Endothelium, smooth muscle, vessels

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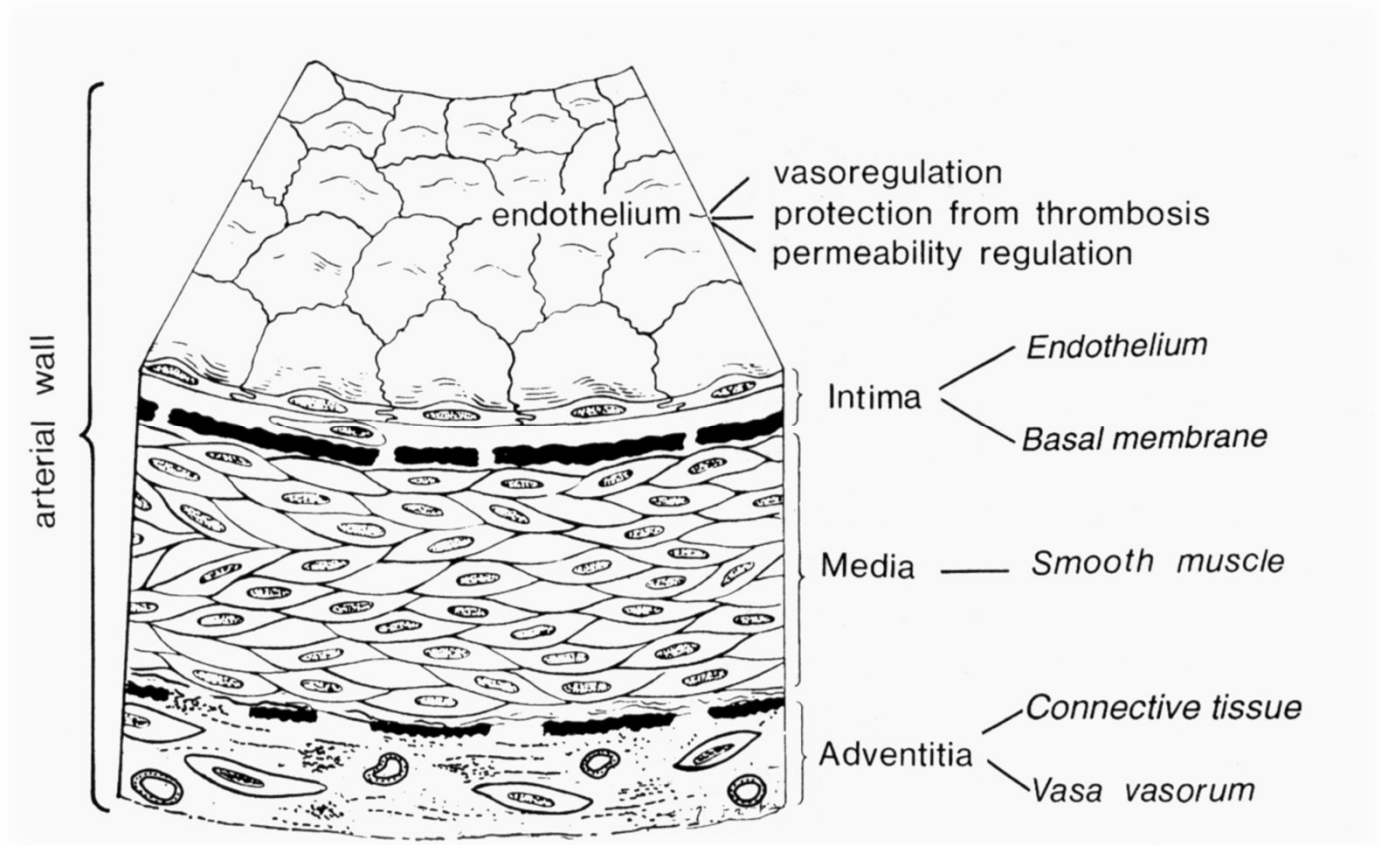
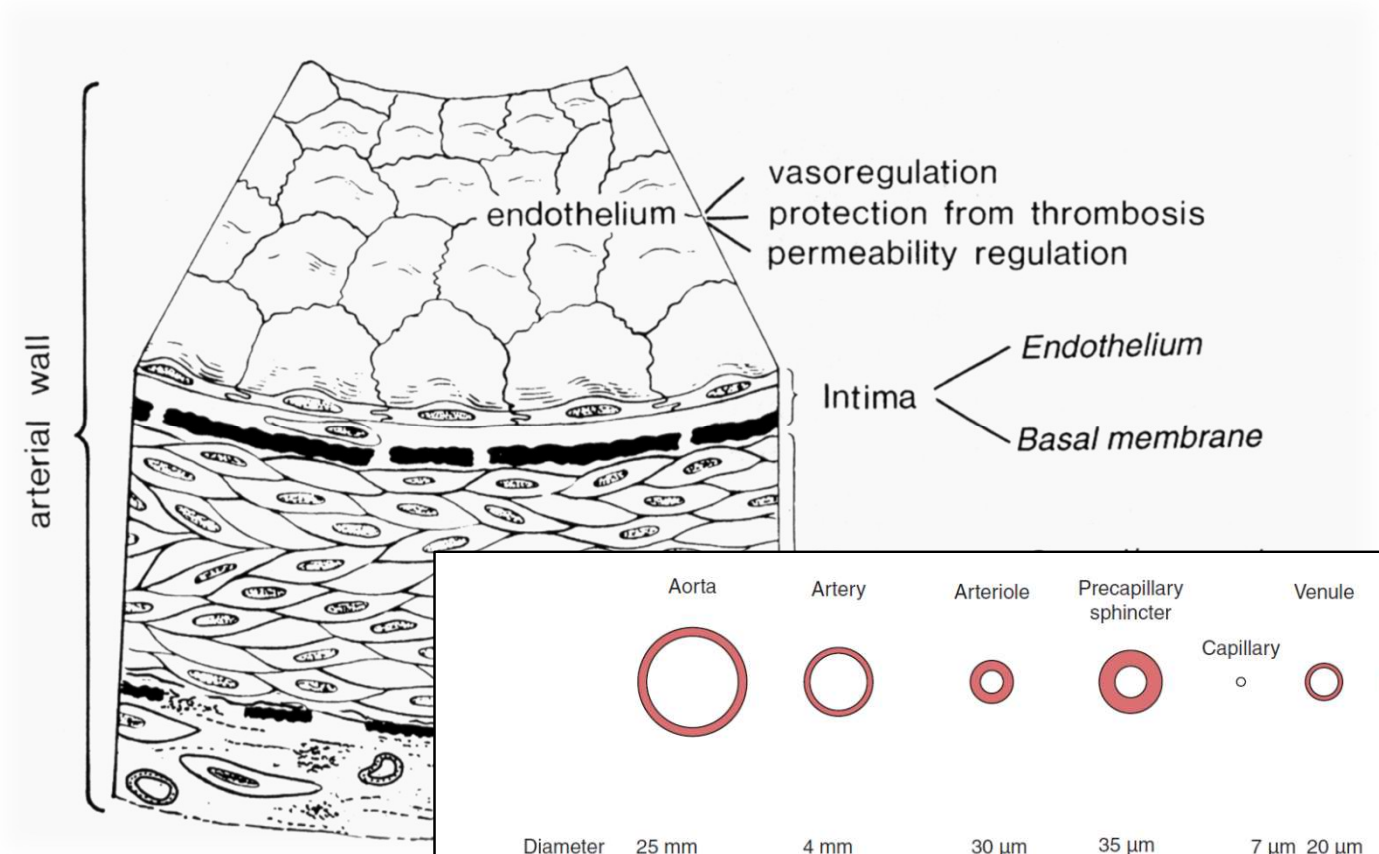
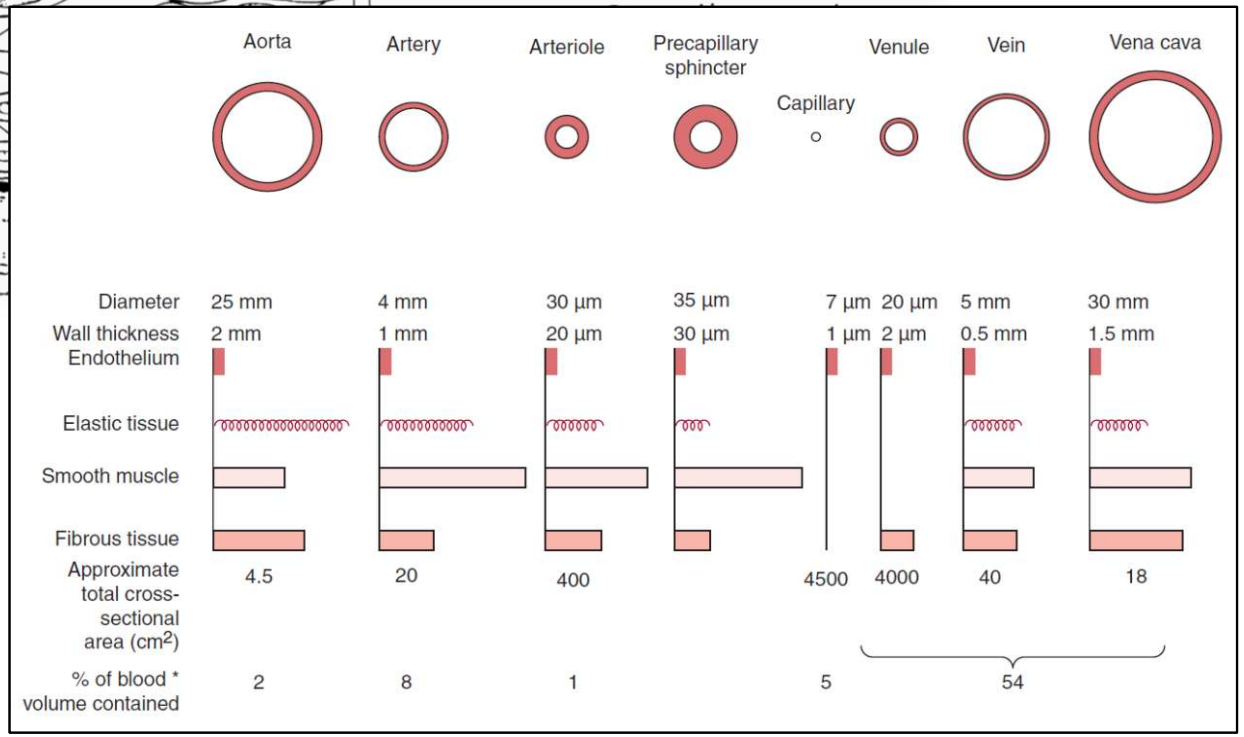
Vessels


