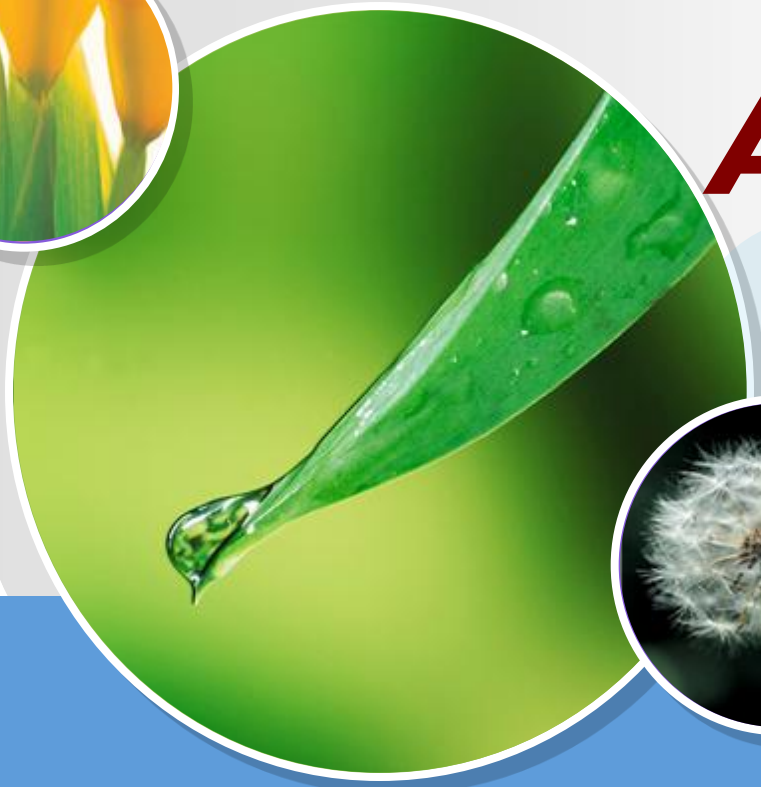
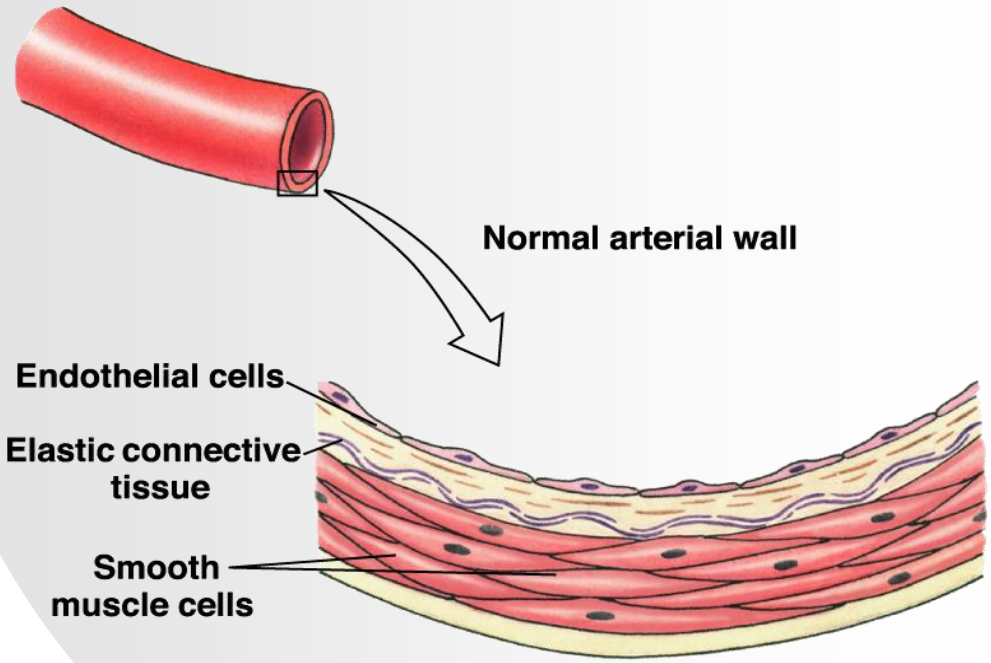


Endothelial Cell & Angiogenesis

Reporter: Yaqi Zhou Date: 11/26/2013

Endothelial Cell

Vascular endothelial cells line the entire circulatory system, from the heart to the smallest capillaries. The arteries and veins have three well-defined layers including intima, media and adventitia, while capillaries consist of little more than a layer of endothelium and occasional connective tissue.



