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LABS:

12	6.2	22
	17.5	

139	102	9	119
3.7	22	0.7	

7.0	4.1
0.7	<0.2
10	9
74	

<u>Diff</u>
Neutrophil %: 0%
Promyelocytes %: 3.5%
Blasts %: 88%
Abs neutrophils: <0.03

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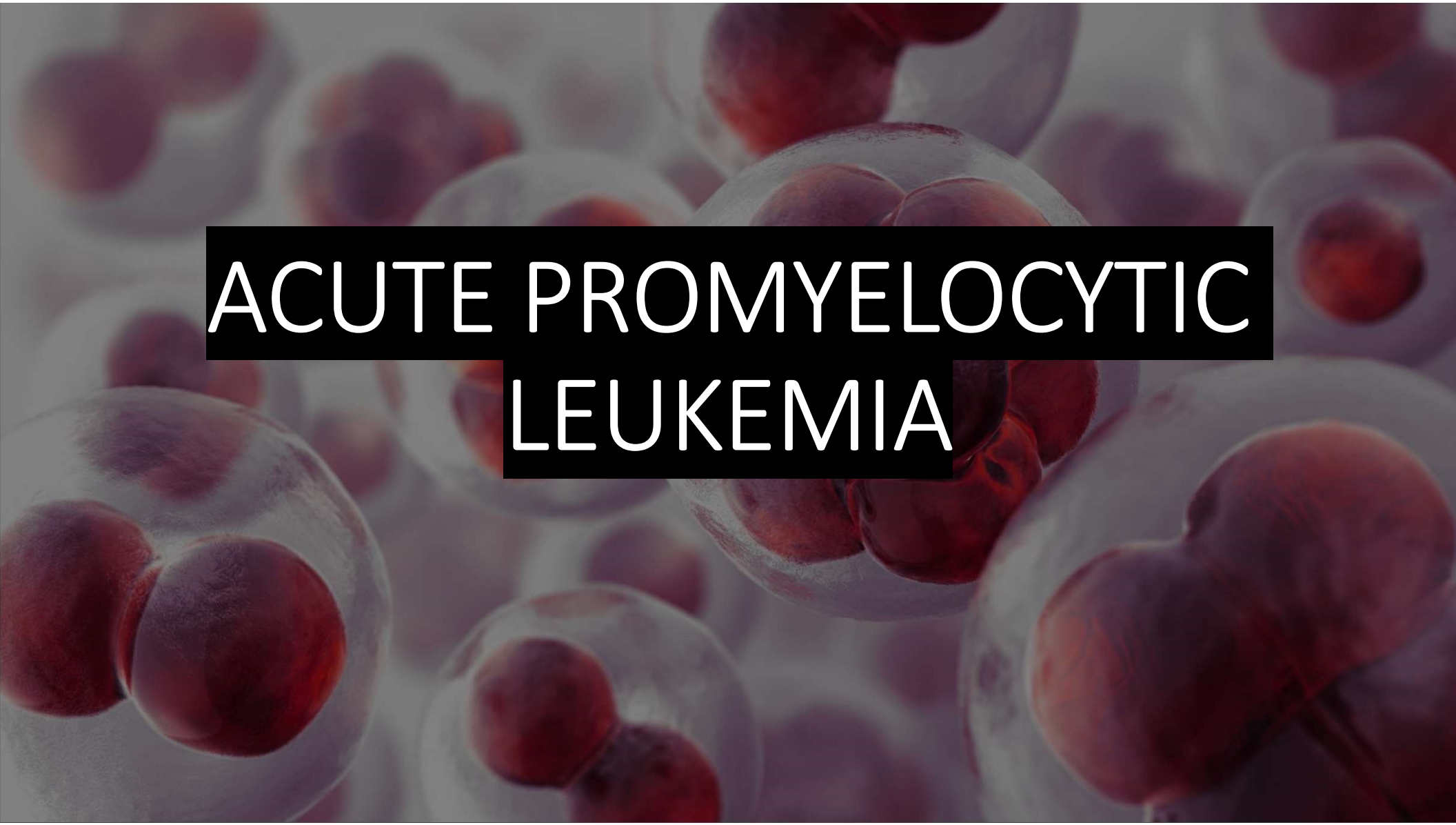
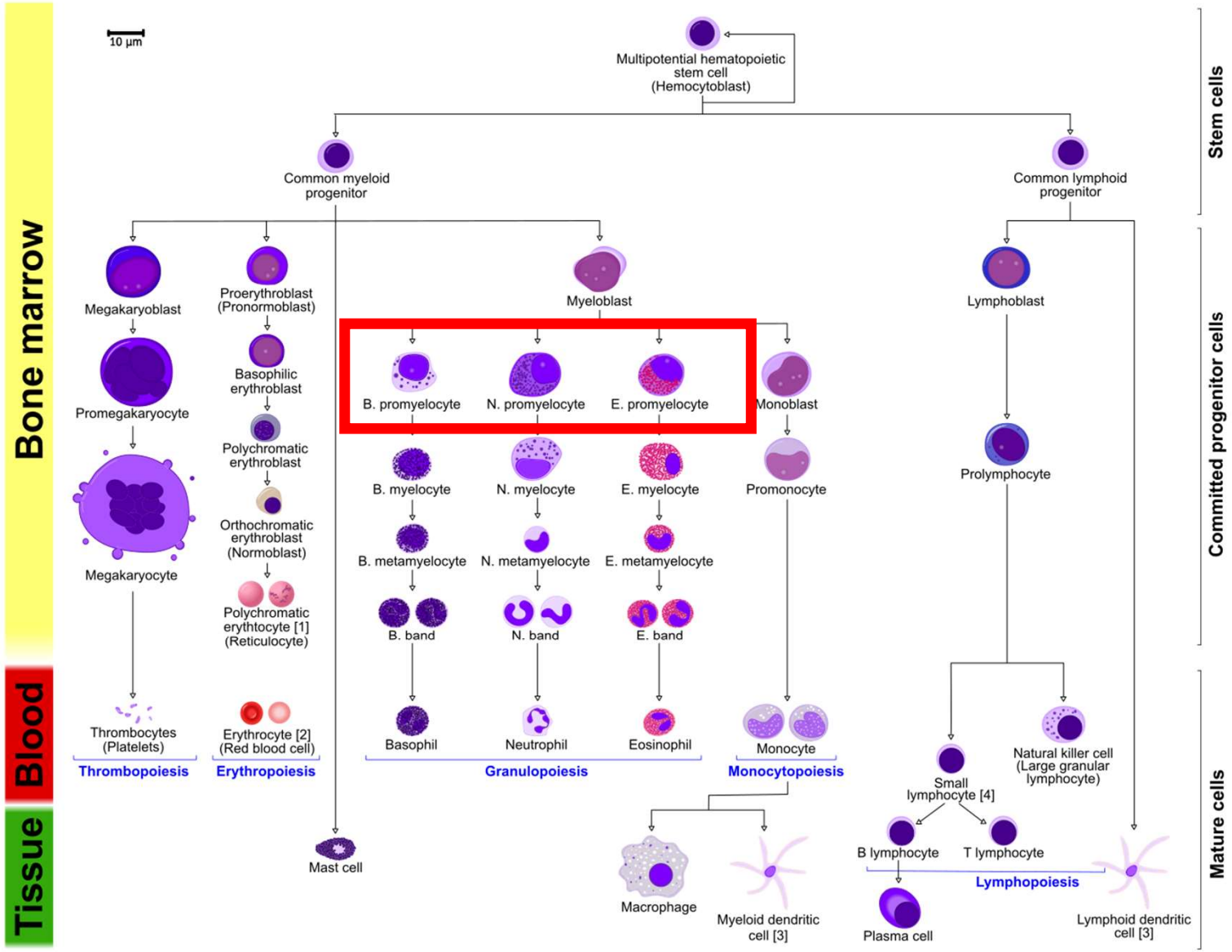