arterial wall
endothelium
vasoregulation
protection from thrombosis
permeability regulation
Intima
Endothelium
Basal membrane
Media
Smooth muscle
Adventitia
Connective tissue
Vasa vasorum

Vessels - endothelium as an organ





Endothelial cells:

~ 1-6*10^{13} cells in adults

weight ~ 1 kg

surface area ~ 1-7 m^2

Functions of vascular endothelium

Release of vasodilator agents

Nitric oxide (EDRF)
Prostacyclin (PGI_2)
Bradikynin
EDHF (endothelium derived hyperpolarizing factor)

Release of vasocontrictor agents

Endothelins

Protection of vascular smooth muscle

vasoconstrictory → to vasodilatory stimuli
(acetylcholine and serotonin)

Antiaggregatory effect

Acts via NO (nitric oxide) and PGI_2 (thrombocyte activation ↓)

Functions of vascular endothelium

Prevention of coagulation

Thromboresistant surface (heparan sulfate – antithrombin cofactor)

Immune and barrier function

Supply of antigens to immunocompetent cells

Secretion of interleukin I, E-selectin (rolling)

Enzymatic activity

Angiotensin-converting enzyme (ACE) and ACE2

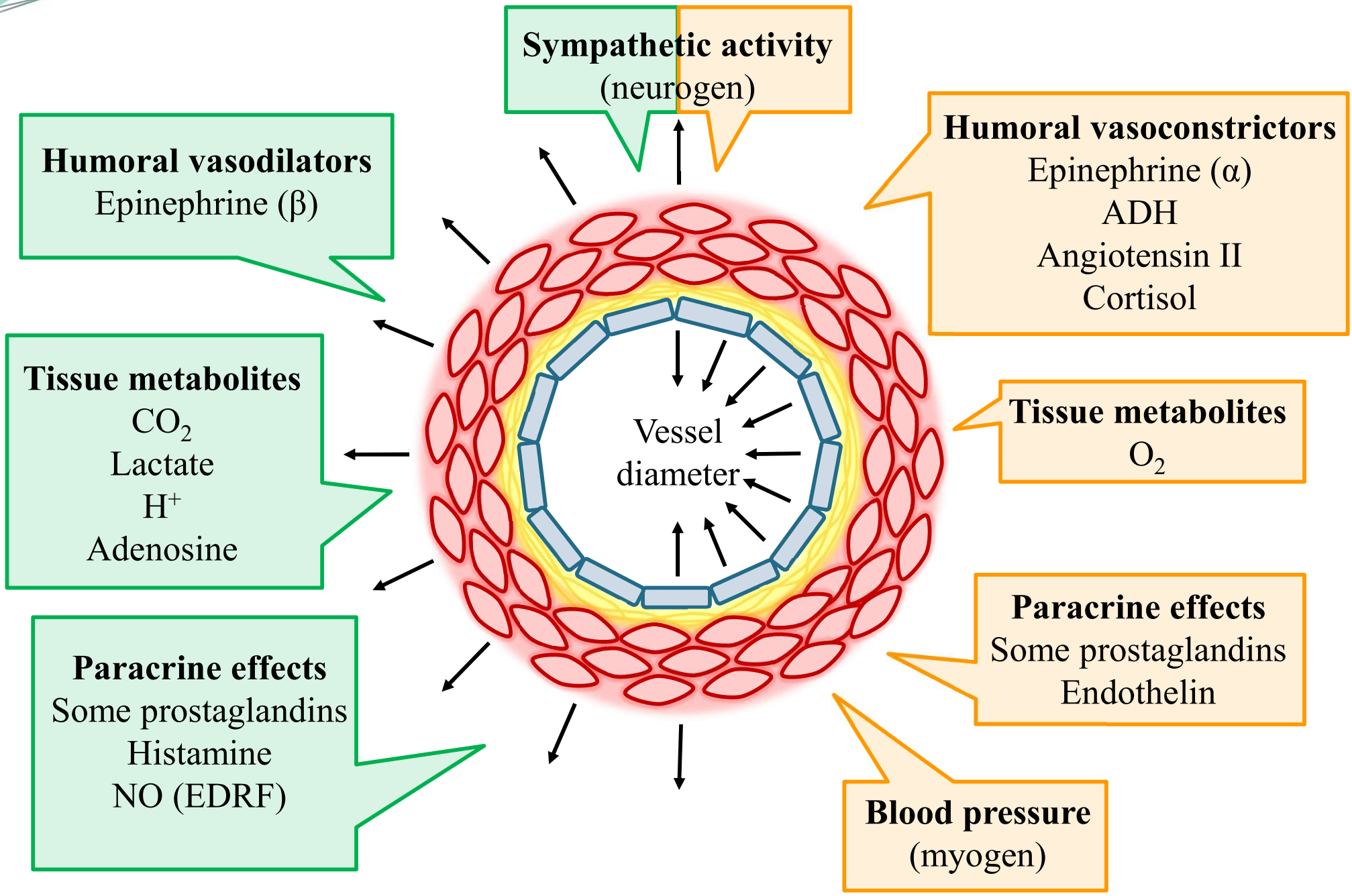
Carbonic anhydrase (large amounts in lung endothelium)

Growth signal to vascular smooth muscle

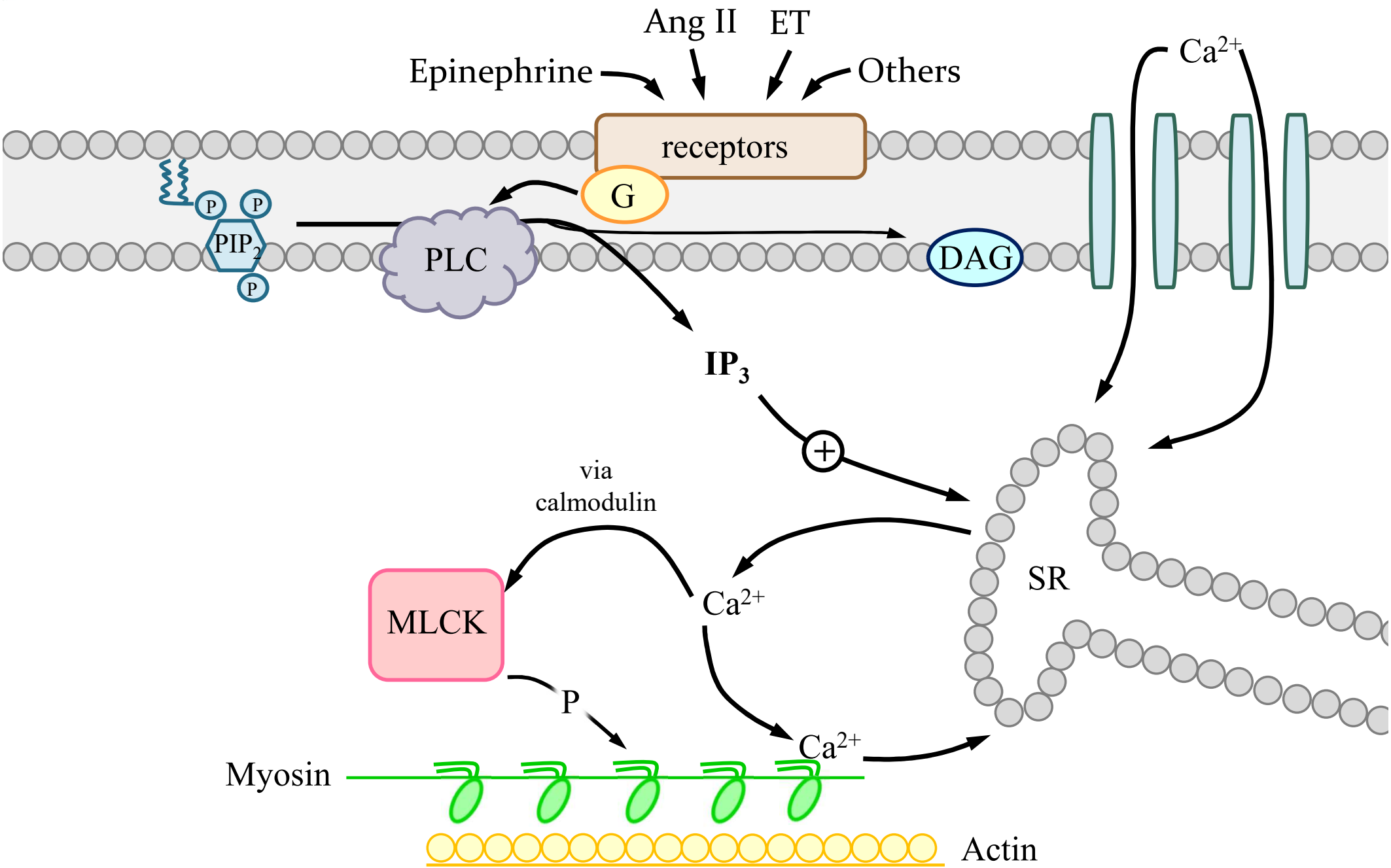
VEGF (vascular endothelial growth factor), angiopoietin