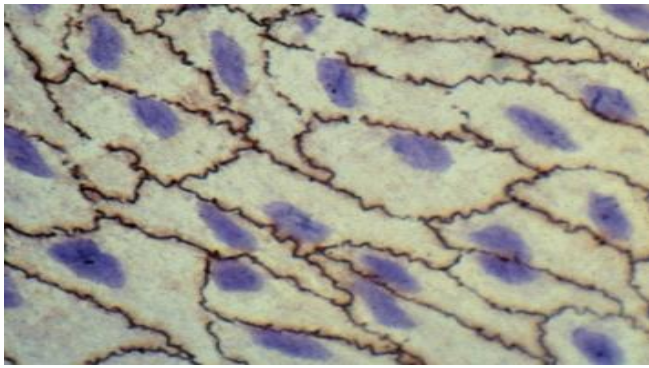


Fig. 1. A surface preparation of arterial endothelium

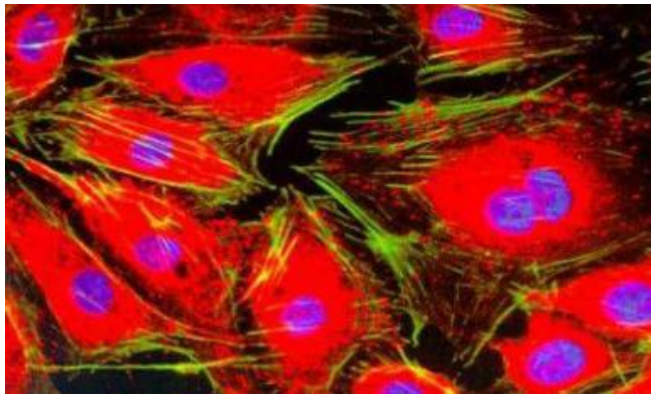


Fig. 2. Endothelial cells under fluorescence microscopy

What's the endothelial cell?

Endothelial Cell

❖ Function

1. Barrier function
2. Endocrine function
   - ① Vasoconstrictors & Vasodilators
   - ② Anticoagulant factors & Procoagulant factors
   - ③ Adhesion molecules
   - ④ Inflammatory mediators
3. Vasoconstriction and Vasodilation
4. Blood clotting (thrombosis & fibrinolysis)
5. Inflammation
6. Formation of new blood vessels (angiogenesis)