ACUTE PROMYELOCYTIC LEUKEMIA

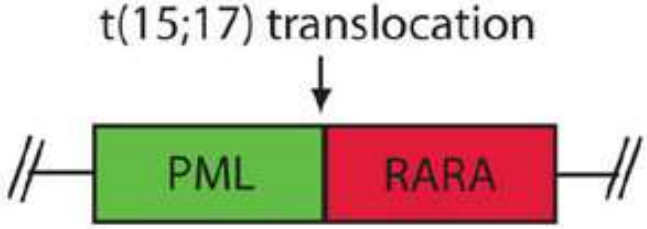
AML vs APL

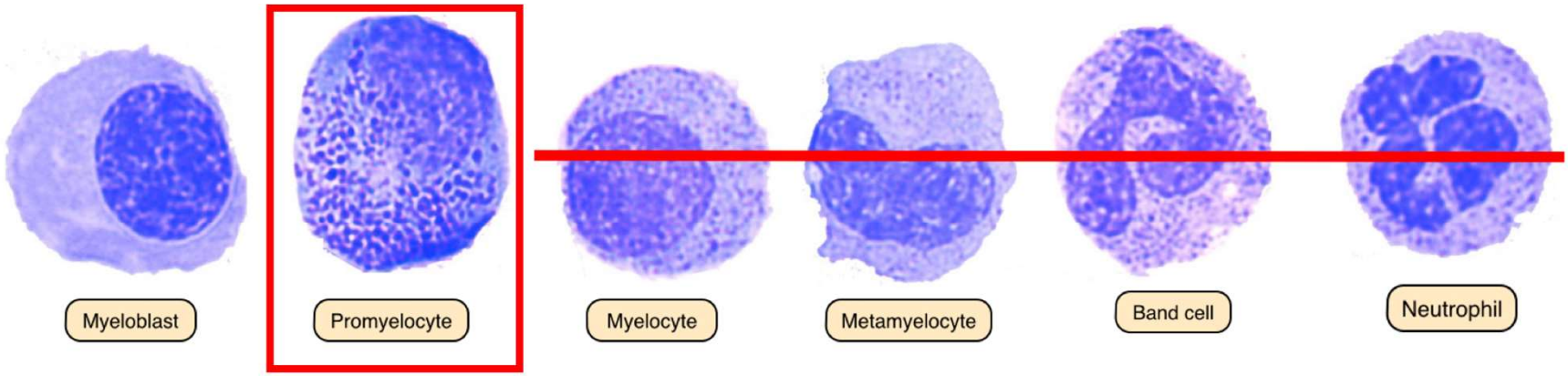
- AML
  - Neoplasm of myeloid cells
  - Adults (50-60s)
  - Fatigue (anemia), infections (ineffective neutrophils), bleeding / bruising (thrombocytopenia)
  - >20% blasts in blood or bone marrow
- APL
  - Variant of AML
  - Adults (20-50s, median 40s)
  - Same clinical presentation as AML
  - **Atypical promyelocytes in blood or bone marrow**


