PHAGOCYTOSIS

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PHAGOCYTIC CELLS

- Macrophages, neutrophils, and dendritic cells in tissues and monocytes in the blood

DEFINITION OF PHAGOCYTOSIS

- Through various cell surface receptors they recognize microbes such as bacteria, extend their plasma membrane to engulf them, and internalize them in phagosomes. Lysosomes then fuse with the phagosomes, delivering agents that kill and degrade the microbes.

PROCESSES OF PHAGOCYTOSIS

- Chemotaxis
- Extravasation
- Pathogen recognition
- Intracellular Killing

CHEMOTAXIS

- A variety of chemotactic stimuli can be involved in the recruitment of leukocytes to the extravascular space. The types of chemotactic factors:

1. Bacterial origin: such as formyl-methionine-leucine-phenylalanine.

2. Complment derivatives: C5a that can be generate in several ways.

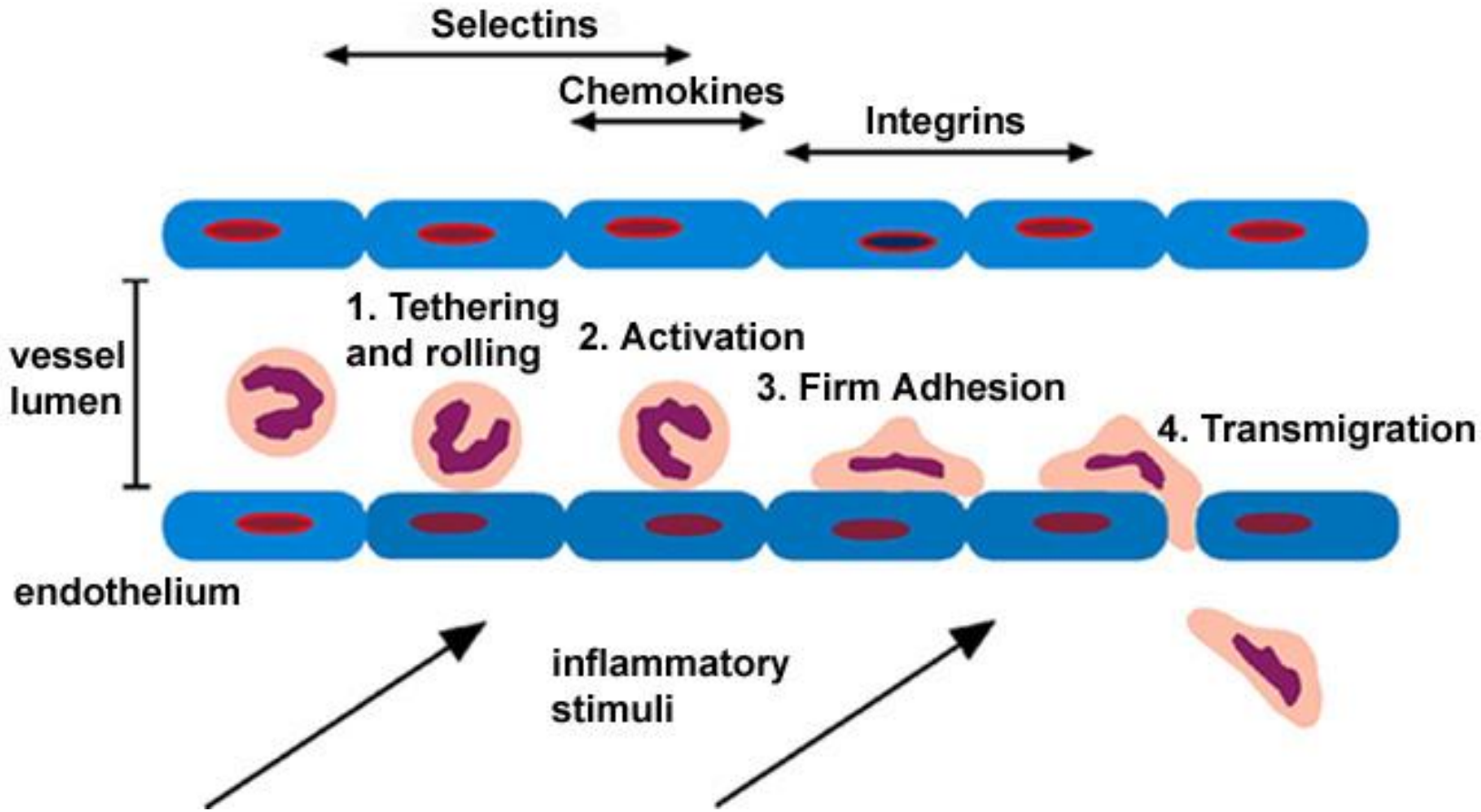
3. Leukotriene B4 released by activated neutrophils and macrophages after inflammation.