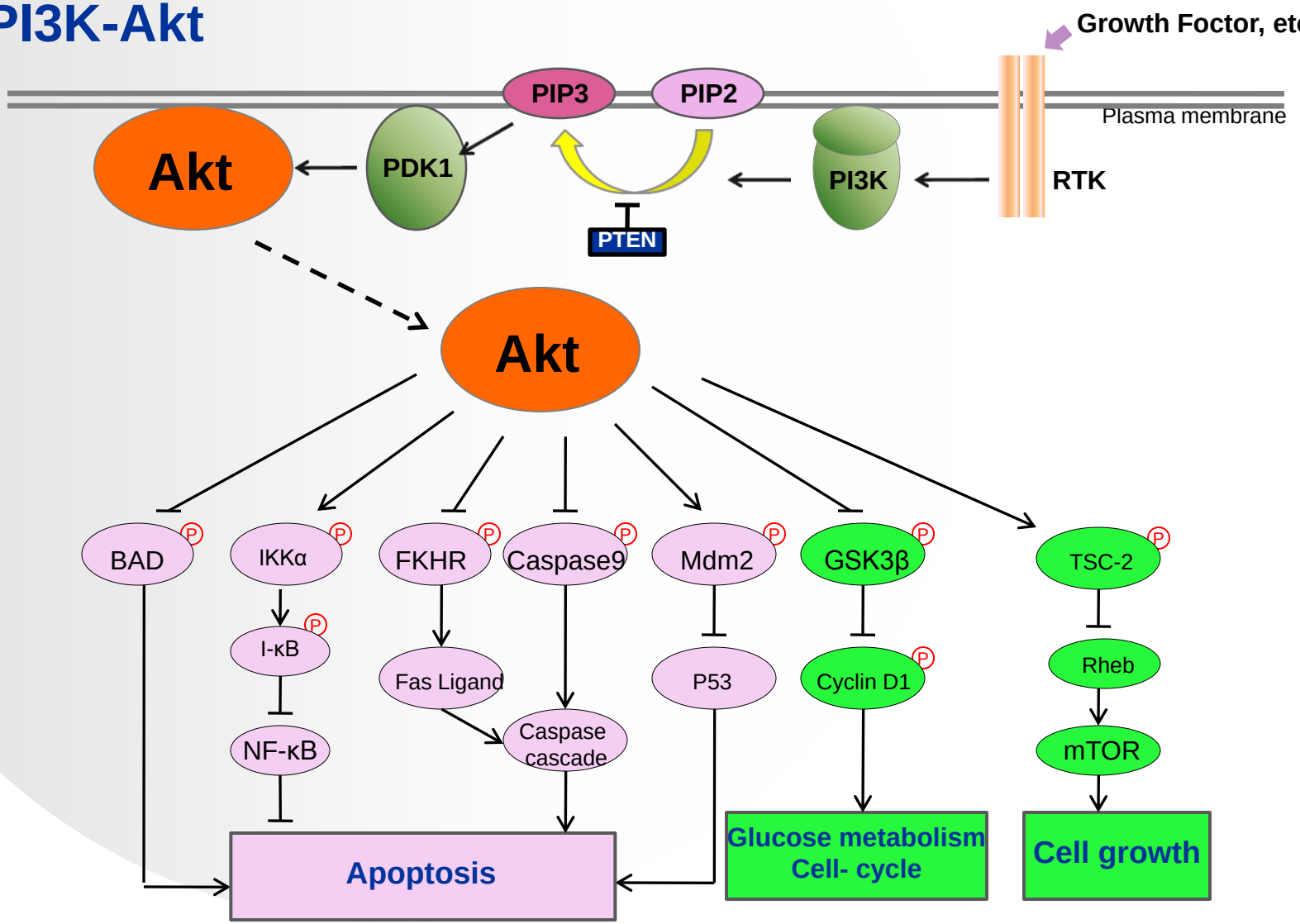
❖ Surface marker

Normal EC: CD34, CD31(PECAM-1), vWF

Activated EC: AMs(P-selectin, E-selectin, ICAM-1, VCAM-1)
ET-1, ACE, t-PA and PAI-1, PAF