Heparin-like inhibitors of growth

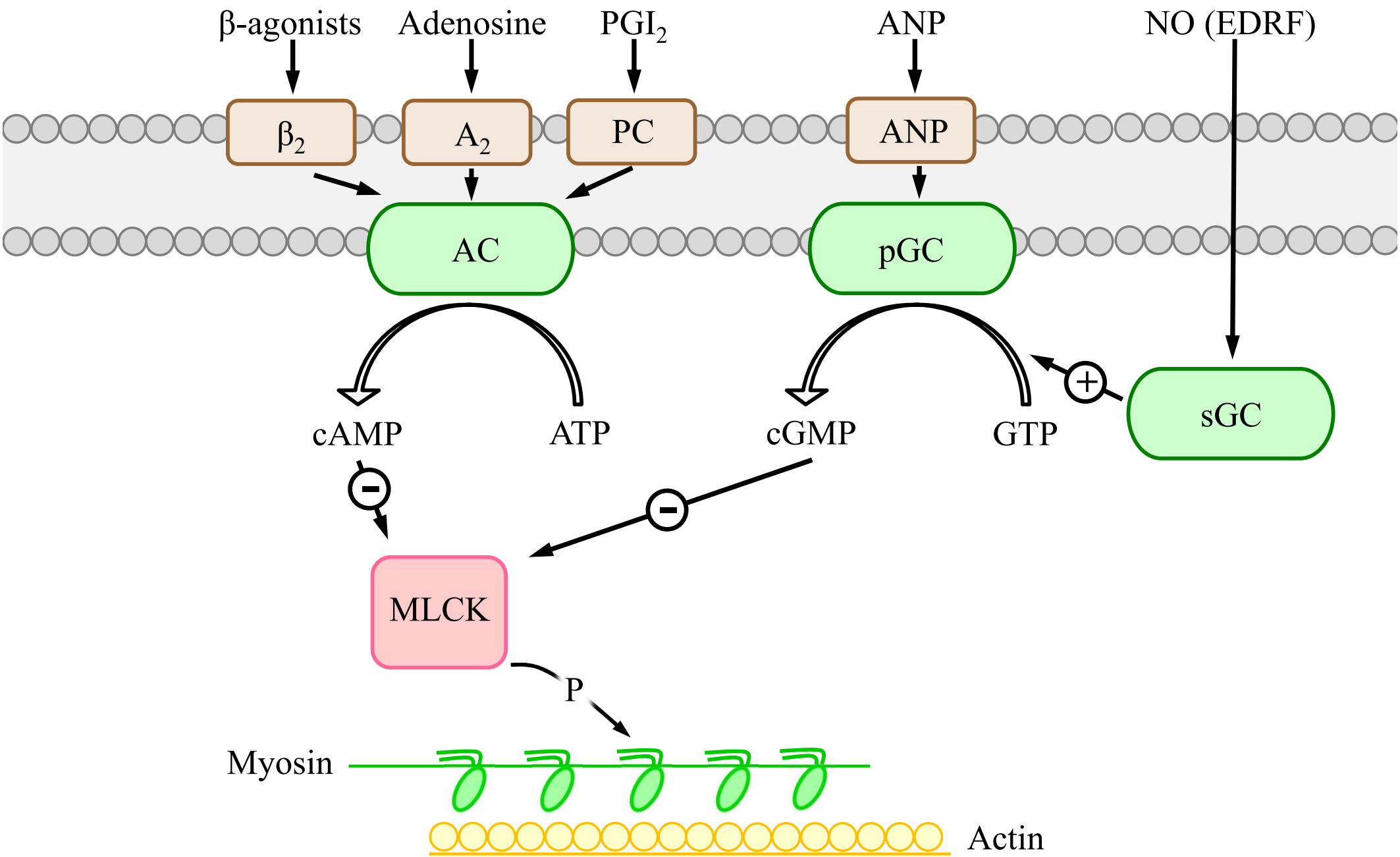
Mediators of vascular control



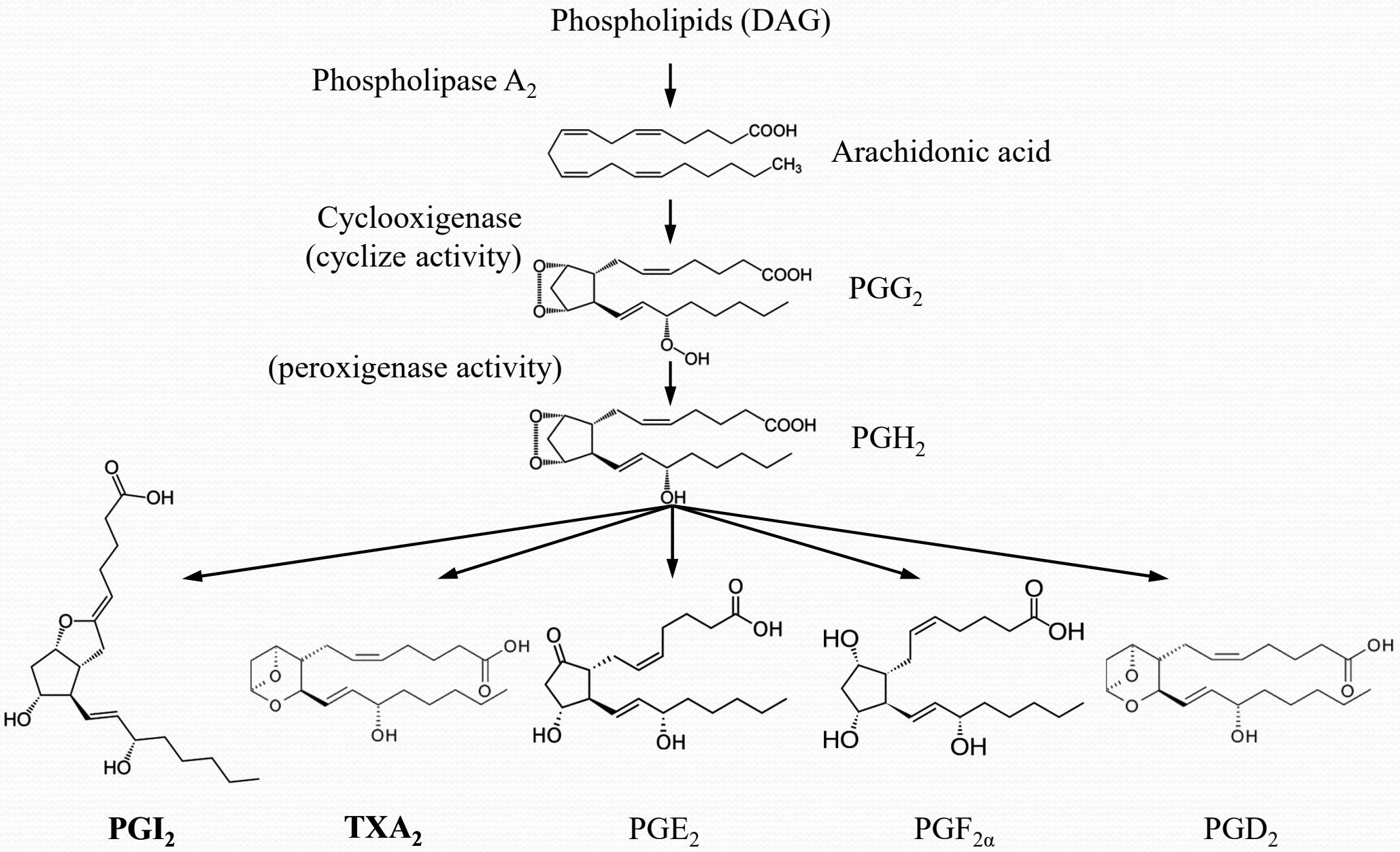
Vasoconstrictor mechanisms



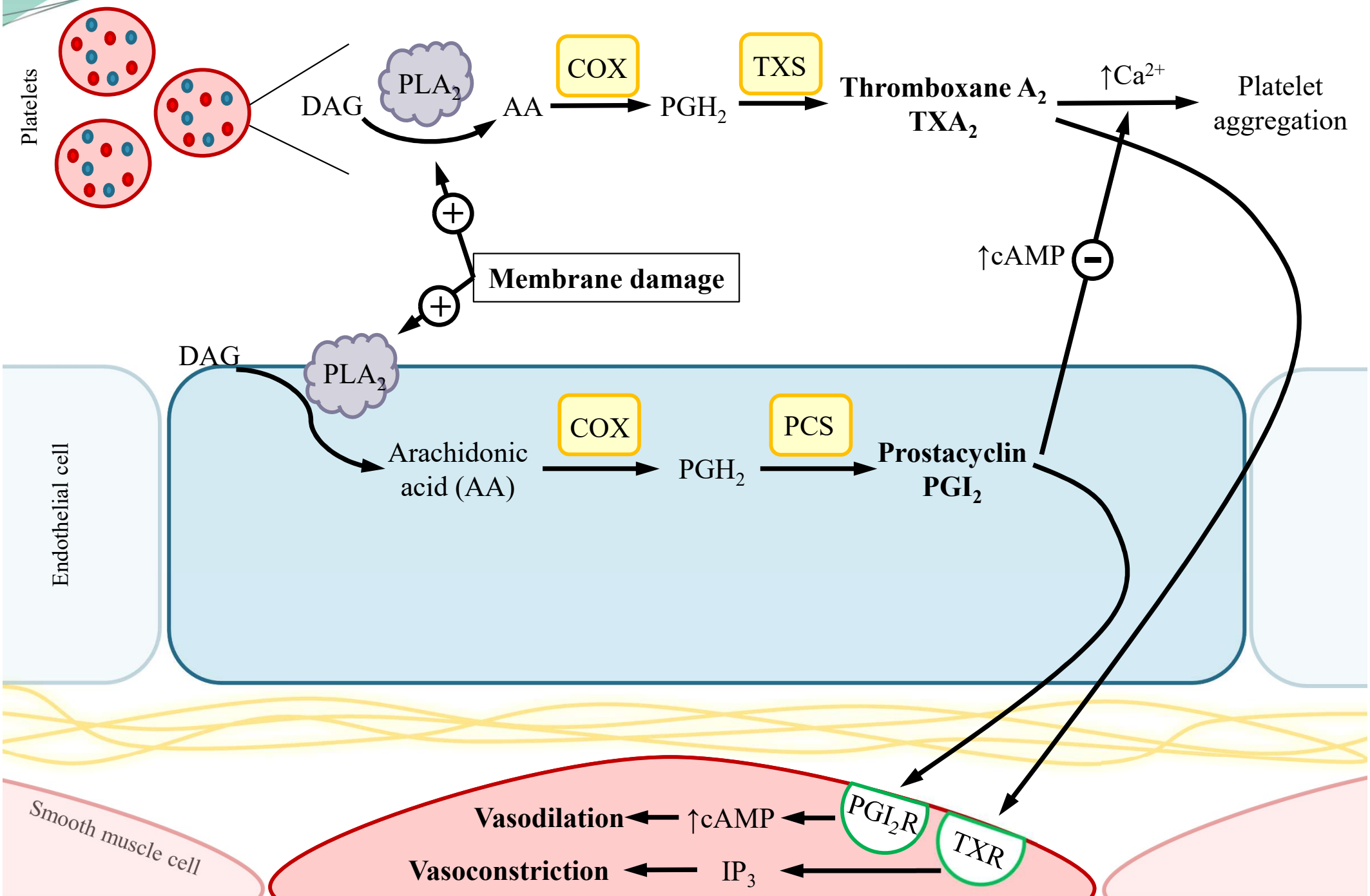
Vasodilator mechanisms



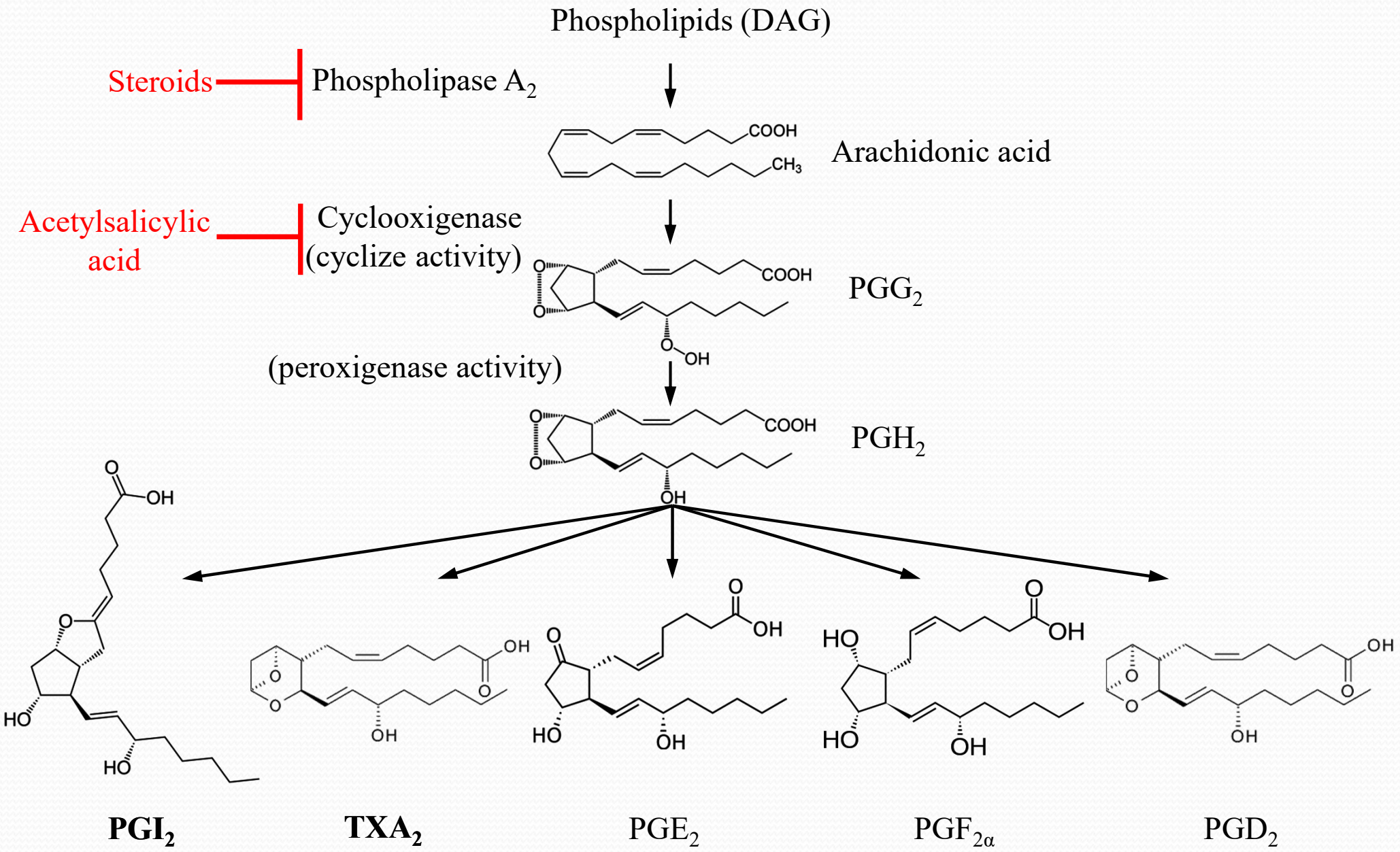
Prostaglandins



