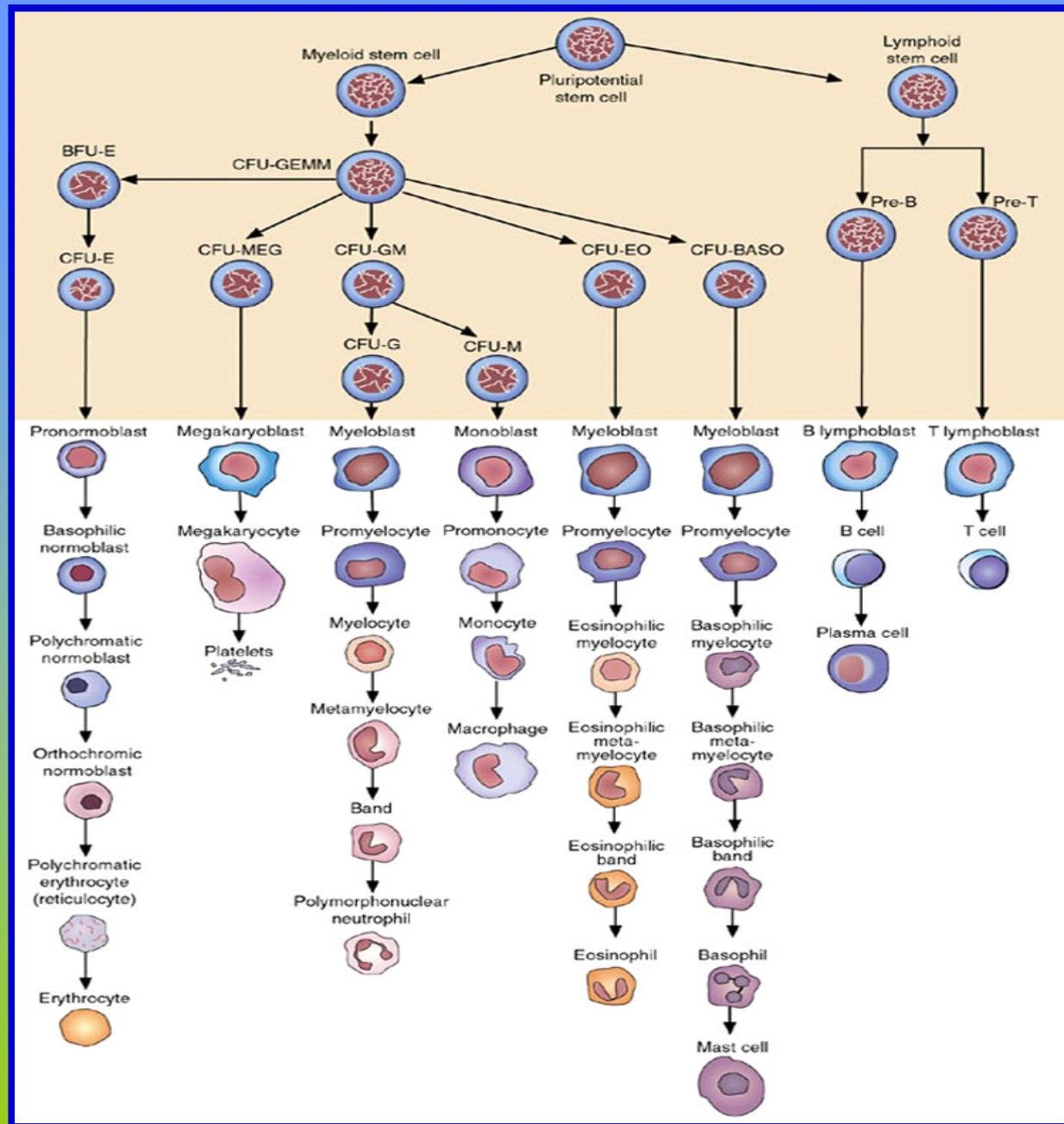
▶ GATA

▶ PAX

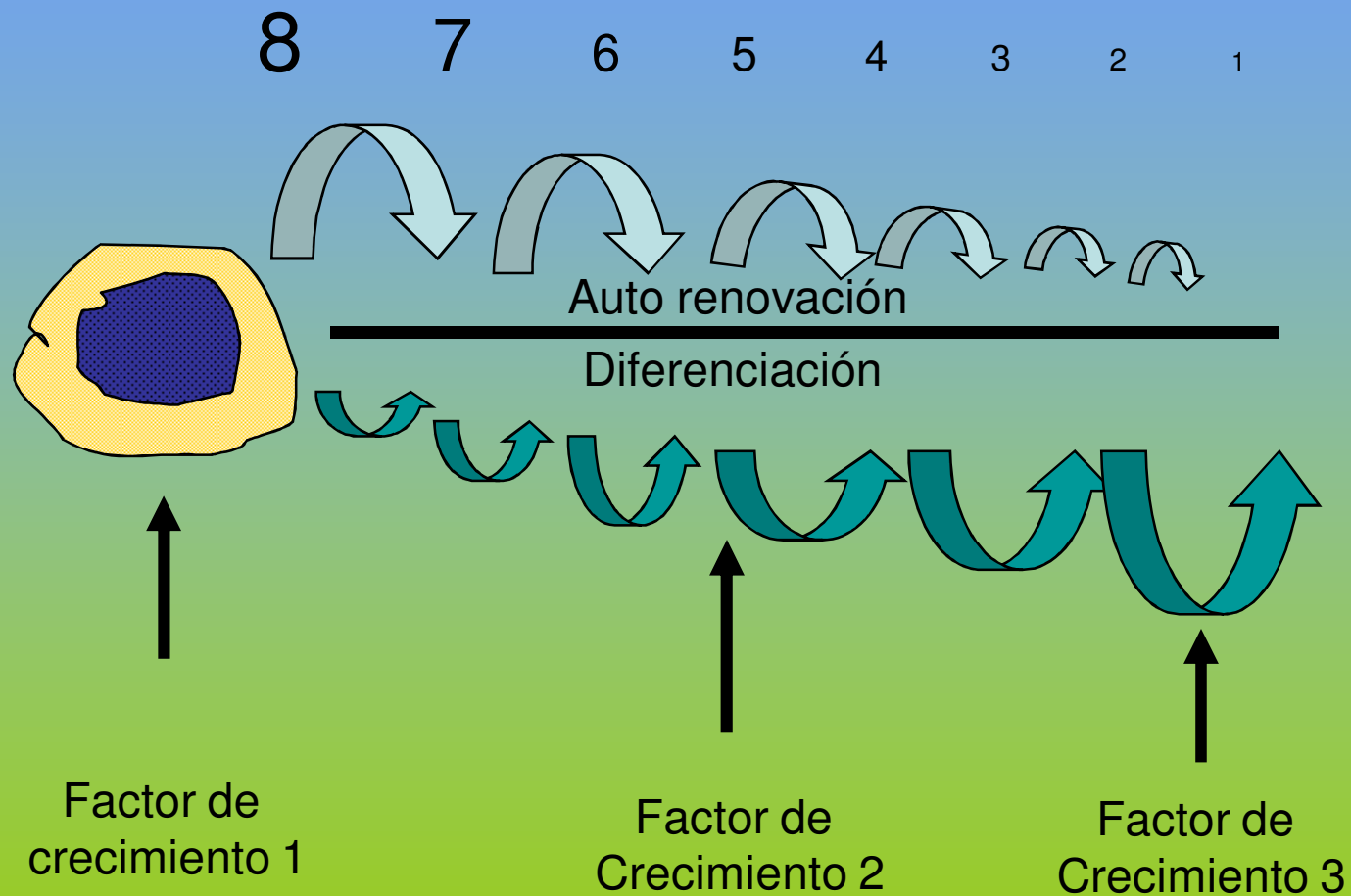


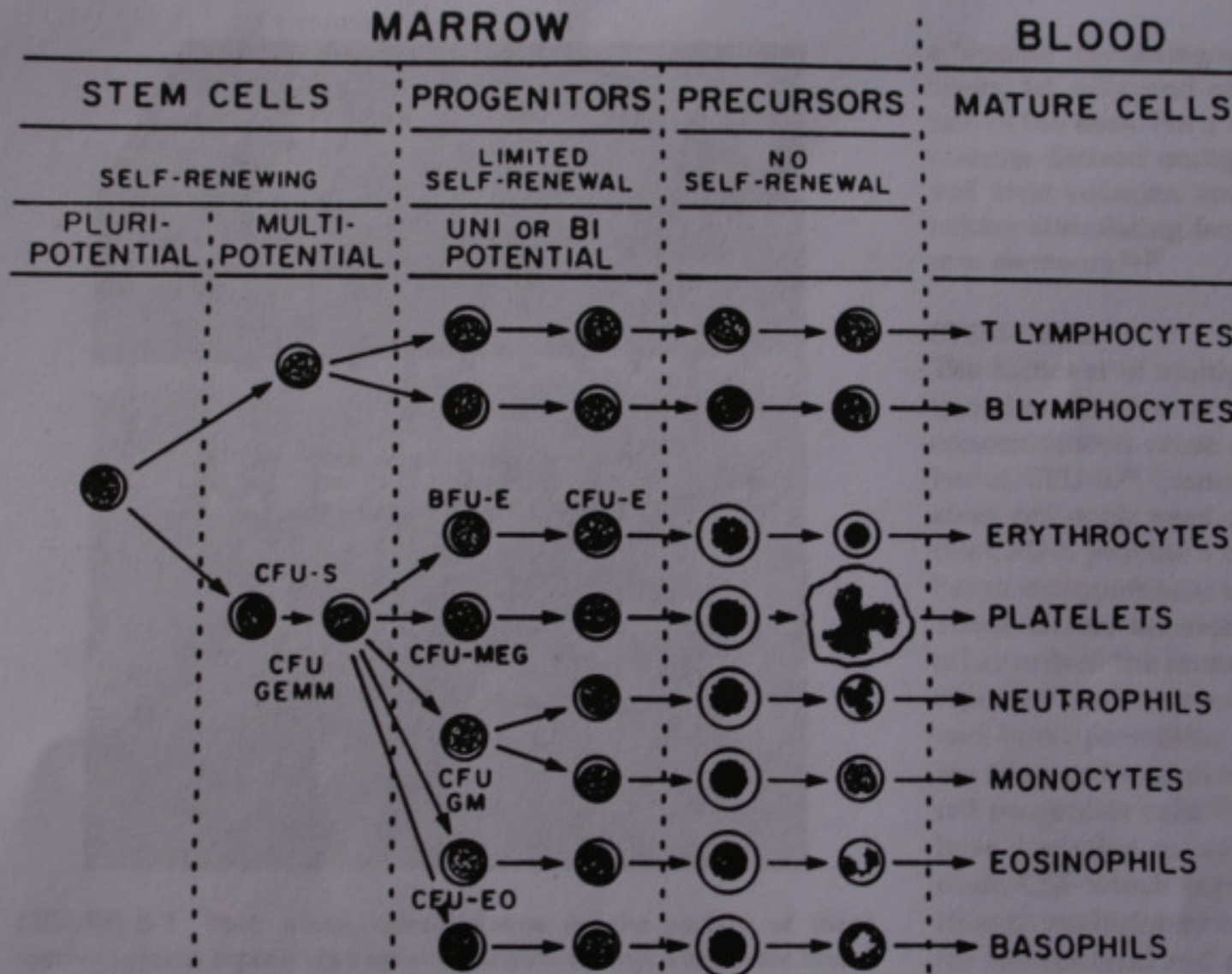
Multilevel targeting of hematopoietic stem cell self-renewal, differentiation and apoptosis for leukemia therapy Tsiftoglou AS, Bonovolias ID, Tsiftoglou SA. Pharmacol Ther. 2009 Mar 21.