EC Proliferation

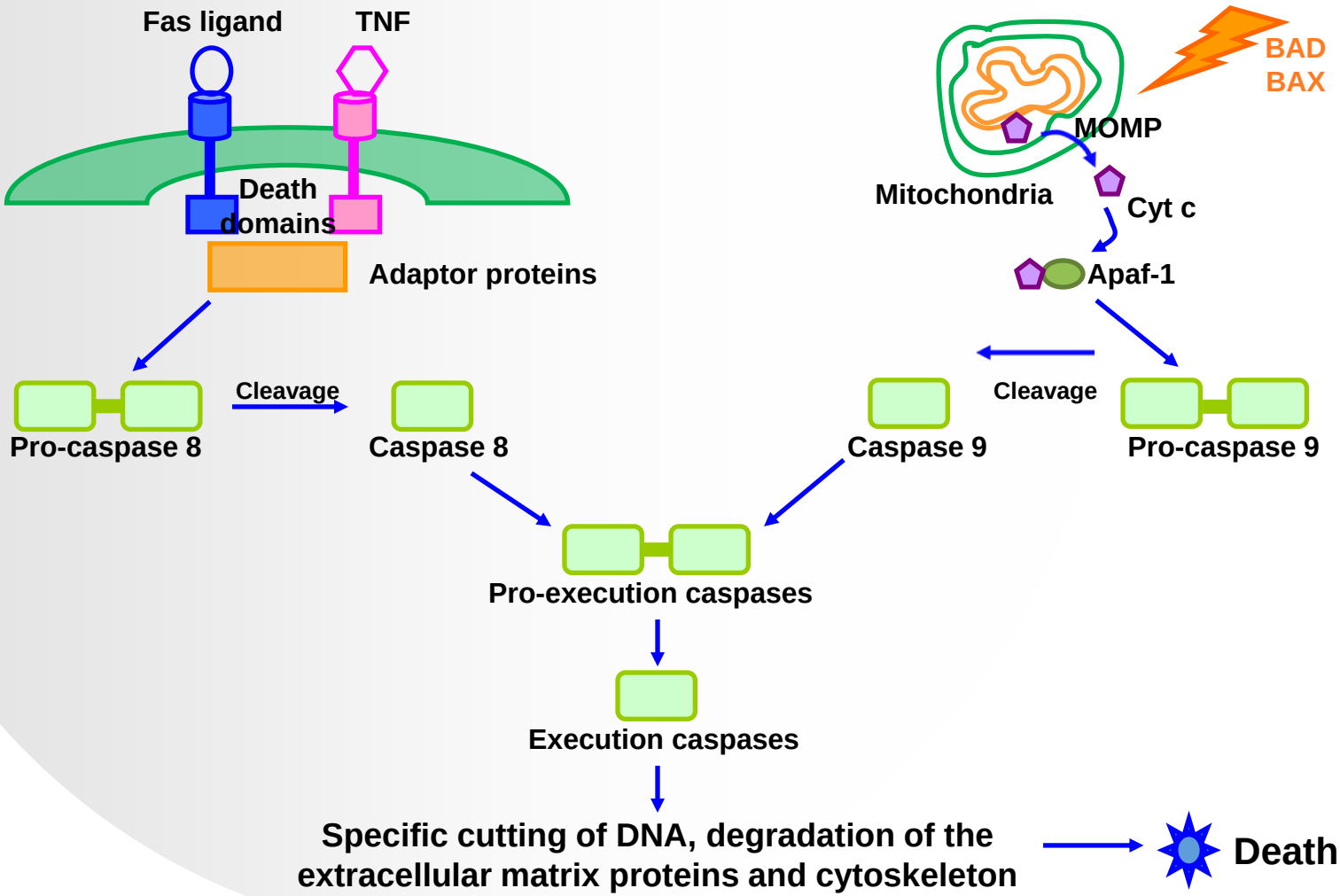
❖ PI3K-Akt



EC Apoptosis

❖ Extrinsic pathway (physiological)

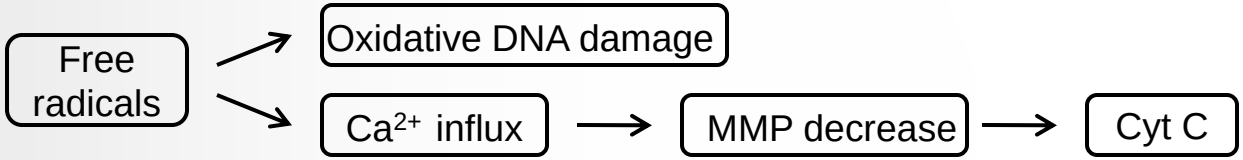
❖ Intrinsic pathway (damage)