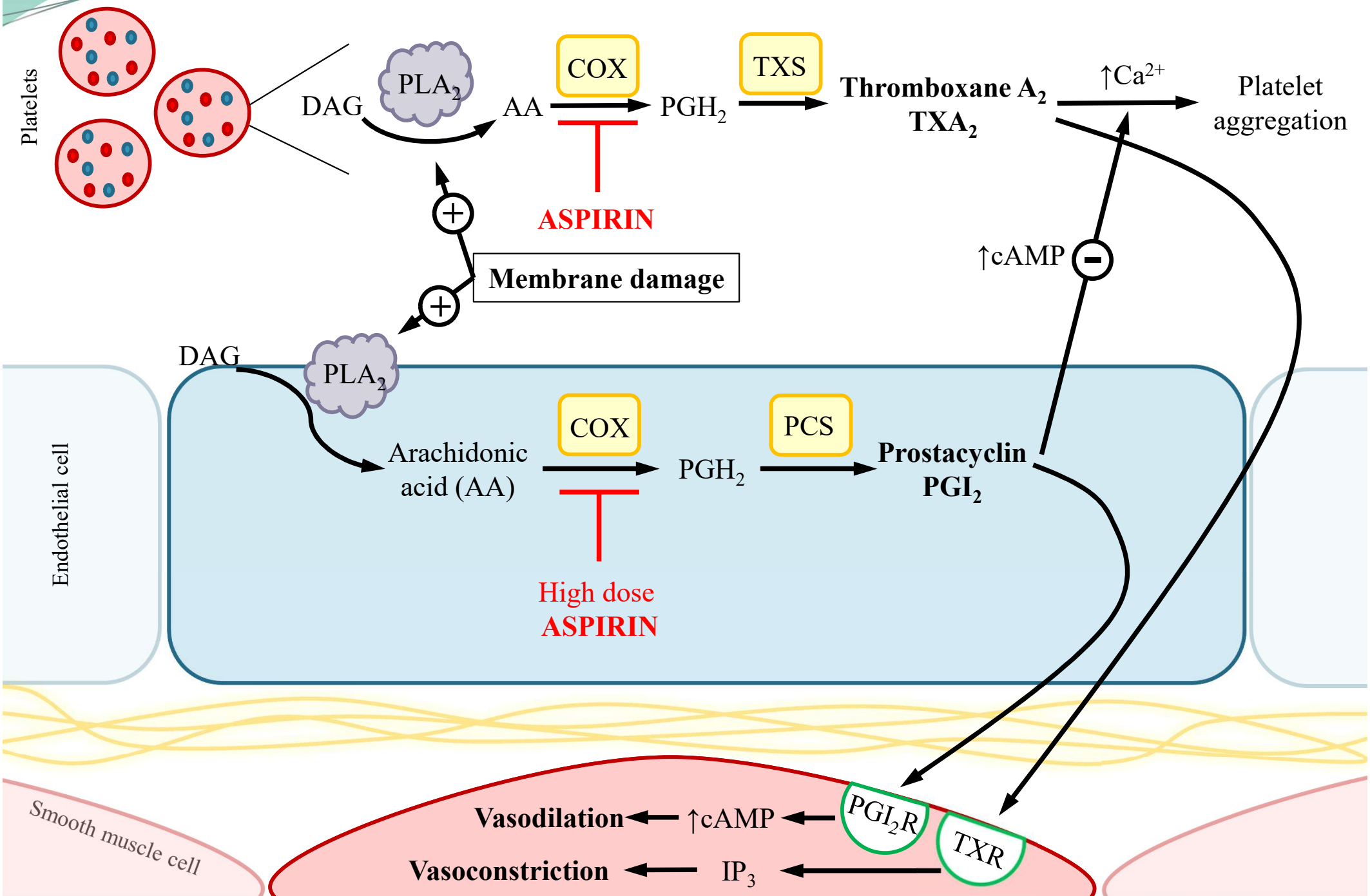
Prostaglandins



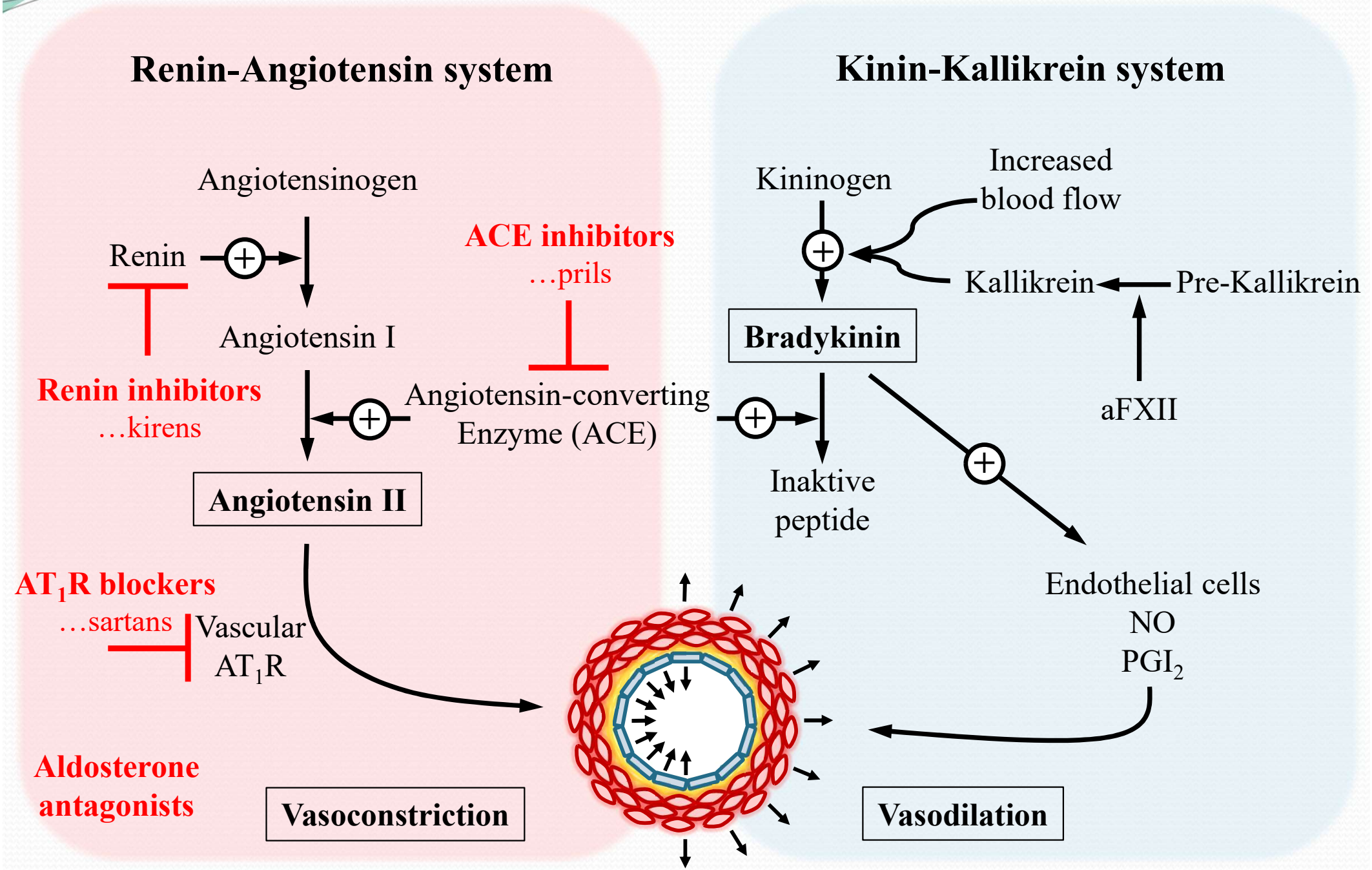
Prostaglandins



Prostaglandins



Angiotensin and Bradykinin



Nitric oxide (NO)

Chemical characteristics: short lived (half-life: seconds), lipophilic, freely diffusible, soluble gas