Bone marrow
Blood
Tissue
10 µm
Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Stem cells
Committed progenitor cells
Mature cells
Megakaryoblast
Promegakaryocyte
Megakaryocyte
Thrombocytes (Platelets)
Thrombopoiesis
Proerythroblast (Pronormoblast)
Basophilic erythroblast
Polychromatic erythroblast
Orthochromatic erythroblast (Normoblast)
Polychromatic erythtocyte [1] (Reticulocyte)
Erythrocyte [2] (Red blood cell)
Erythropoiesis
Mast cell
Myeloblast
B. promyelocyte
N. promyelocyte
E. promyelocyte
B. myelocyte
N. myelocyte
E. myelocyte
B. metamyelocyte
N. metamyelocyte
E. metamyelocyte
B. band
N. band
E. band
Basophil
Neutrophil
Eosinophil
Granulopoiesis
Monoblast
Promonocyte
Monocyte
Monocytopoiesis
Macrophage
Myeloid dendritic cell [3]
Lymphoblast
Prolymphocyte
Small lymphocyte [4]
Natural killer cell (Large granular lymphocyte)
B lymphocyte
T lymphocyte
Lymphopoiesis
Plasma cell
Lymphoid dendritic cell [3]

APL DIAGNOSIS

- **Promyelocytes in blood or bone marrow**
- **t(15;17) translocation**
- Results in a **fusion PML-RARα gene**
  - PML-RARα protein blocks differentiation at the promyelocyte stage