EC Apoptosis

❖ Apoptosis inducer

1. Free radicals (ROS, NOS)



2. High glucose

◆ Mitochondrial electron transport chain → O_2^{2-}

3. Ang Ⅱ

◆Release of ox-LDL by mitochondria
◆ICAM-1

4. Ox-LDL

◆ROS carrier
◆LOX-1

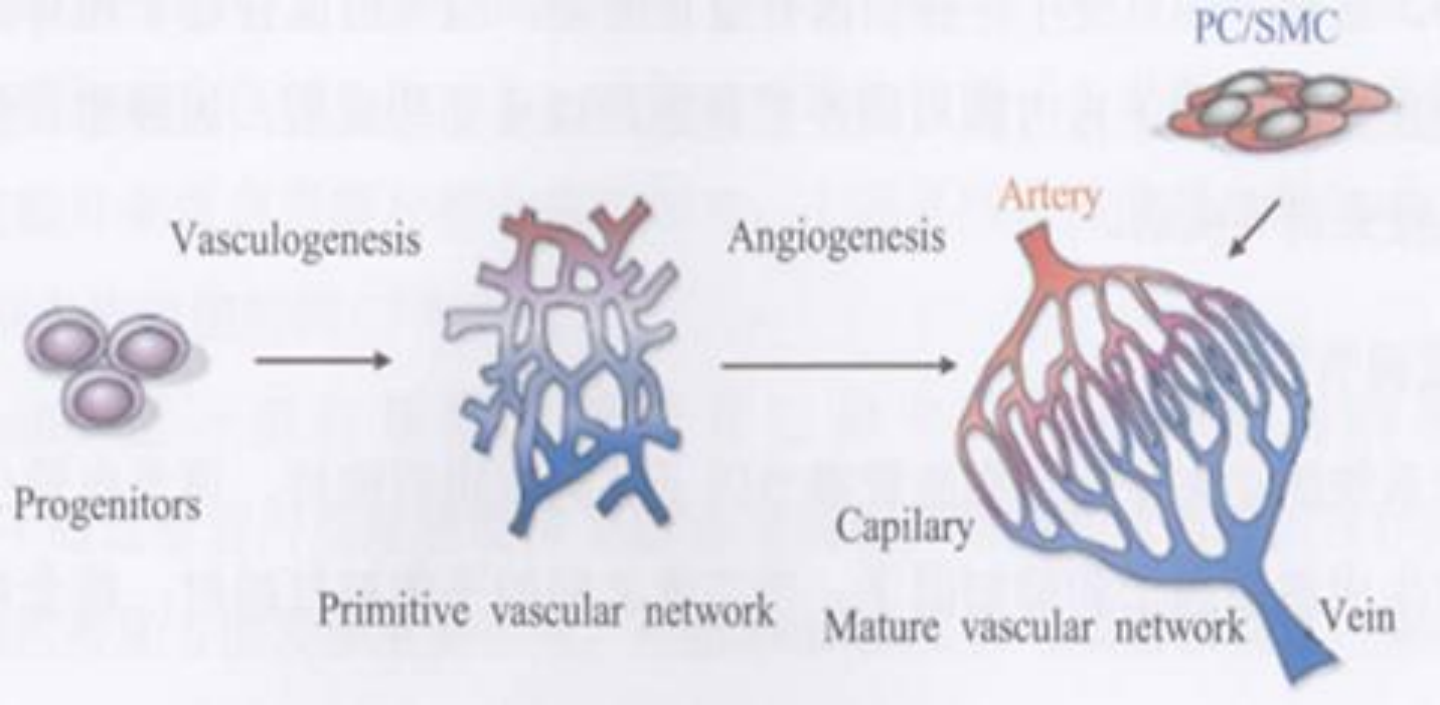
5. TGF-β

◆TβR-Ⅰ and TβR-Ⅱ

EC apoptosis is closely related to angiogenesis.