Synthesis of NO: (NOS = **N**itric **O**xide **S**ynthase)

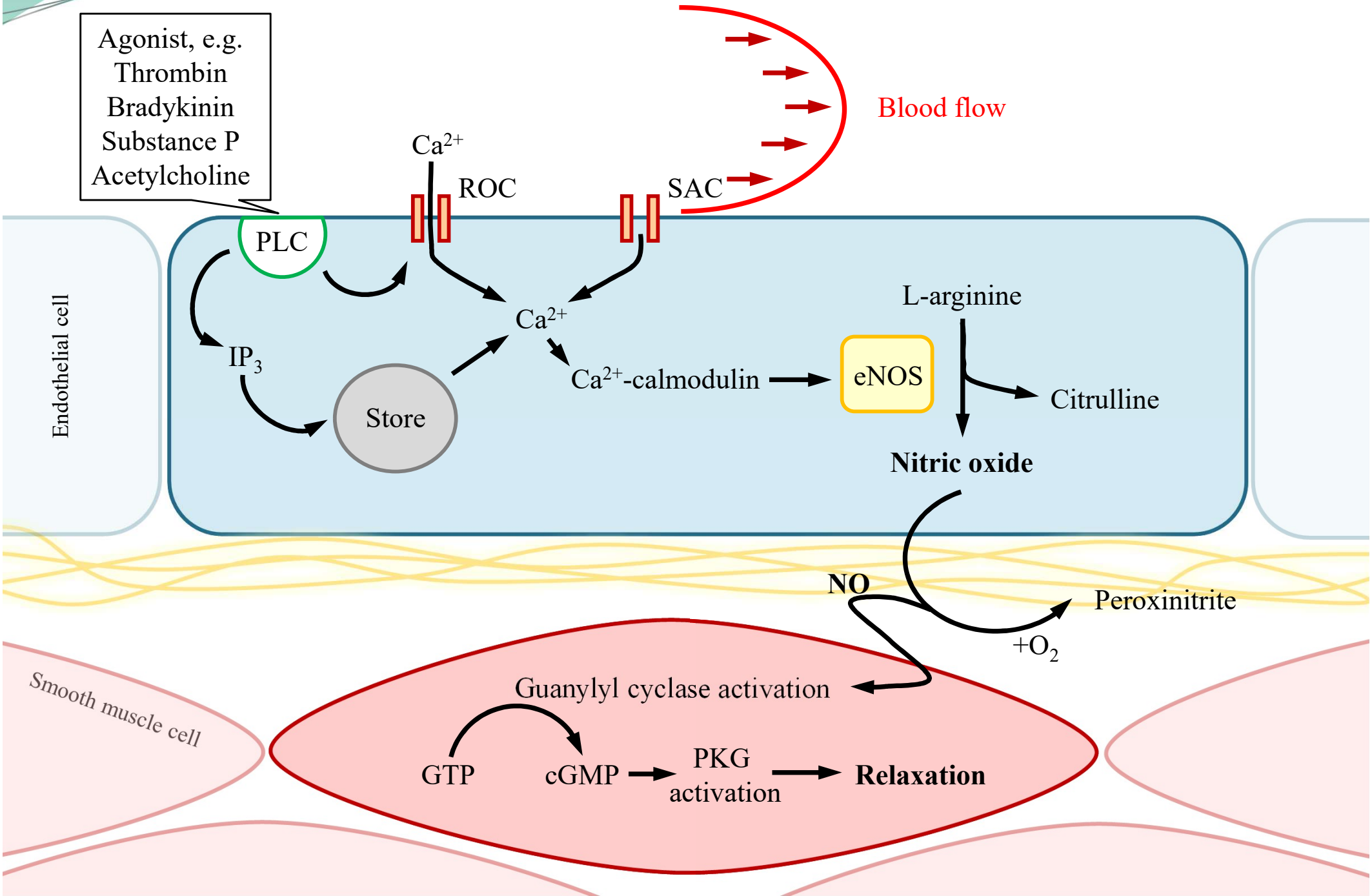
nNOS = NOS I (in nervous system)
iNOS = NOS II (inducible [macrophages, endothelium])
eNOS = NOS III (endothelial or constitutive form), upregulated by oestrogens, insulin and chronic increases in wall shear stress