GATA-2 L359 V mutation is exclusively associated with CML progression but not other hematological malignancies and GATA-2 P250A is a novel single nucleotide polymorphism Zhang SJ, Shi JY, Li JY. Leuk Res. 2009 Mar 20.

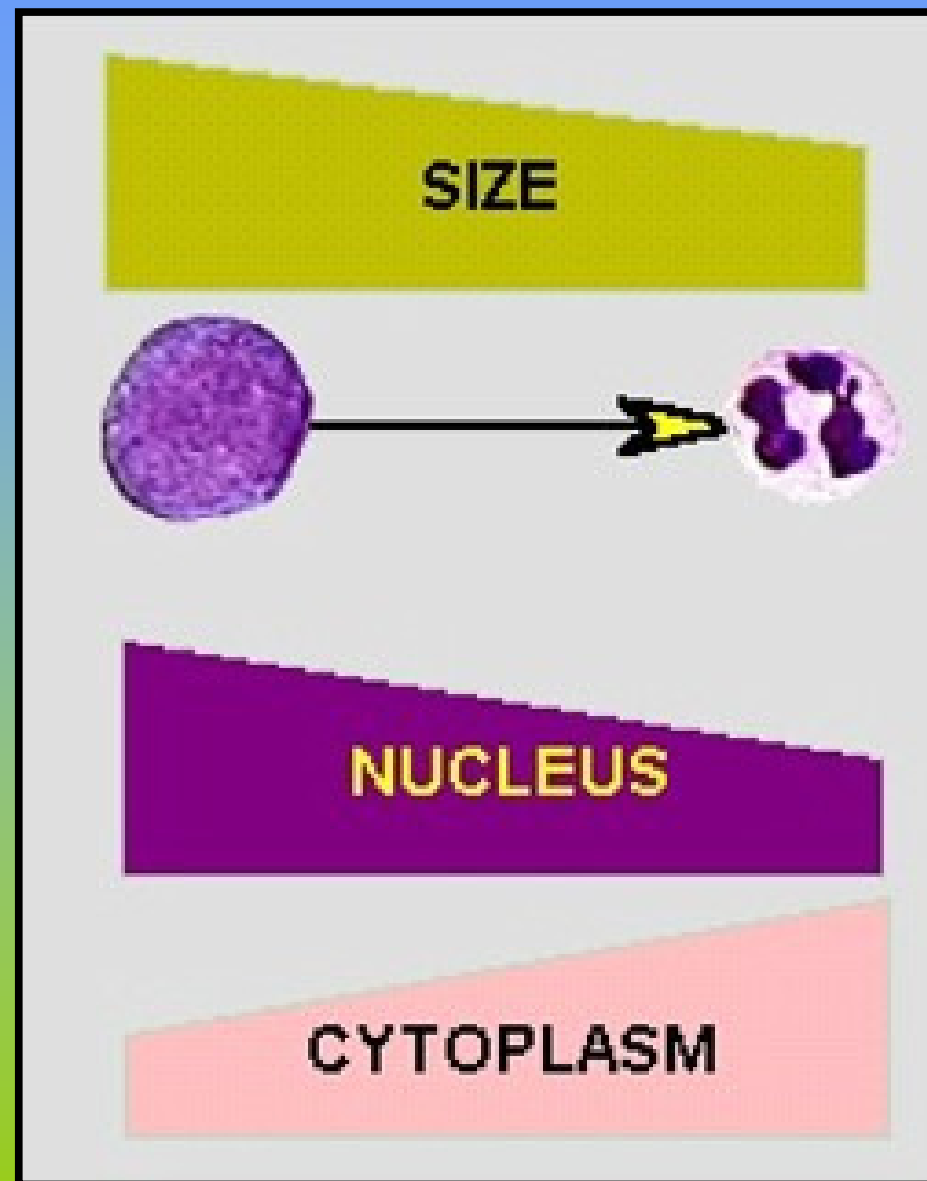


Potencialidad de multilinaje

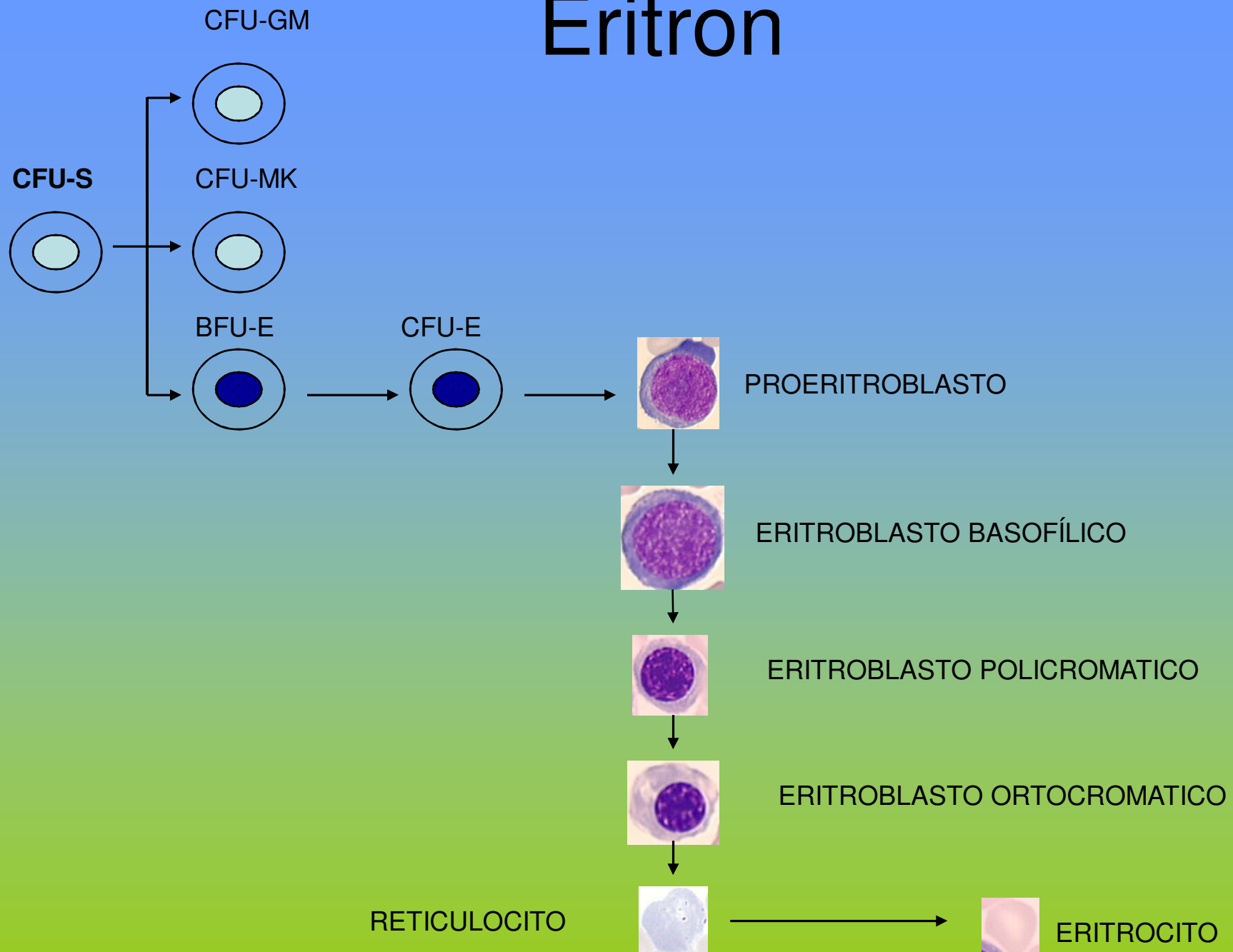




Maduración celular

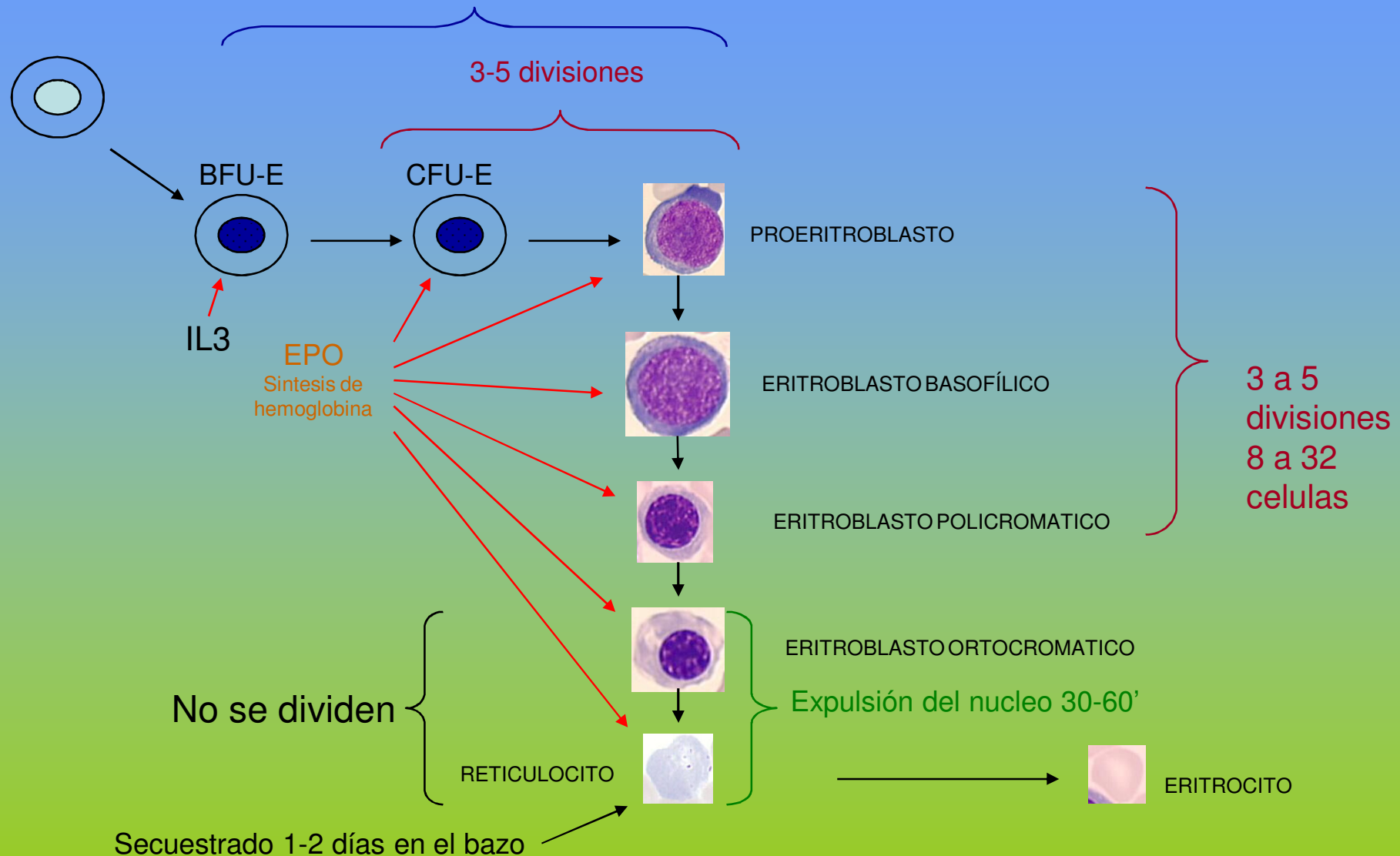


Eritron