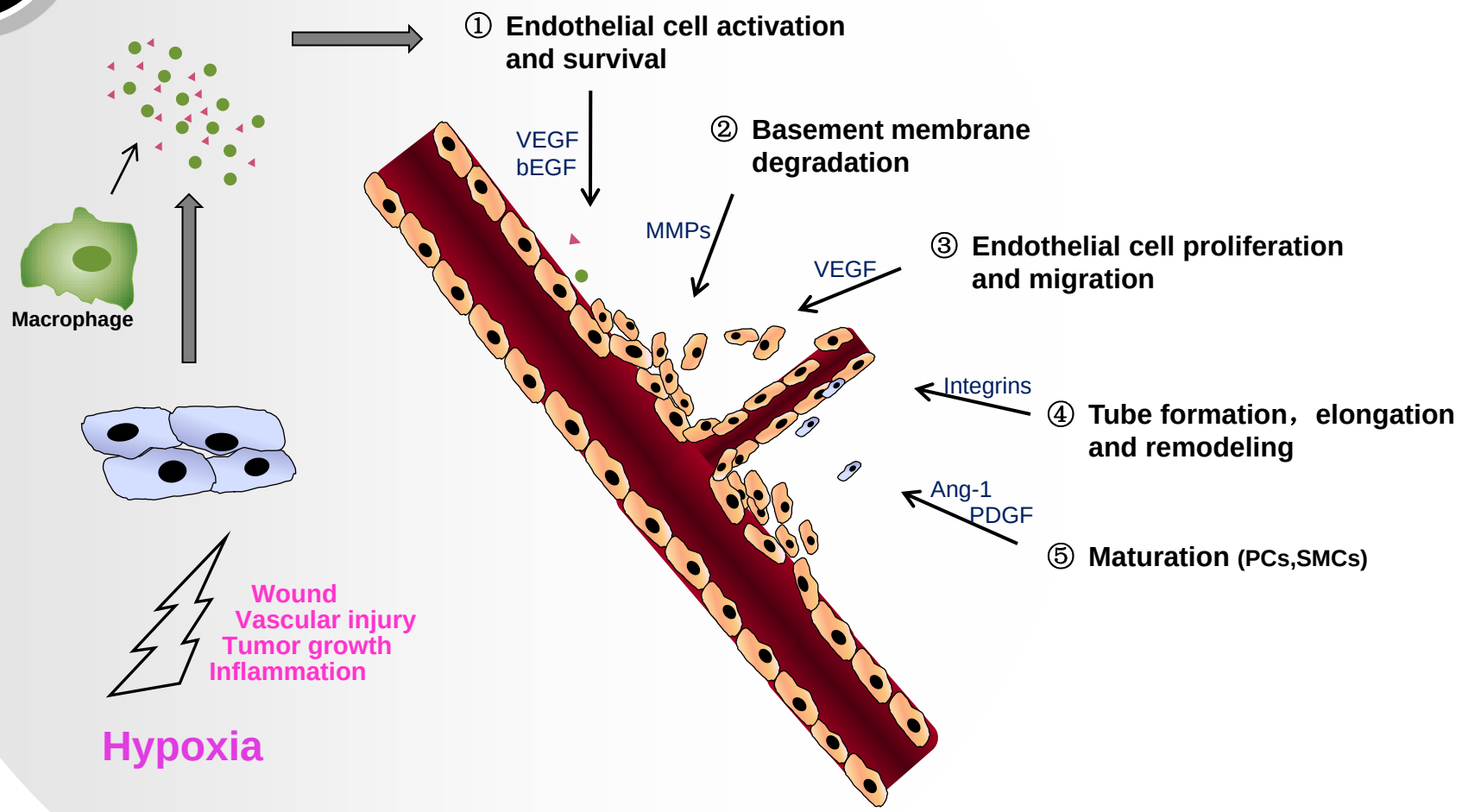
Angiogenesis

Angiogenesis is the physiological process through which new blood vessels form from pre-existing vessels. There are two main types: sprouting angiogenesis and intussusceptive angiogenesis. The former is the most classic way.