Chemical reaction:

$$\textbf{L-arginine} + NADPH + H^+ + O_2 \rightarrow Citrulline + \textbf{NO} + NADP^+$$

Cofactors: NADPH, tetrahydrobiopterine

Intercellular communications



Agonists of NO production

1. Humoral agonists of <u>eNOS</u> increase $[Ca^{2+}]_i$:

acetylcholine (M_3-receptor), bradykinin, thrombin, substance P, vasoactive intestinal polypeptide (VIP), insulin, histamine

2. Mechanical agonists (<u>wall shear stress</u>):

- flow induced vasodilatation
- mechanosensitive ion channels

3. Inflammation and endotoxin shock (<u>iNOS</u>):

in inflammation:- in reaction to interleukins (e.g. IL-1) and TNF
- contributes to reddening (rubor) and local heat (calor) in inflammation

in shock: - lipopolysacharide induced shock
- direct reaction to TNFα from macrophyages
- results <u>too much NO</u> → general vasodilation

4. Organic nitrates: - glyceryl trinitrate
- isosorbid mononitrate
- sodium nitroprusside

EDHF (endothelium derived hyperpolarizing factor)

Soluble secretion of EDHF during Ach/ bradykinin evoked SM hyperpolarization/ relaxation when NO and PGI_2 productions blocked.

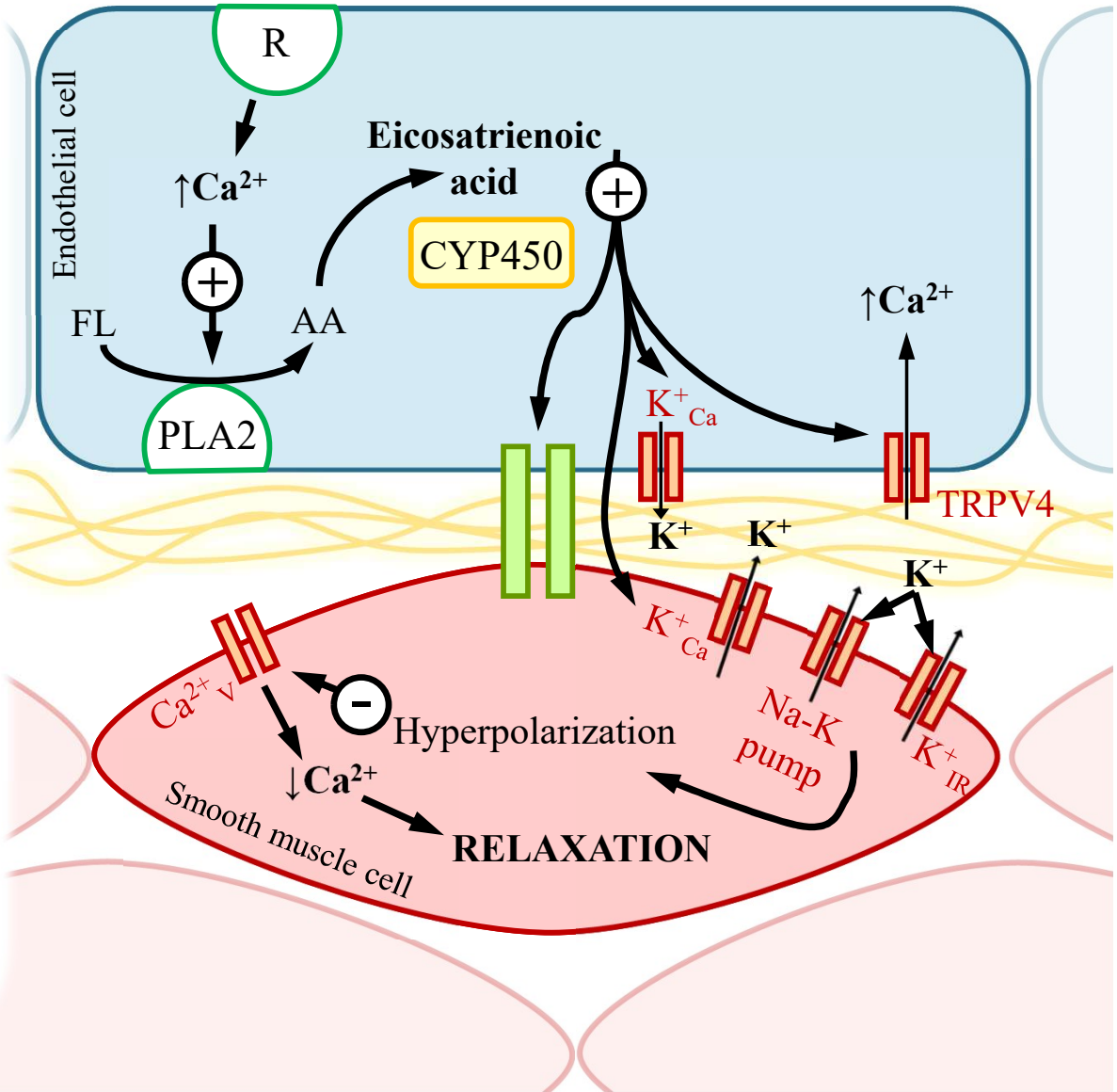
Chemical structure is uncertain: CYP450 product, K^+, H_2O_2 …

Half-life of action ~70 sec

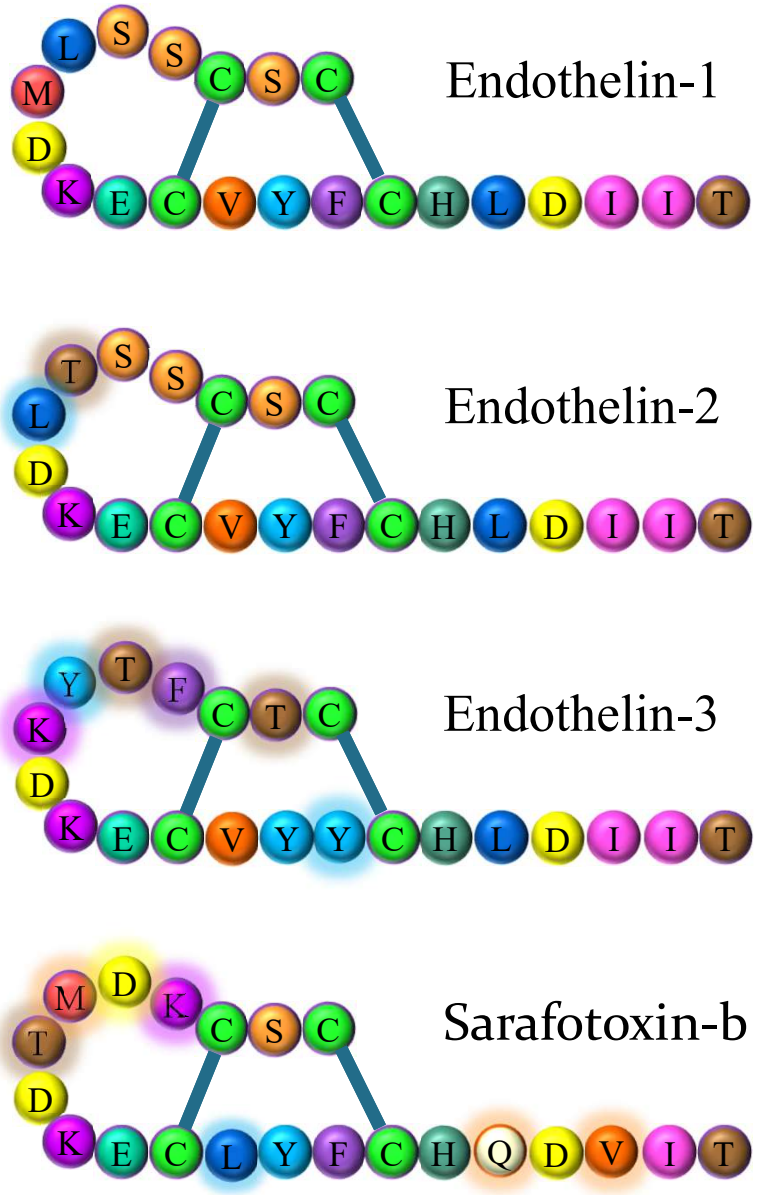
EDHF: in vessels with smaller diameter (resistance vessels)
NO: in vessels with higher diameter