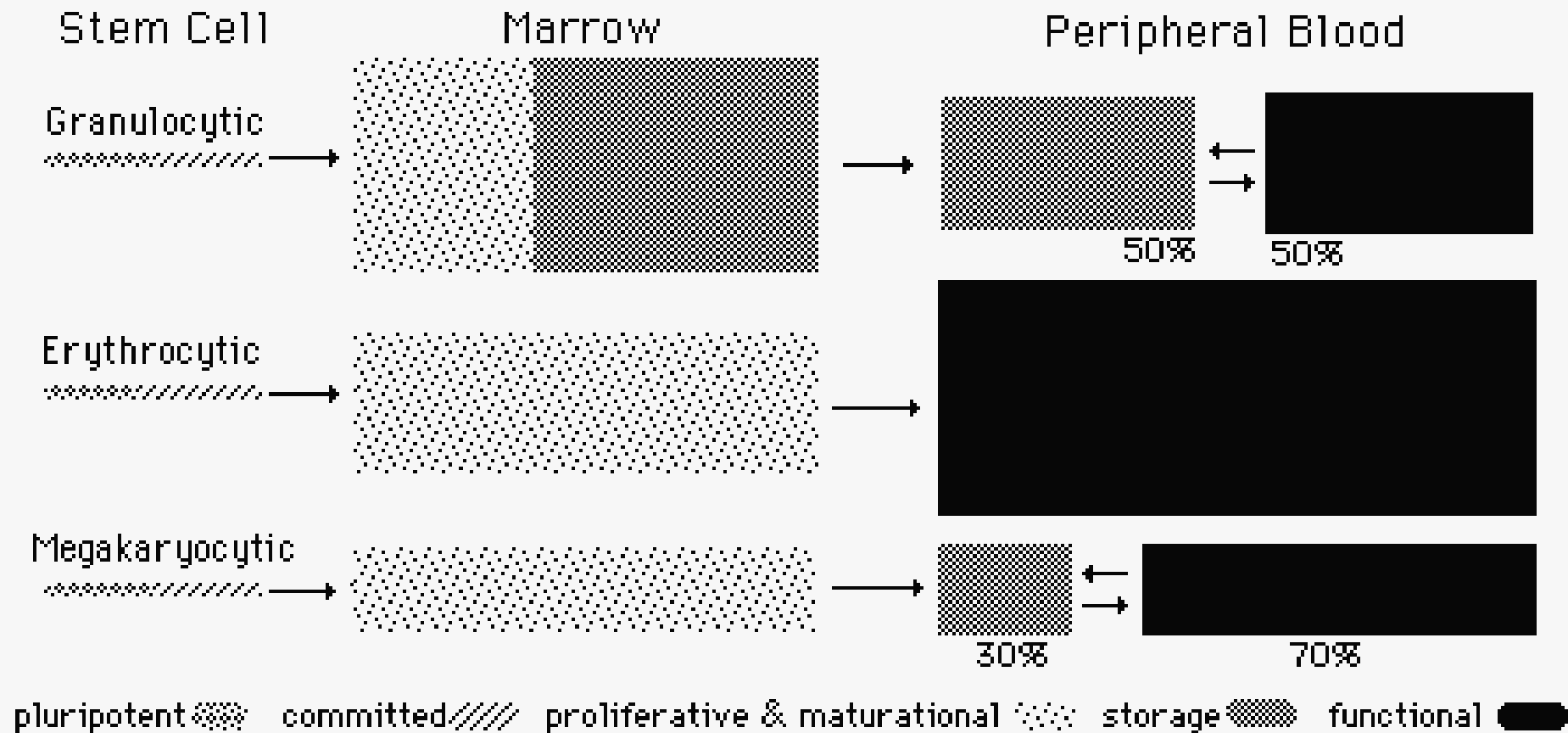


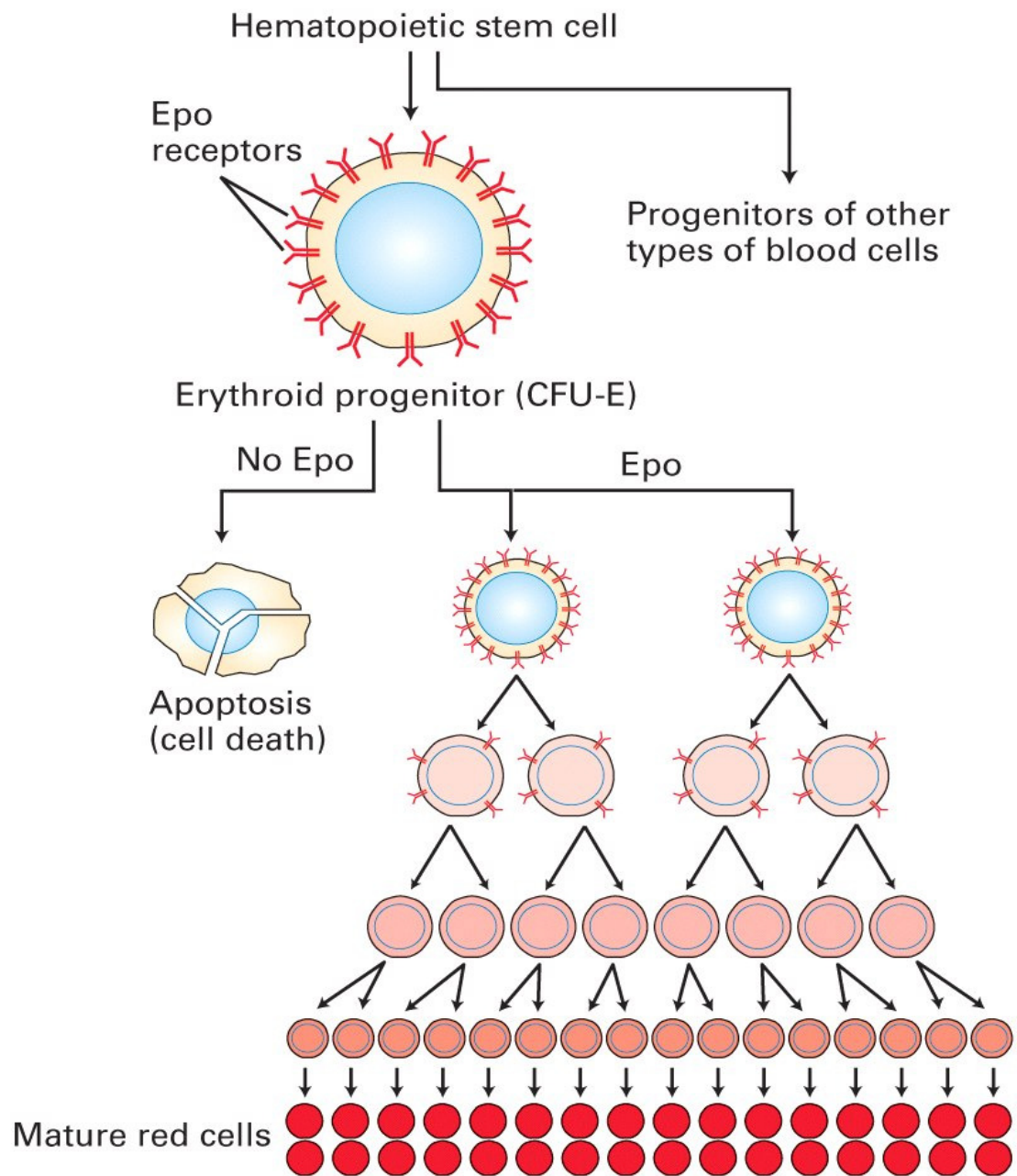
Poliferación y maduración del eritron

12-15 días

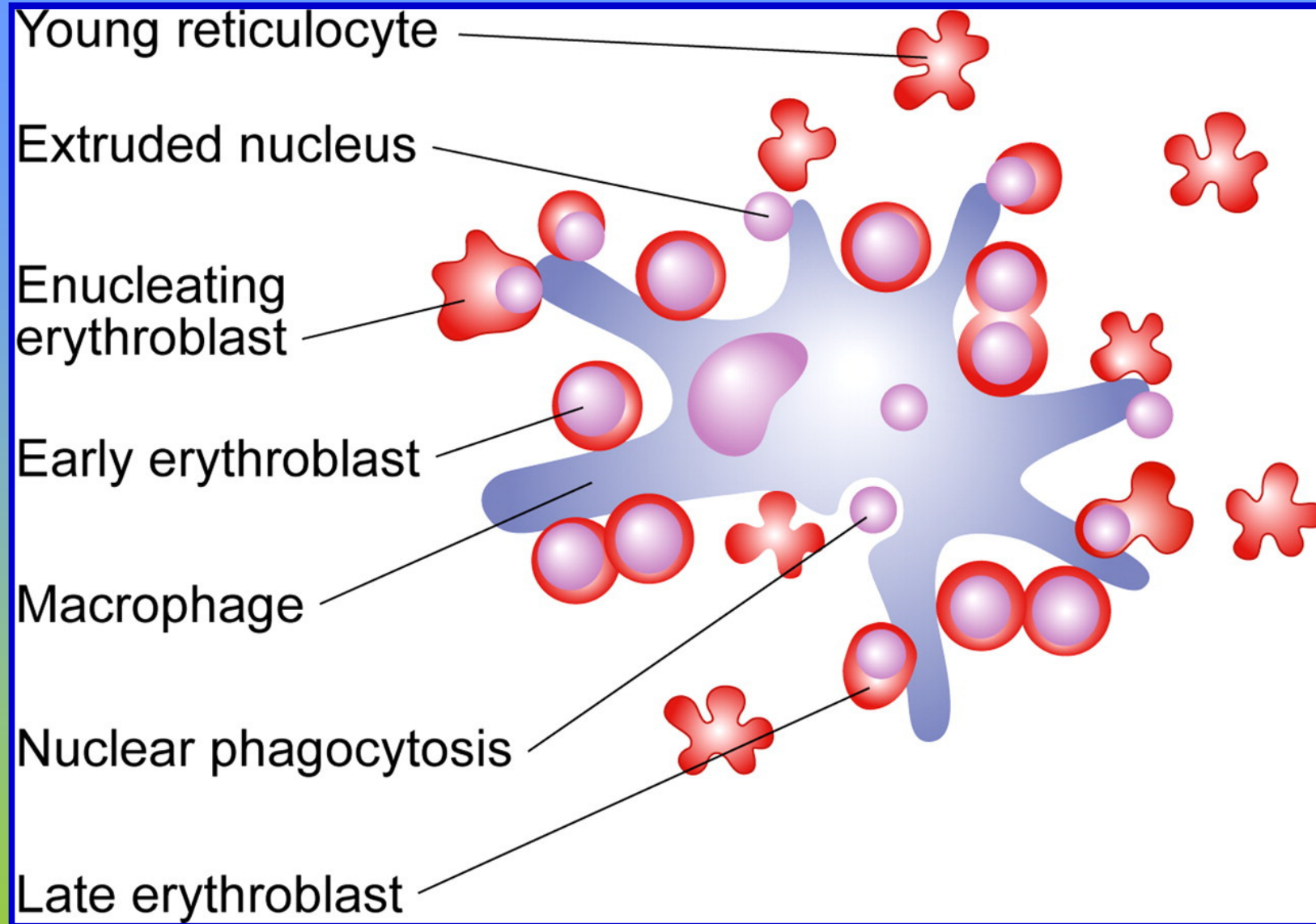


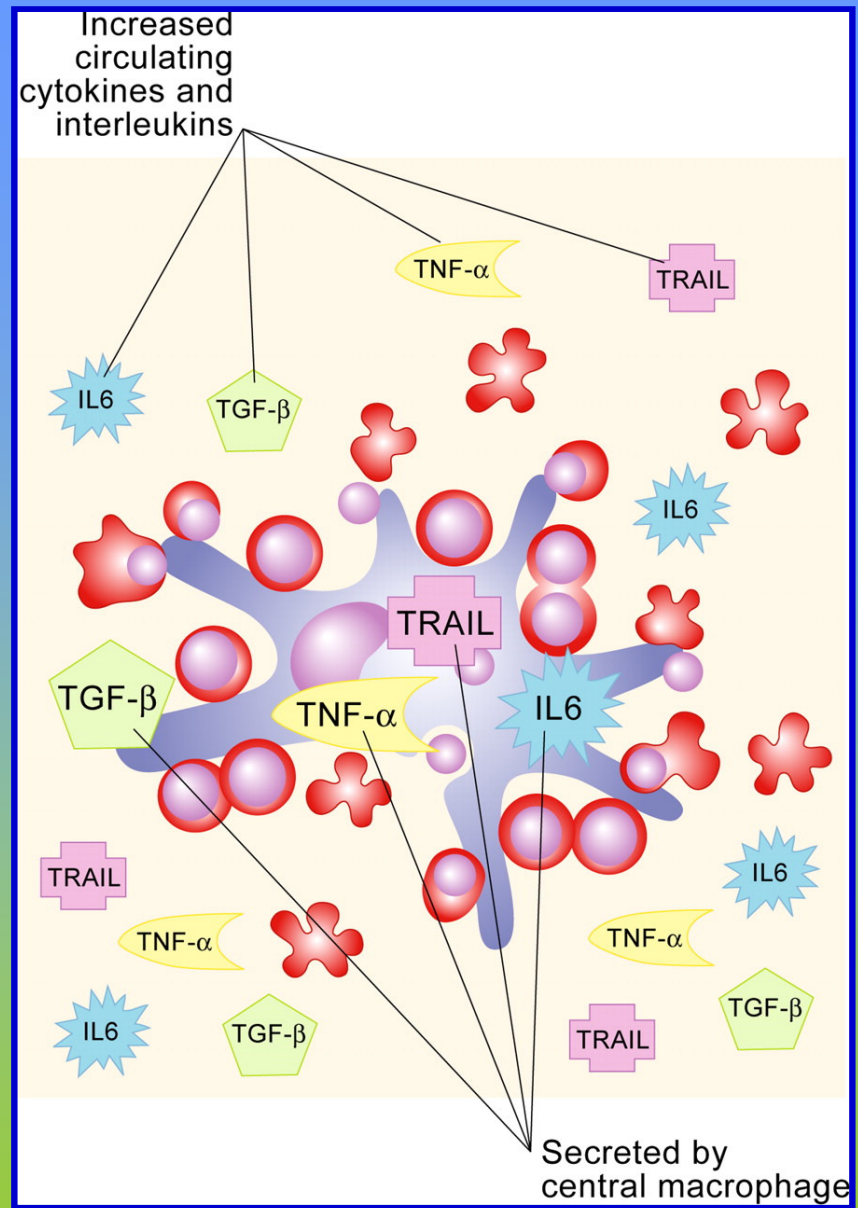