Vasculogenesis ≠ Angiogenesis

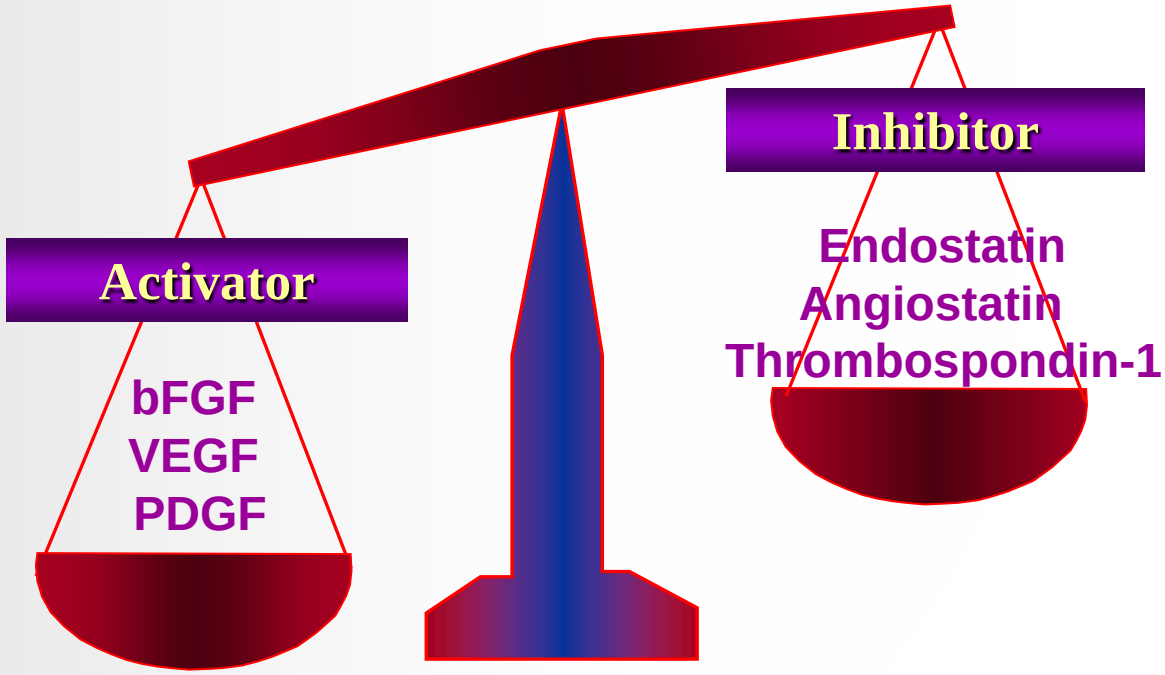
The Angiogenic Process



The proliferation and apoptosis of ECs play key roles in angiogenesis.

Regulation Mechanism

Angiogenesis is a complex process which controlled and regulated by pro-angiogenic and anti-angiogenic factors. If the balance between them was destroyed under certain condition, it will result in vascular degeneration or angiogenesis.



Within a disease orientation, such as tumor, the pro-angiogenic factors show a clear advantage, which then lead to angiogenesis.

Regulation Mechanism

❖ Regulatory factors in angiogenesis

	Factor	Function/Role
Activator	VEGF	Endothelia cell activation, proliferation and migration
	bFGF	Endothelia cell differentiation, proliferation and migration
	PDGF	Cell growth and division, pericyte and smooth muscle cell recruitment and proliferation Induce endothelia cell to secrete MMPs
	Angiopoietin	Vessel maintenance, growth and stabilization
Inhibitor	Endostatin	Inhibit endothelial cell migration by combining with $\alpha_V\beta1$ Induce endothelial cell apoptosis
	Angiostatin	Inhibit endothelial cell proliferation and migration Induce endothelial cell apoptosis
	Thrombospondin-1	Block endothelial cell proliferation, migration and lumen formation
	Platelet factor-4	Inhibit the combination of bFGF with its receptor

VEGF: vascular endothelial growth factor; bFGF: basic fibroblast growth factor; PDGF, platelet-derived growth factor ; MMP, matrix metalloproteinase

VEGF

❖ Member

- In mammals: VEGF-A, VEGF-B, VEGF-C, VEGF-D, PLGF
- Structurally related proteins: VEGF-E, VEGF-F

❖ Receptor

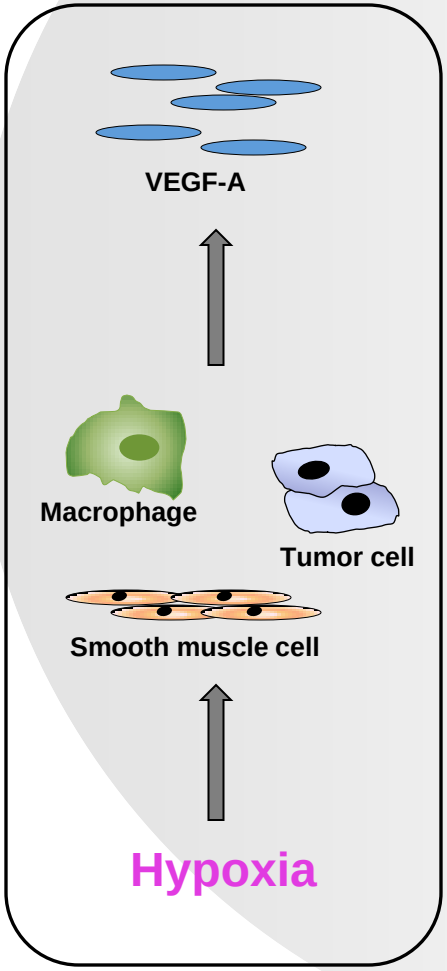
1. Receptor Tyrosine Kinases(RTKs)