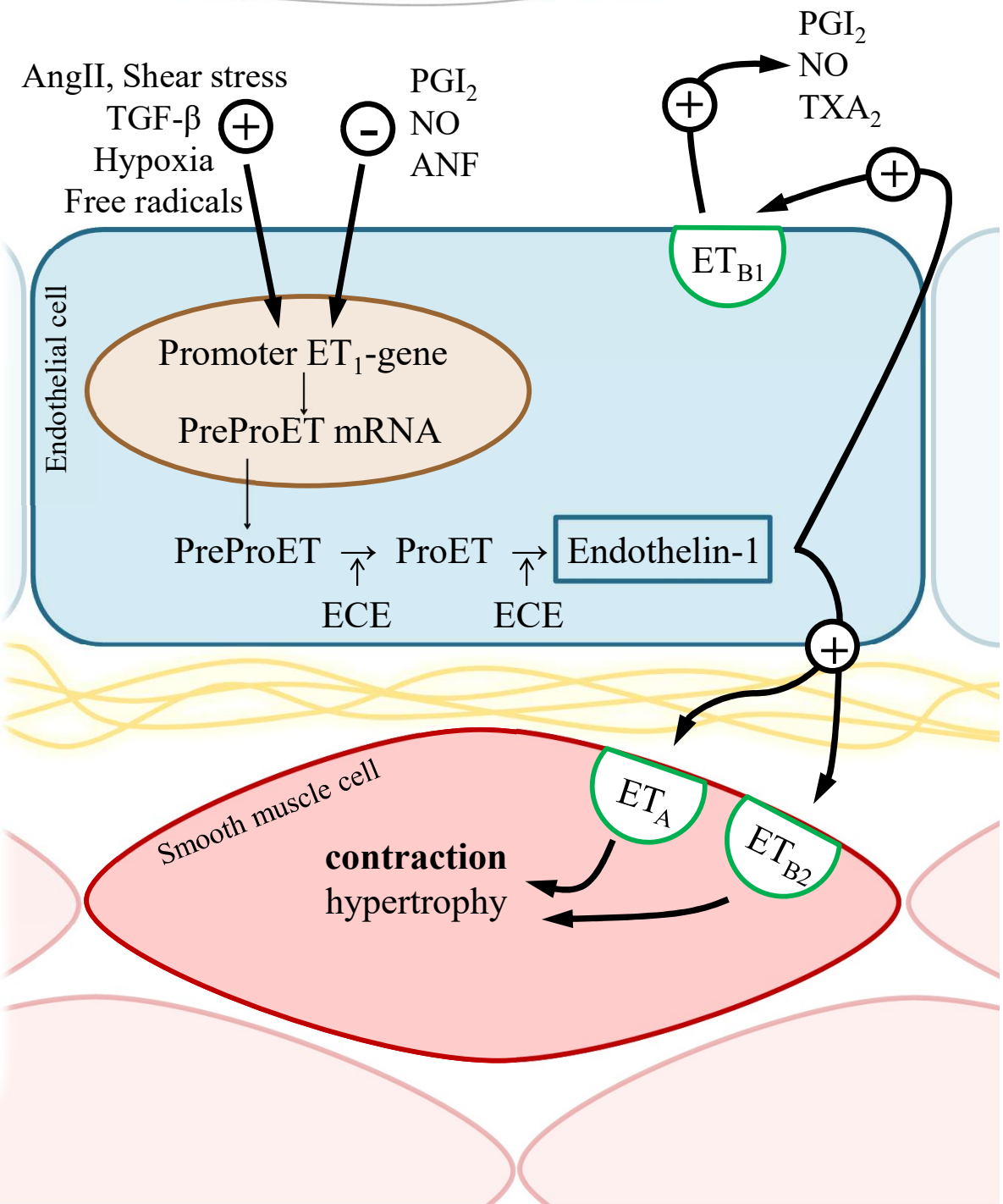
EDHF independent SM hyperpolarization may occur because of myoendothelial gap junctions.

(If junctions are blocked, Ach induced hyperpolarization develops only in endothelial cells.
Ach → Ca^{2+}↑ → $I_{K,Ca}$ open → hyperpol.)