Hematopoietic Compartments





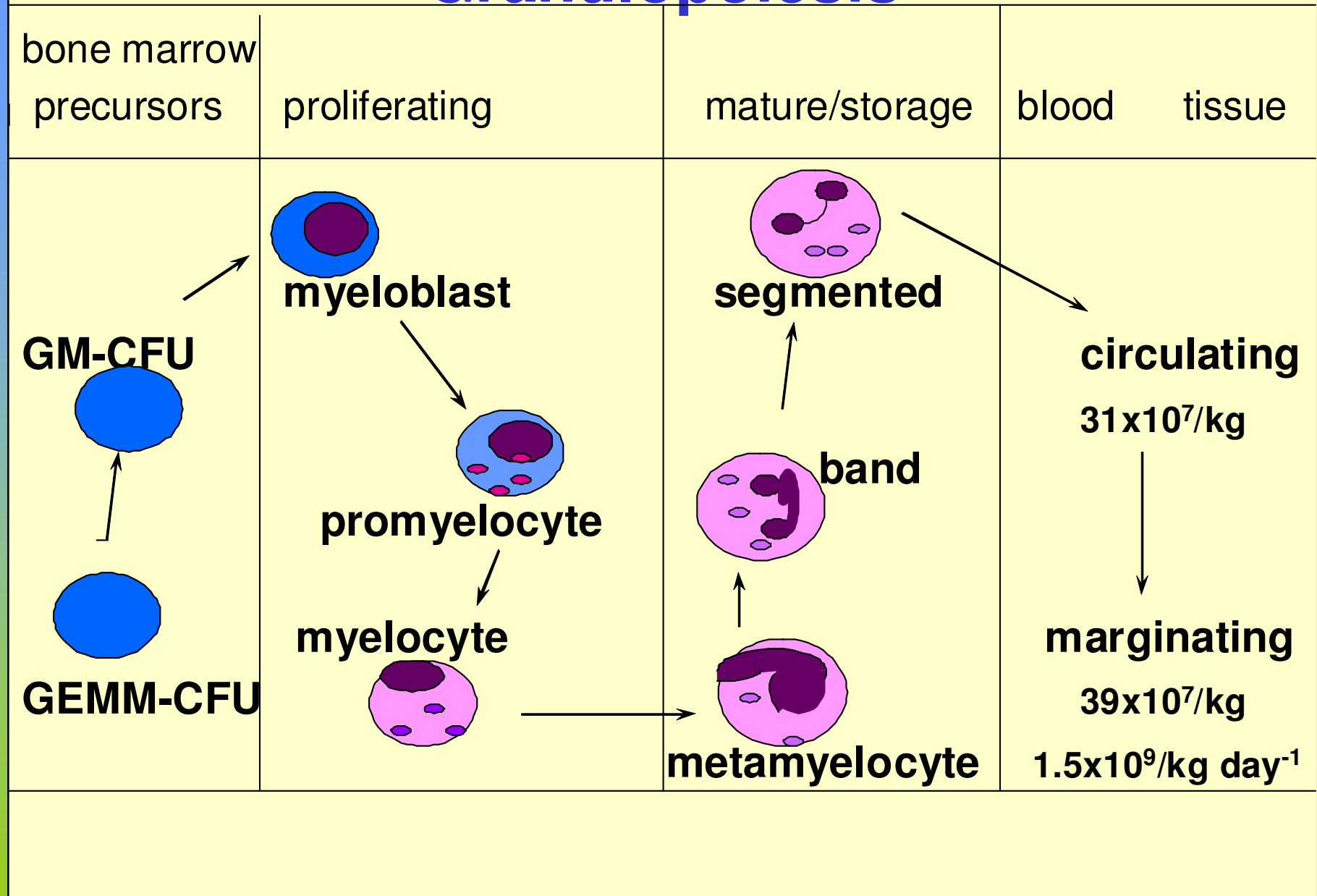


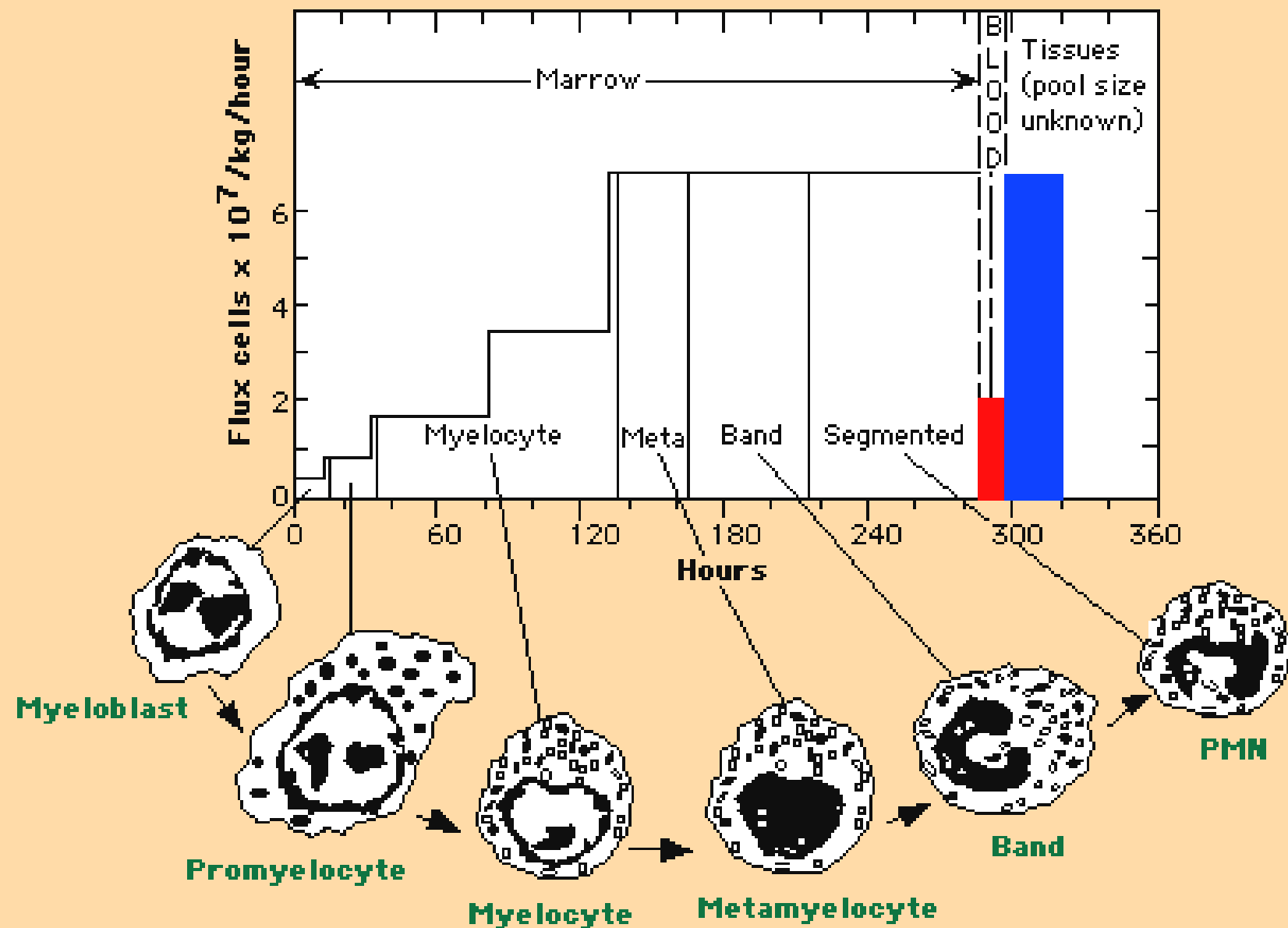




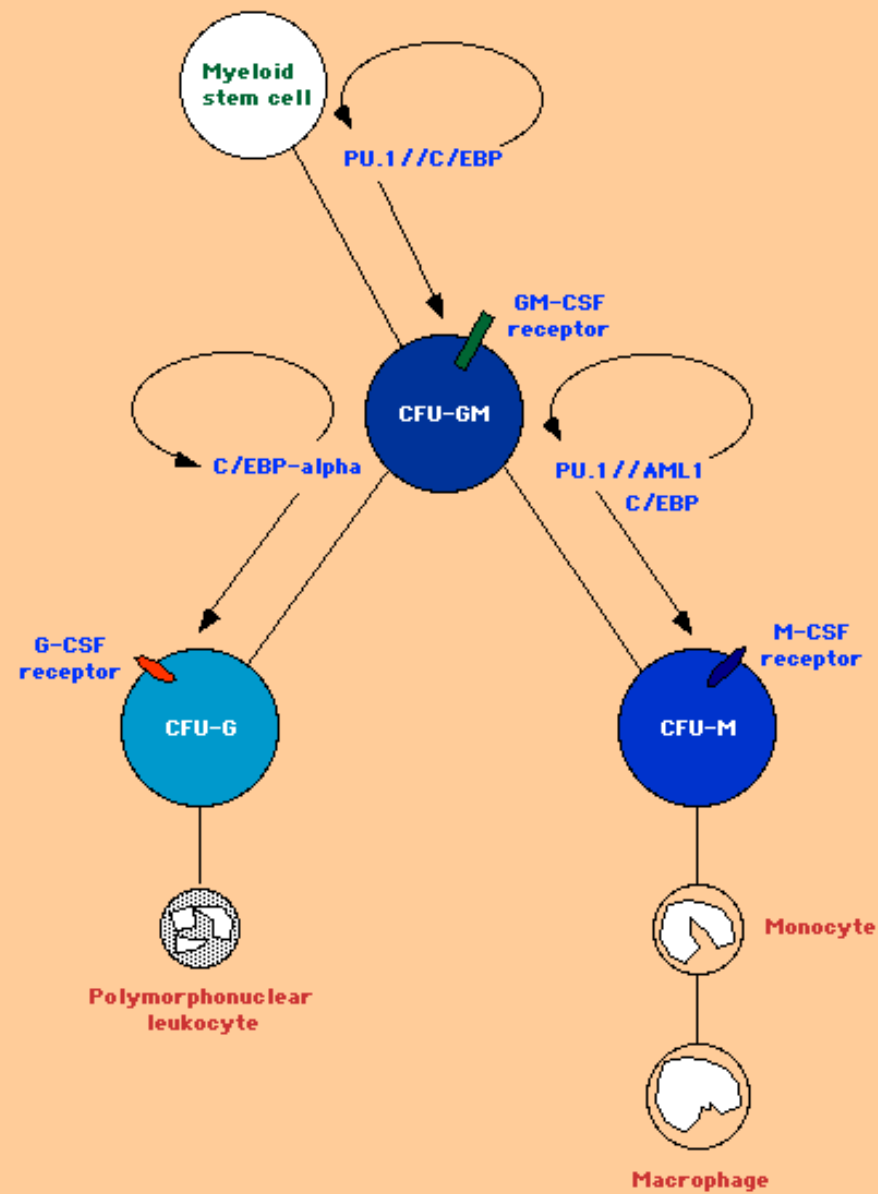
Chasis, J. A. et al. Blood 2008;112:470-478