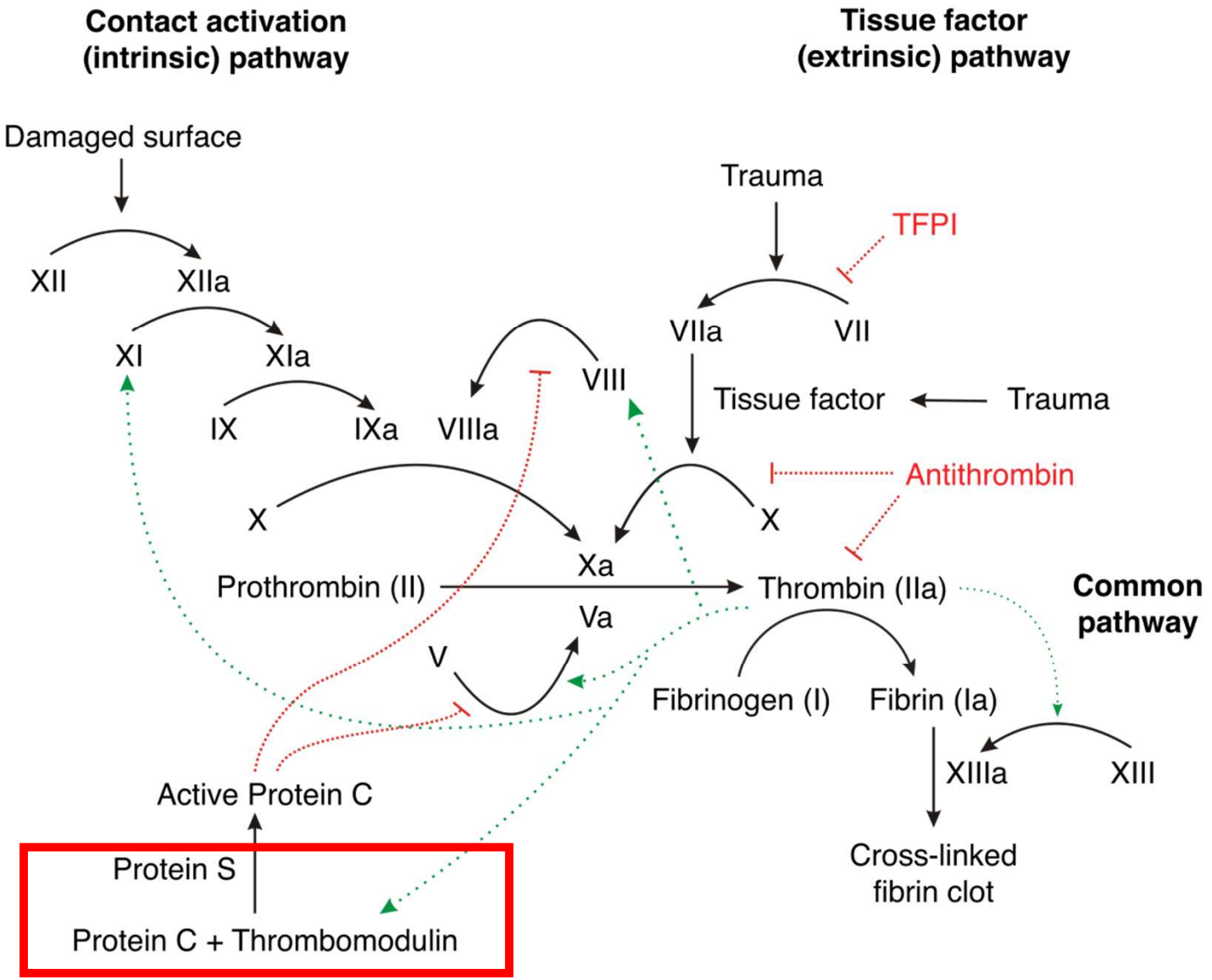


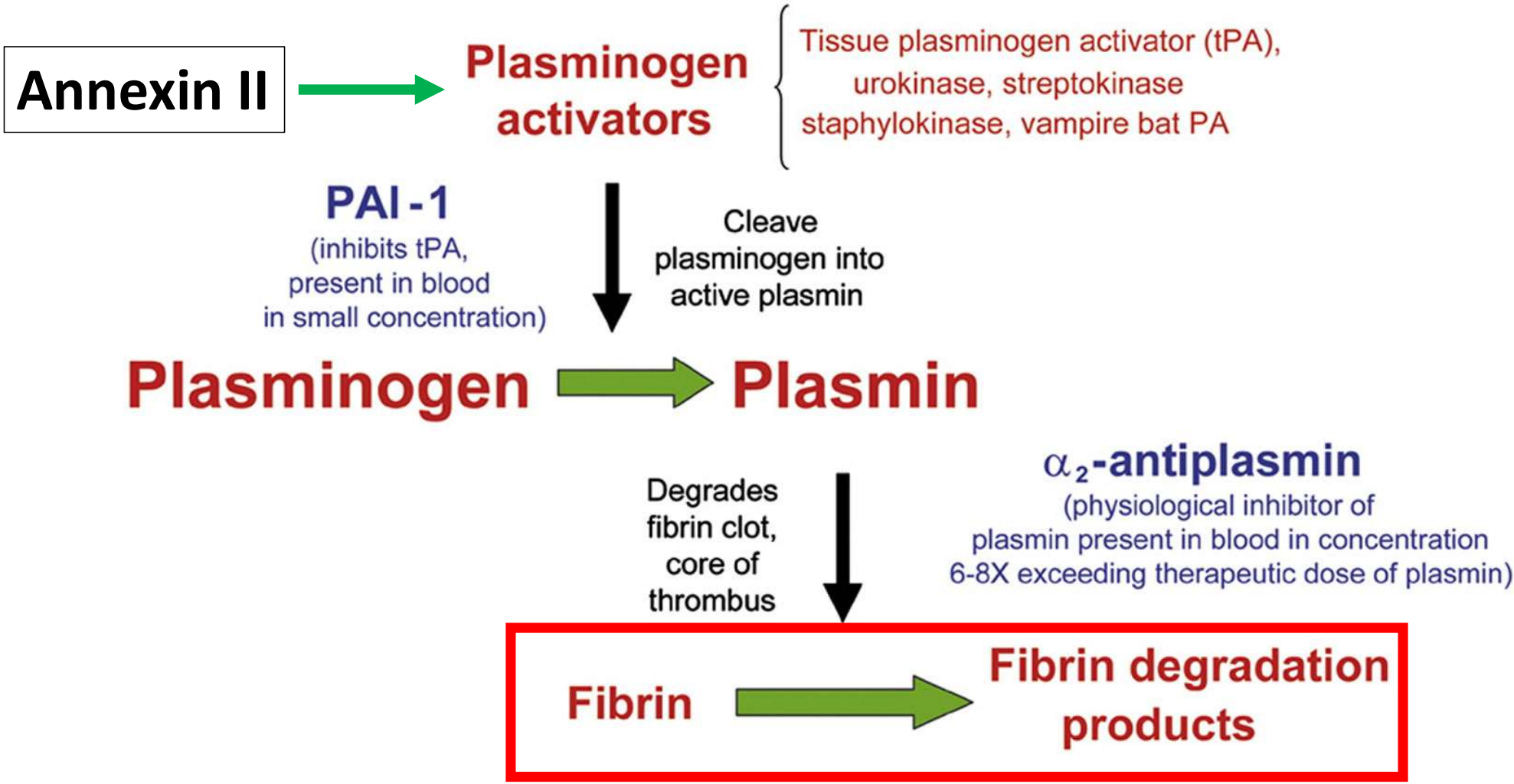
http://medcell.med.yale.edu/systems_cell_biology/haematopoiesis_lab.php