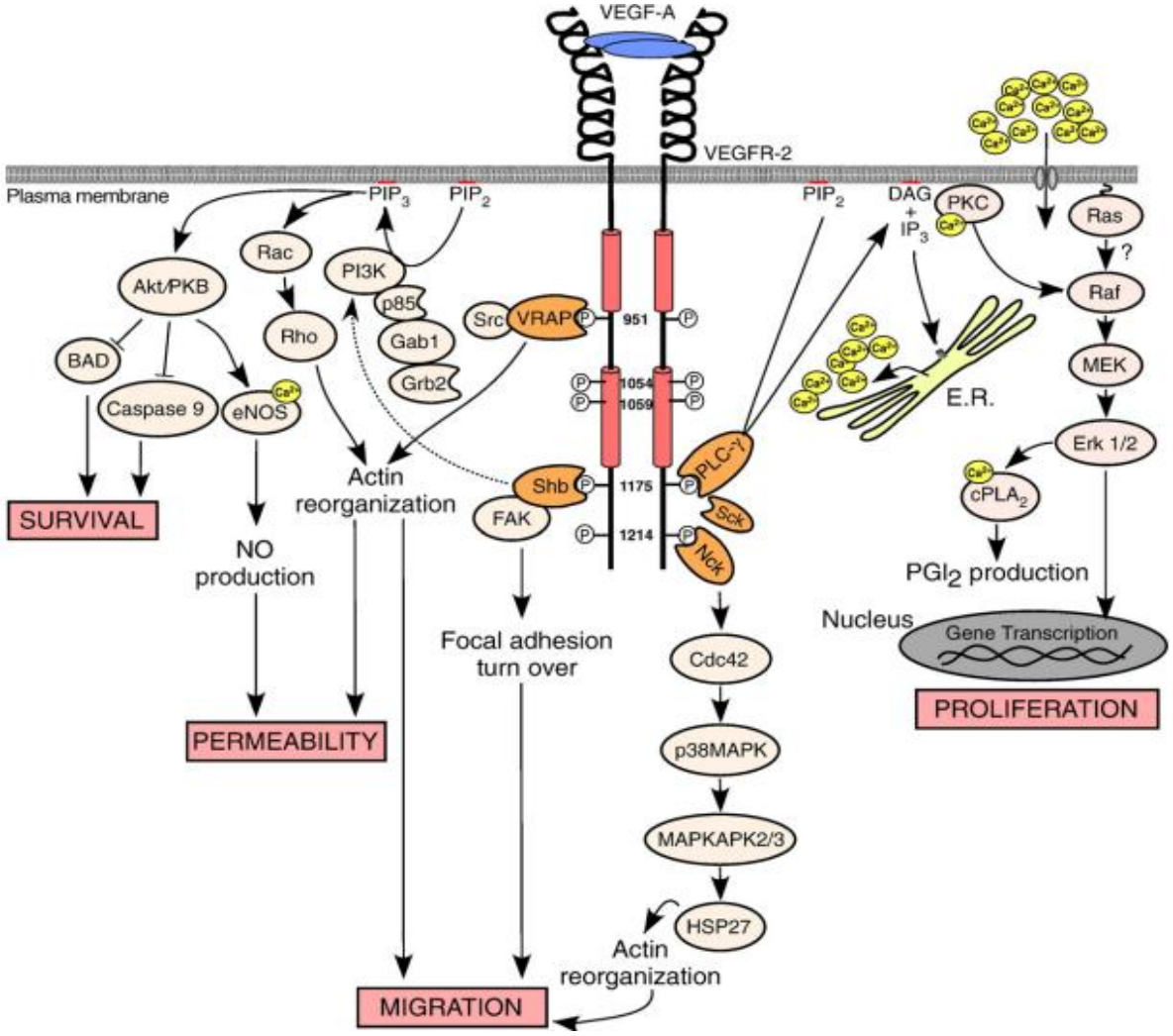
Receptor	Ligand	Physiological effect	Cellular expression
VEGFR-1(Flt-1)	VEGF-A, VEGF-B, PLGF	Haematopoiesis	haematopoietic stem cells, monocytes, macrophages, vascular endothelial cells
VEGFR-2(Flk-1/KDR)	VEGF-A, VEGF-C, VEGF-D, VEGF-E	Vasculogenesis Angiogenesis	vascular endothelial cells, lymphatic endothelial cells
VEGFR-3(Flt-4)	VEGF-C, VEGF-D	Lymphangiogenesis	lymphatic endothelial cells

2. Neuropilins(NRP)

VEGF-A/VEGFR-2 signalling is the major pathway that activates angiogenesis by inducing the proliferation, survival and migration of ECs, and also by increasing endothelial permeability.

VEGFR-2 signaling pathway





K. Holmes et al. Cellular Signalling 19 (2007) 2003-2012

Thank You !