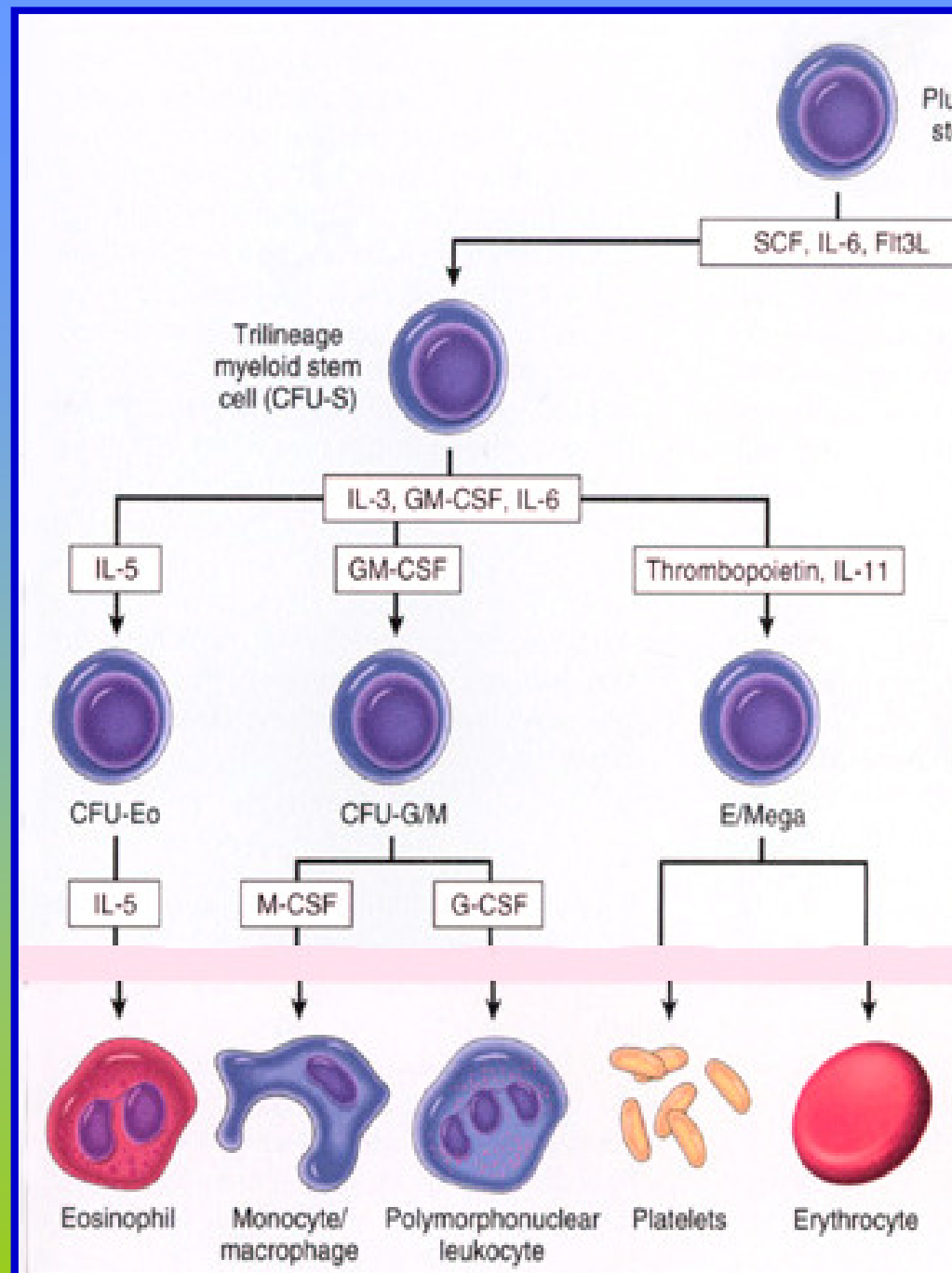
Granulopoiesis

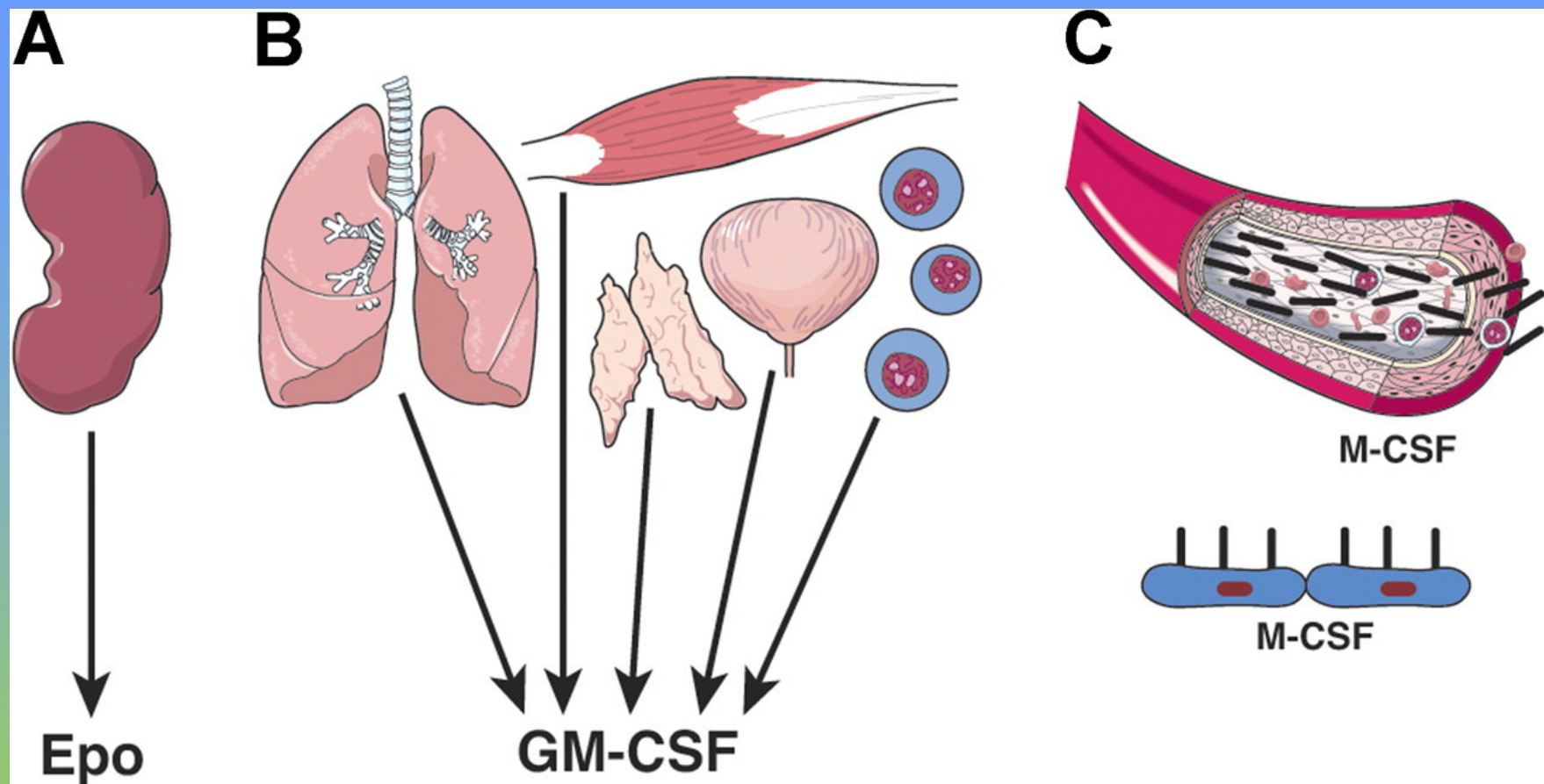




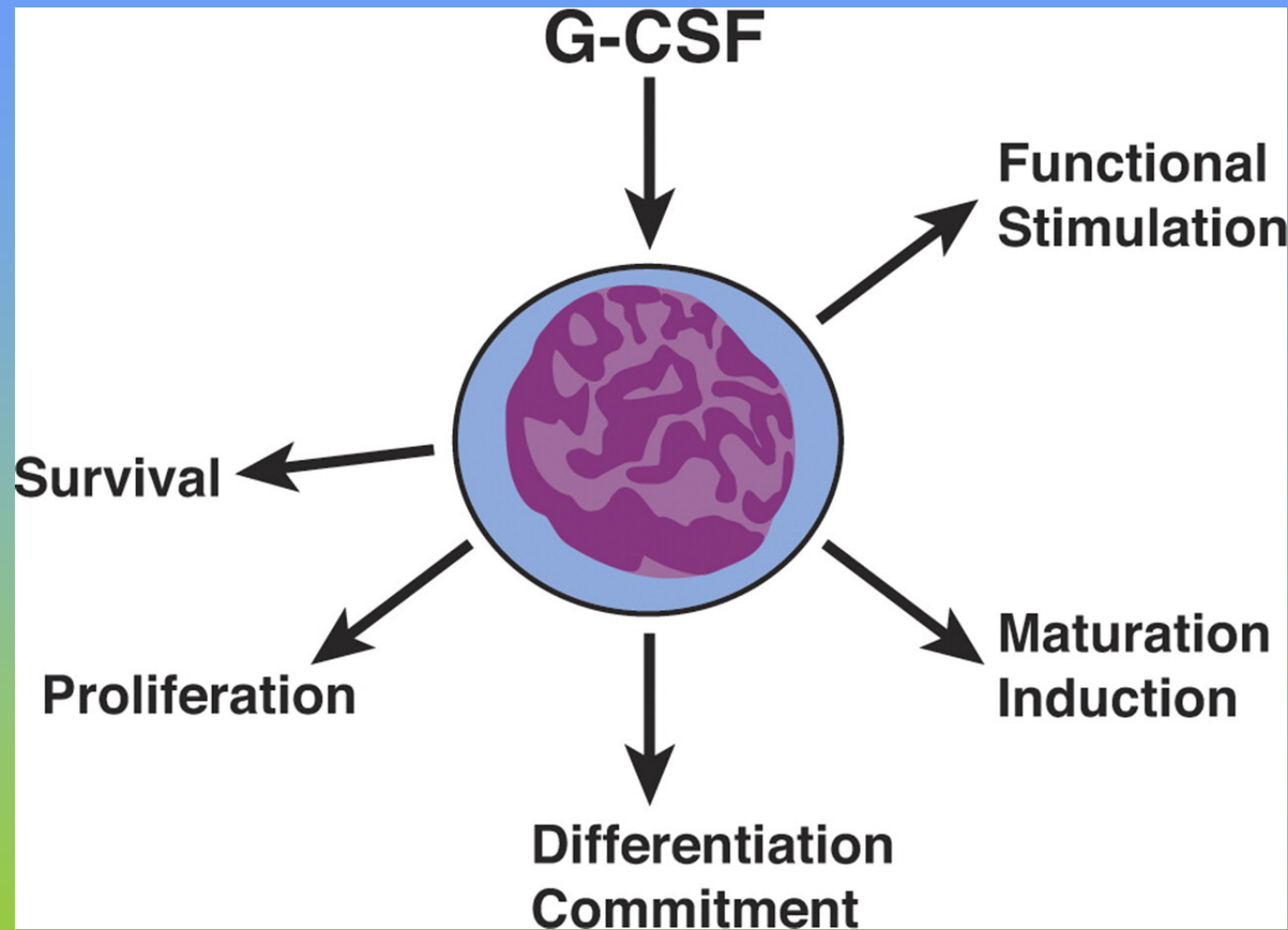
Transcription Factors and Myelopoiesis



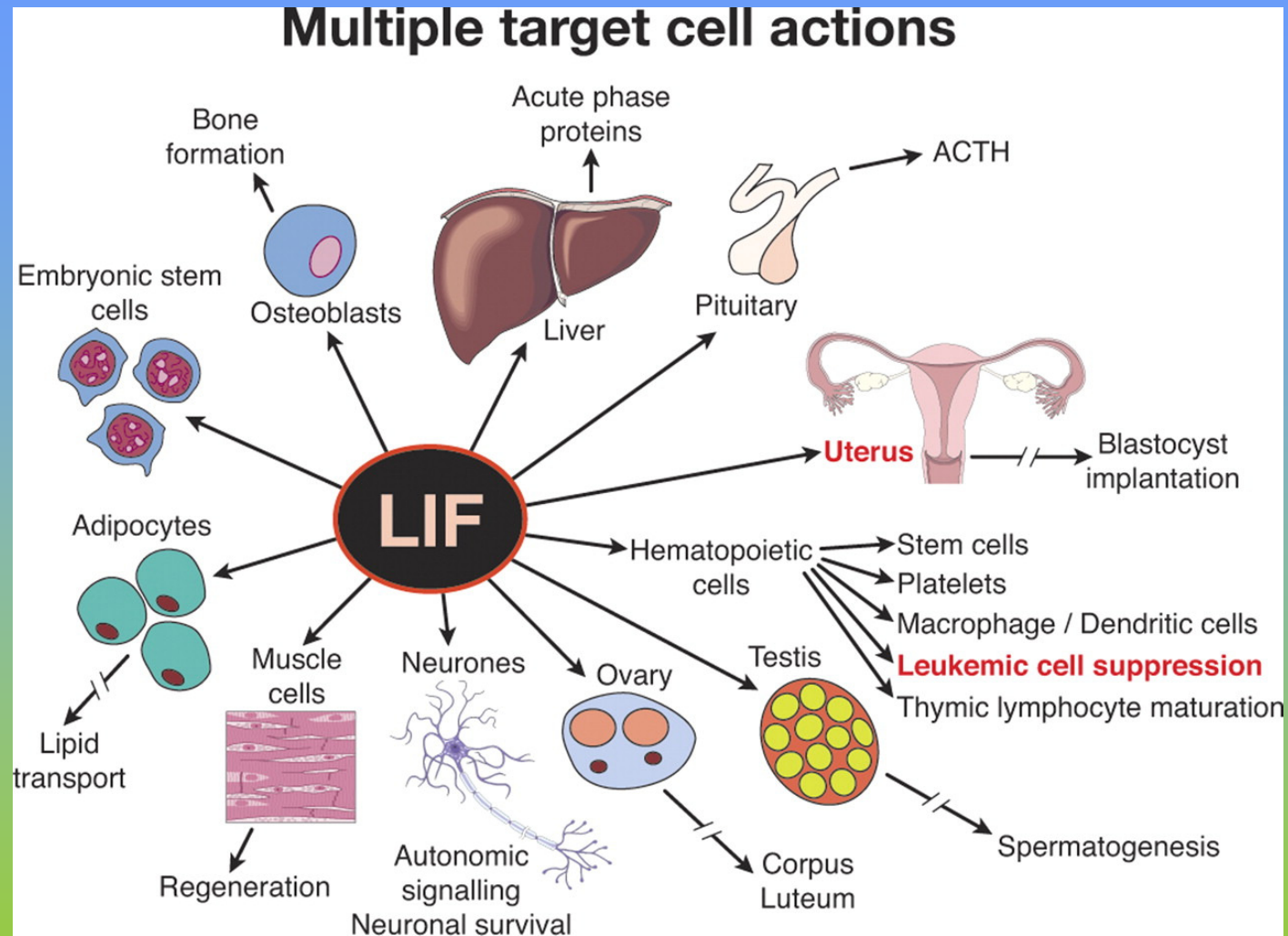