APL PROGNOSIS & COMPLICATIONS

- Prognosis
  - If untreated, short-term survival is VERY POOR; median survival < 1 month
  - APL associated with highest proportion of remission due to modern therapy!

- Complications
  - High risk for DIC and bleeding
  - **Hemorrhage** is one of the most common causes of early mortality
  - If untreated, **up to 40% can have fatal head bleeds**!
  - **Neuro exam** is important!


Contact activation
(intrinsic) pathway
Tissue factor
(extrinsic) pathway
Damaged surface
XII
XIIa
XI
XIa
IX
IXa
VIIIa
VIII
Trauma
TFPI
VIIa
VII
Tissue factor
Trauma
Antithrombin
X
X
Xa
Prothrombin (II)
Thrombin (IIa)
Common
pathway
Va
V
Fibrinogen (I)
Fibrin (Ia)
XIIIa
XIII
Cross-linked
fibrin clot
Active Protein C
Protein S
Protein C + Thrombomodulin


Annexin II
Plasminogen activators
Tissue plasminogen activator (tPA), urokinase, streptokinase staphylokinase, vampire bat PA
PAI-1
(inhibits tPA, present in blood in small concentration)
Cleave plasminogen into active plasmin
Plasminogen
Plasmin
Degrades fibrin clot, core of thrombus
α_2-antiplasmin
(physiological inhibitor of plasmin present in blood in concentration 6-8X exceeding therapeutic dose of plasmin)
Fibrin
Fibrin degradation products

APL TREATMENT

- **All-trans-retinoic acid (ATRA)**
  - ATRA binds to one or more nuclear receptors to **decrease proliferation & induce differentiation of promyelocytes**

- Despite high early mortality, remission rate can be >90 with treatment!
- ATRA as soon as you suspect APL

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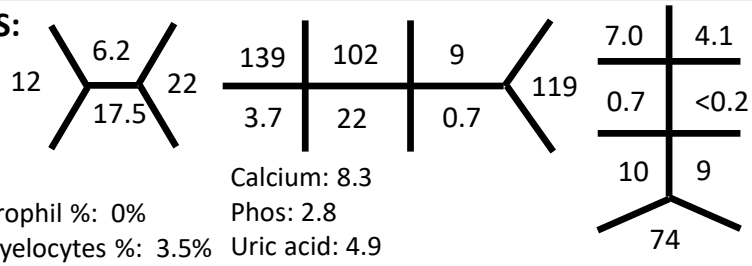

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  - **Atypical promyelocytes** in blood or bone marrow
  - **t(15;17) translocation** & **PML-RARα** gene fusion → blocks myeloid differentiation, cells stuck at promyelocyte stage
  - **DIC & hyperfibrinolysis → hemorrhage** (up to 40% w/ fatal brain bleeds); Do a **neuro exam**!
  - Treat w/ **ATRA**, even if only suspect APL