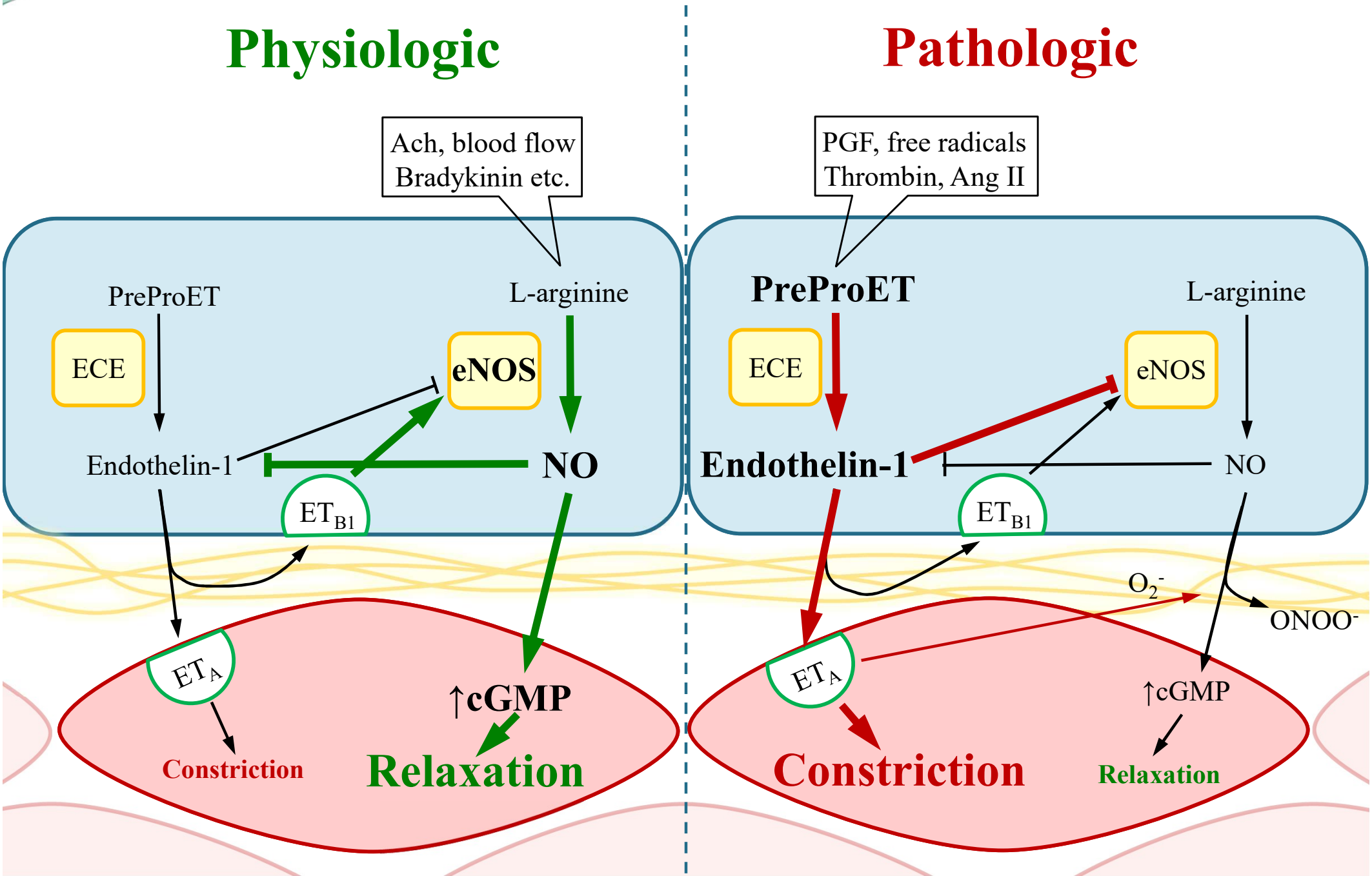


Endothelin

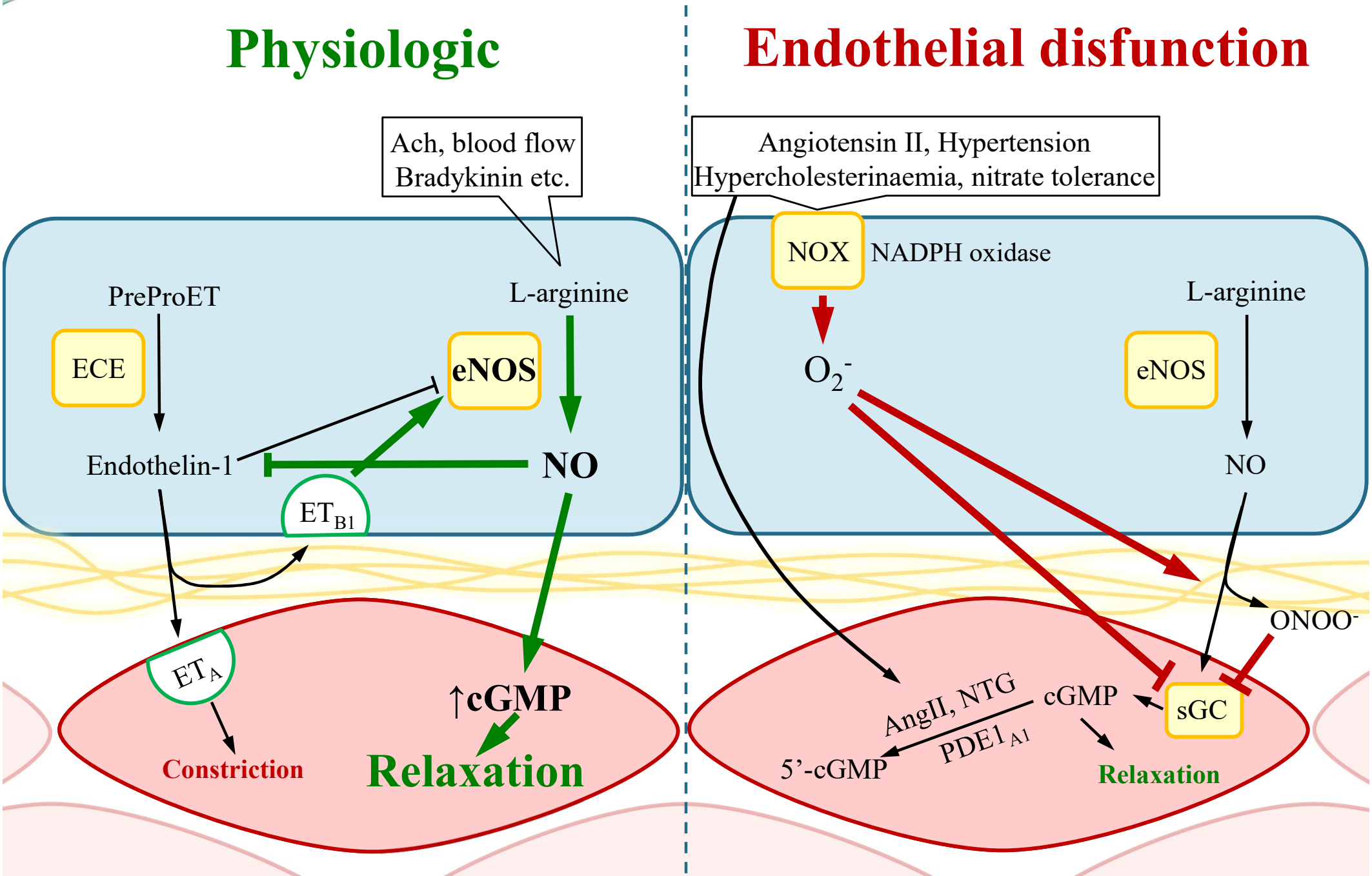

Endothelin-1
Endothelin-2
Endothelin-3
Sarafotoxin-b


AngII, Shear stress
TGF-β
Hypoxia
Free radicals
PGI2
NO
ANF
PGI2
NO
TXA2
ETB1
Endothelial cell
Promoter ET1-gene
PreProET mRNA
PreProET
ProET
Endothelin-1
ECE
ECE
Smooth muscle cell
ETA
ETB2
contraction
hypertrophy

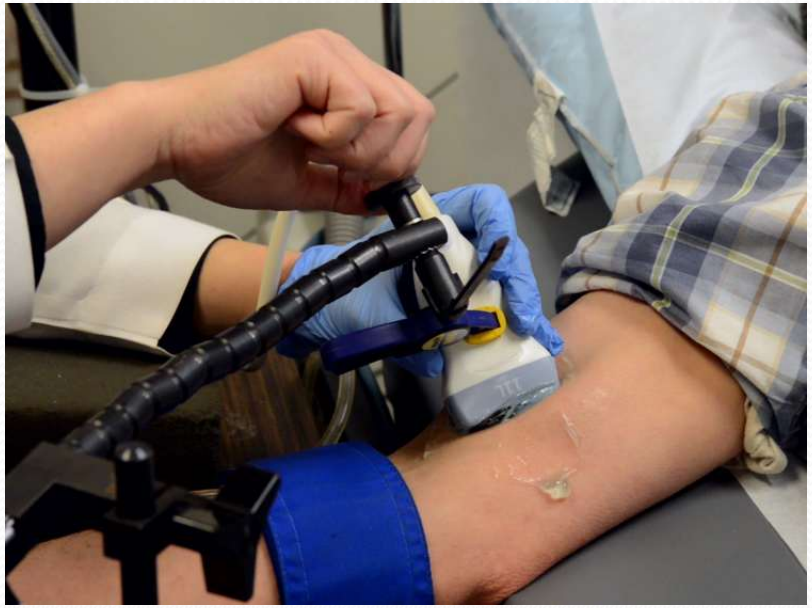
Interactions during health and disease

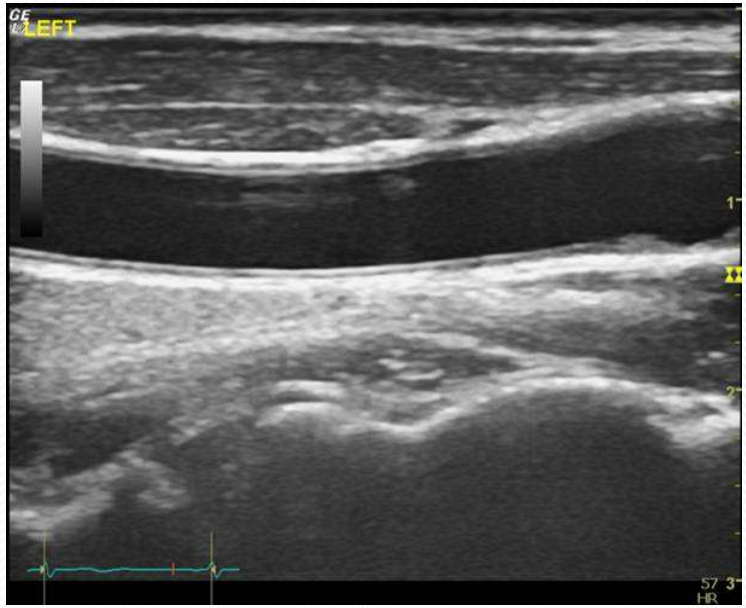


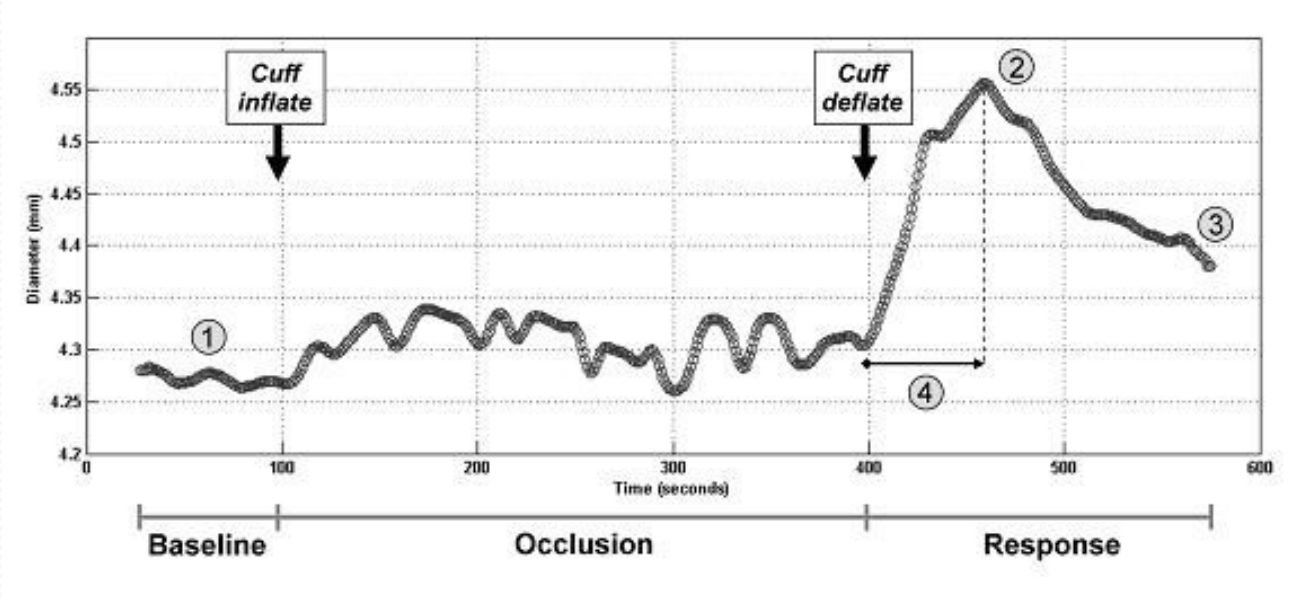
Interactions during disease



Flow-mediated vasodilatation

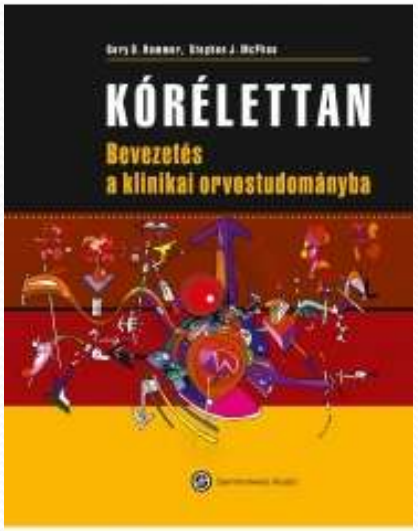






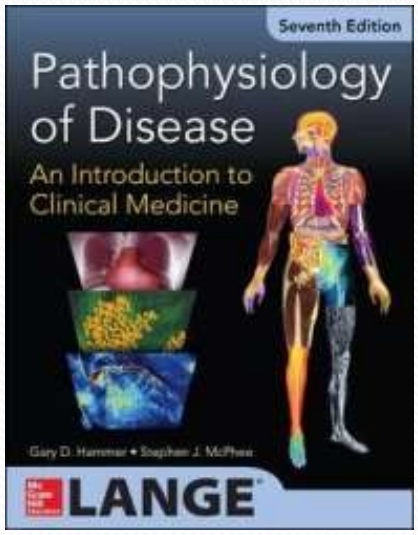
Sources: doi.org/10.3791/54011; https://www.augusta.edu/mcg/dphs/gpi/research/livep2.php; doi.org/10.1186/1471-2261-7-11

Literature



Kórélettan – Bevezetés a klinikai orvostudományba
Szerkesztők: Gary D . Hammer, Stephen J. McPhee

Oldalszám: 299 - 314 o.



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