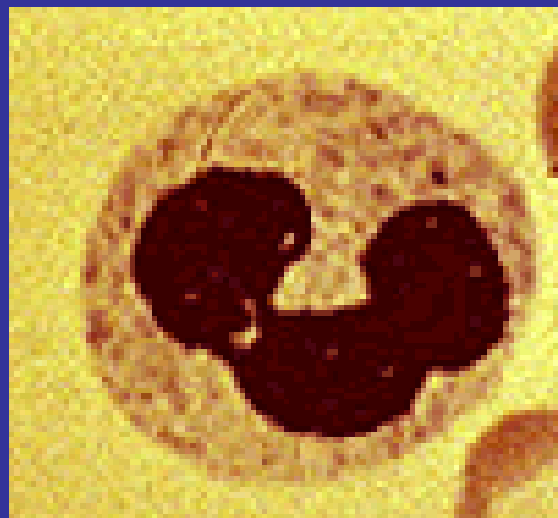
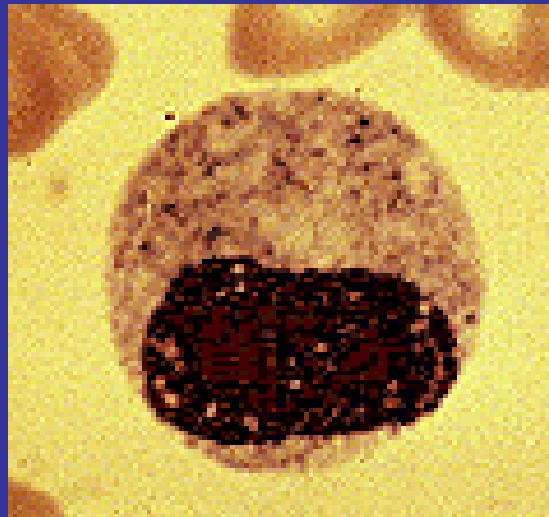
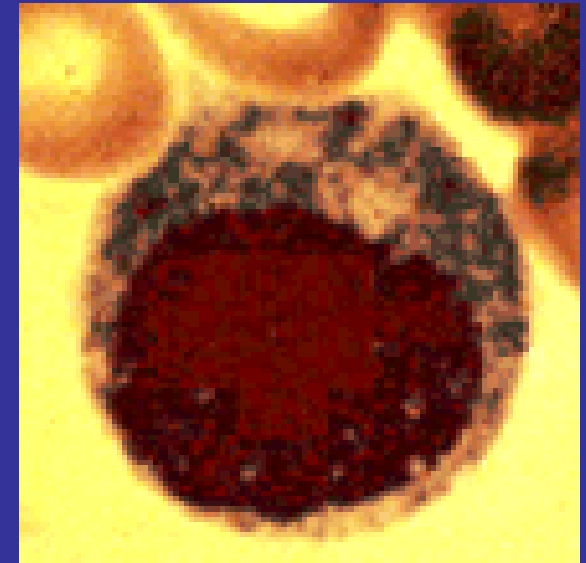
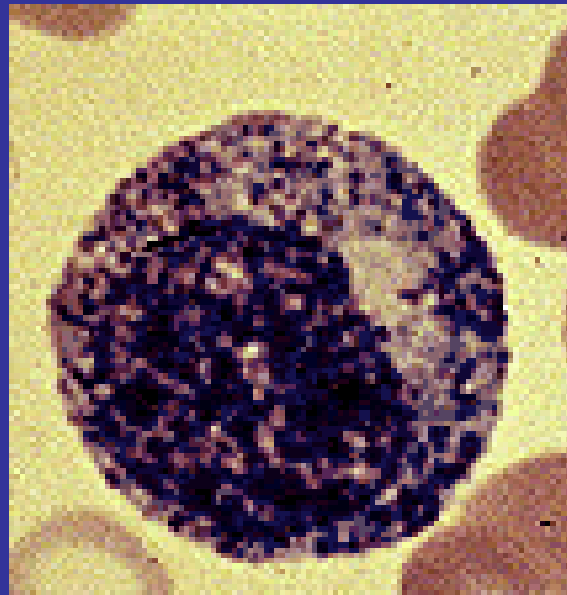
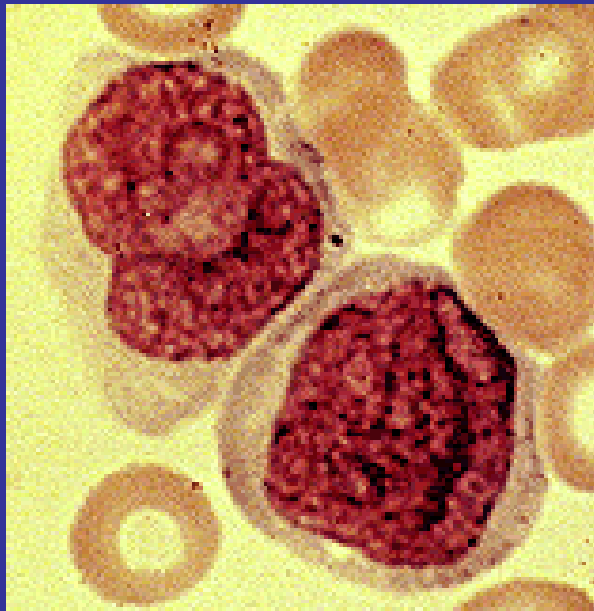
Hematopoietic cytokines are polyfunctional



The confusing nature of some hematopoietic cytokines as illustrated by LIF



Metcalfe, D. Blood 2008;111:485-491



Content of Human PMN Granule Subsets†

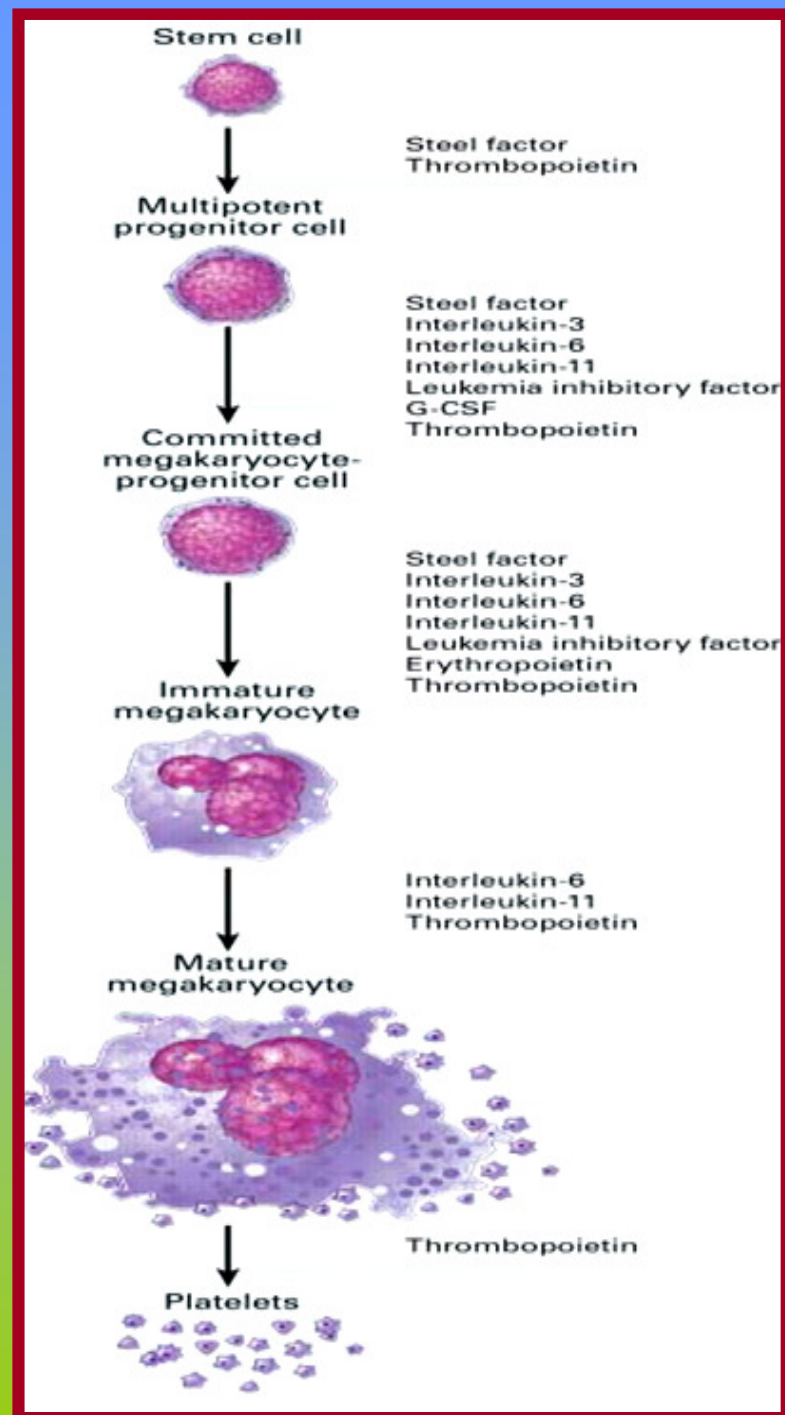
Granule	Azurophil	Specific	Gelatinase	Secretory vesicles
Marker enzyme	Myeloperoxidase	Lactoferrin	Gelatinase	Alkaline phosphatase
Membrane	CD 63 granulophysin CD 68	CD15,CD66,CD67 CD11b/CD18	CD11b/CD18	CD10,CD13,CD45, CD35 (CR1) CD11b/CD18
Matrix				
Microbicidal	Myeloperoxidase Nitric oxide synthase Lysozyme BPI protein Defensins Serprocidins Elastase Cathepsin G Proteinase 3 Azurocidin (CAP 37)	Lactoferrin Lysozyme	Lysozyme	
Hydrolases	Acid beta glycerophosphatase alpha Mannosidase beta Glucuronidase beta Glycerophosphatase N-acetyl-beta glucosaminidase Sialidase	Gelatinase Collagenase Histaminase Heparanase NGAL Sialidase	Gelatinase Acetyltransferase	
Other	Acid mucopolysaccharide Heparin binding protein	Beta-2 microglobulin Plasminogen activator Vitamin B12 binding protein	Beta-2 microglobulin	Plasma proteins

Blasto

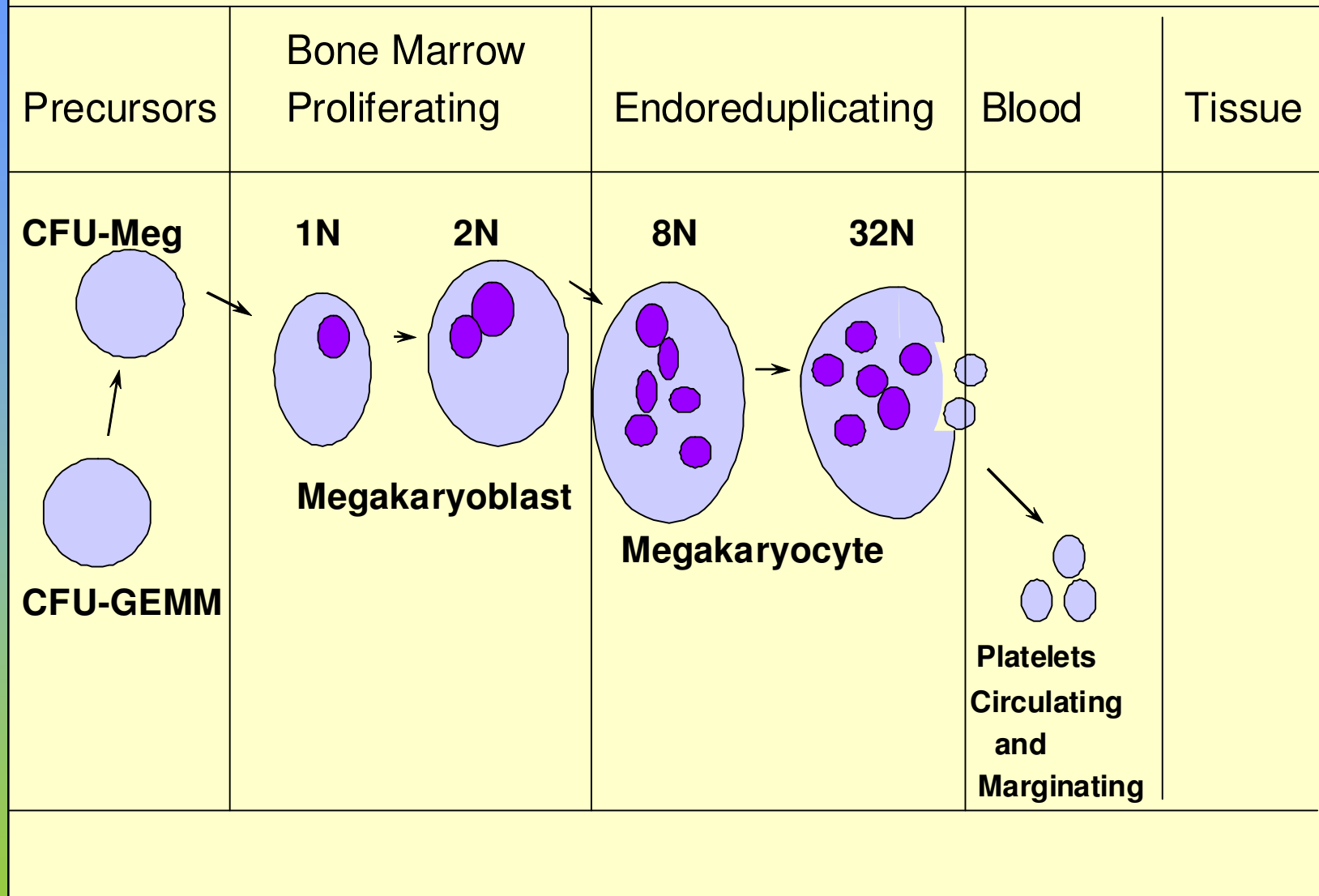


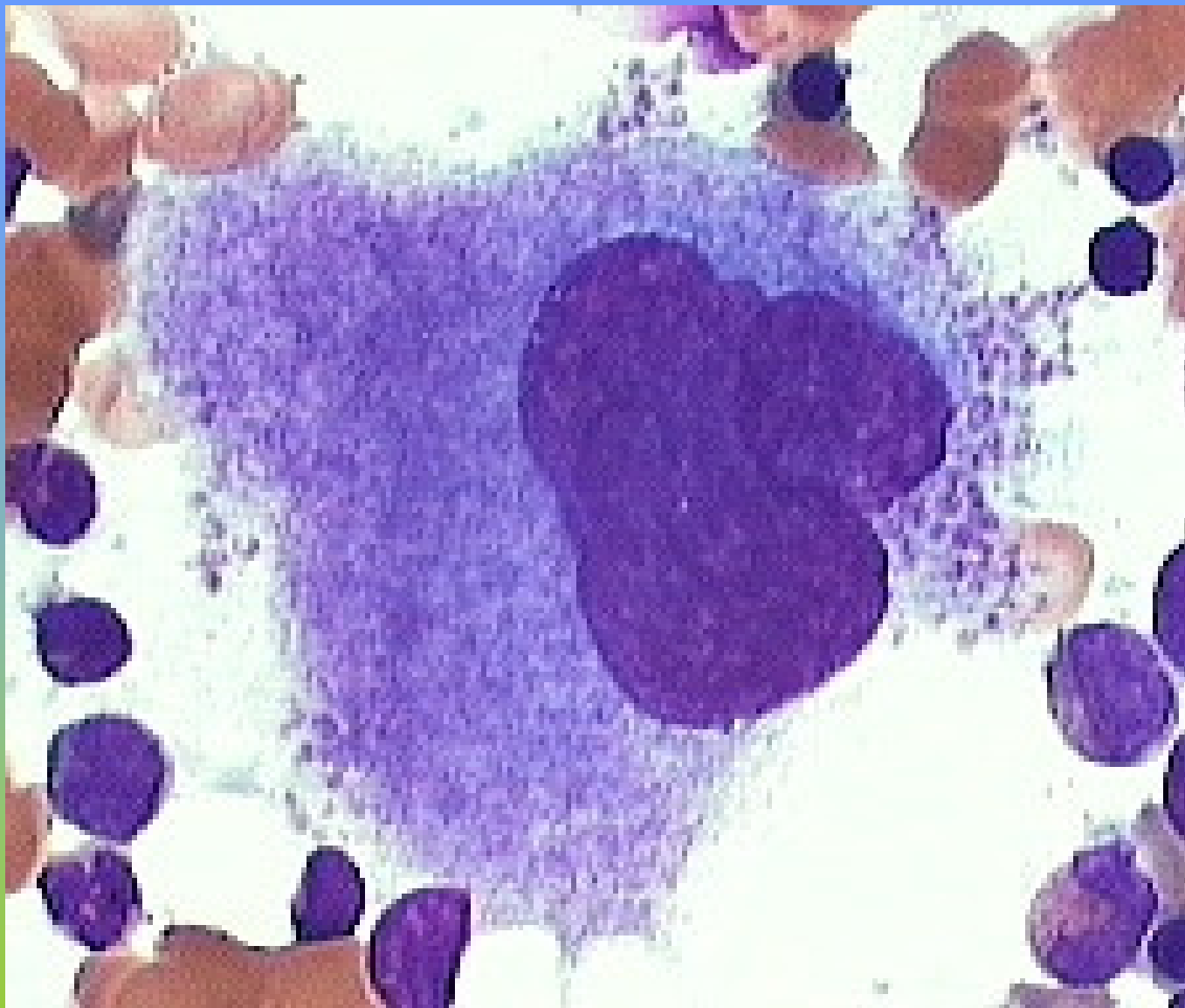
Gránulos





Thrombopoiesis





Neoplasias hematológicas