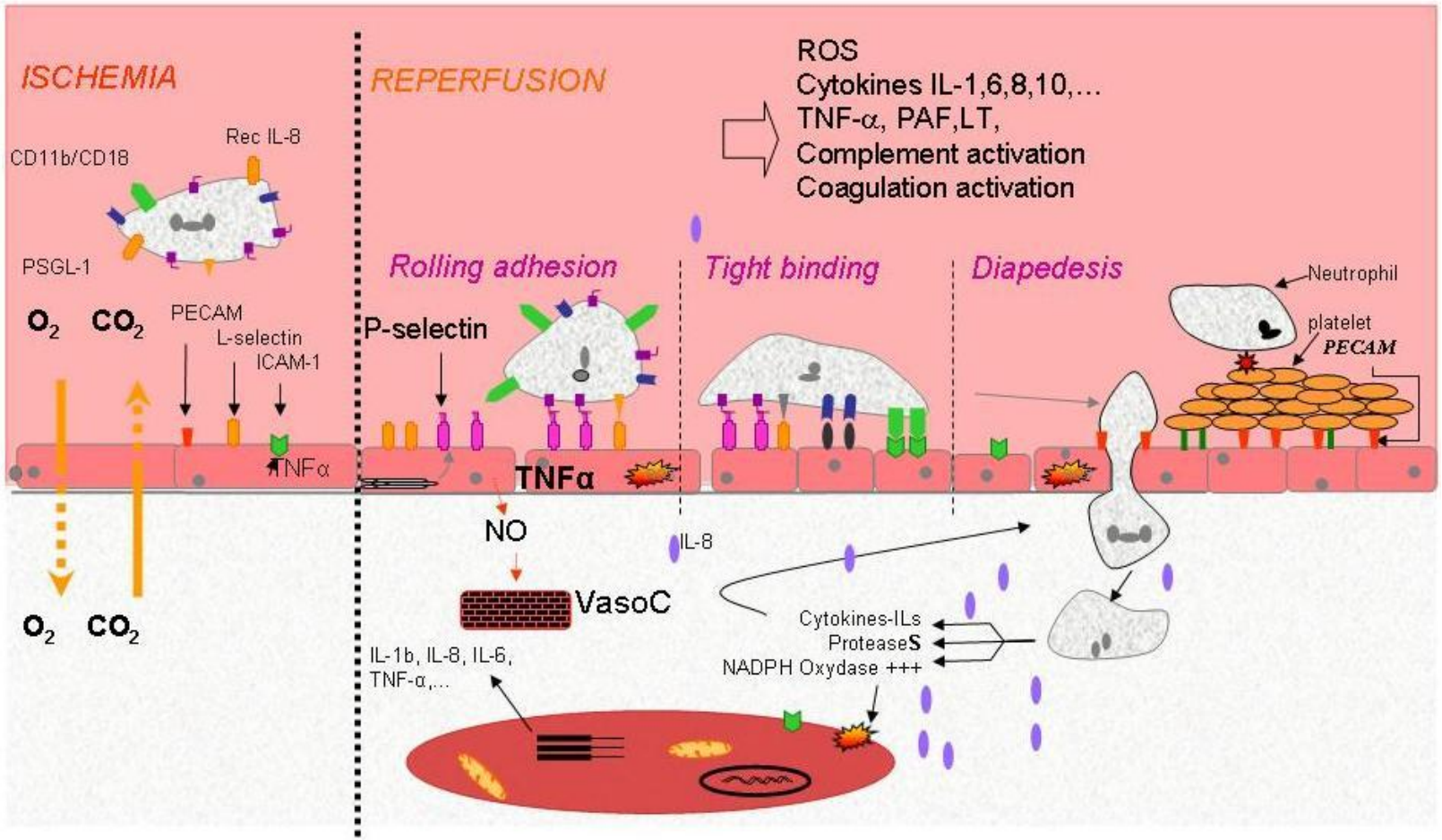
4. Chemokines such as IL-8, monocyte chemotactic protein -1 and RANTES.

EXTRAVASATION

- The neutrophils undergo changes in the cell membrane and become ruffled due to increased expression of cell adhesion molecule (CAM).
- CD11a and CD11b on neutrophils interact with ICAM-1, ICAM-2 and VCAM-1 on endothelial cells.
- The interaction of leukocyte with PECAM-1 which is expressed at the intracellular junctions between endothelial cells and this interaction mediate the process of diapedesis, by which leukocytes squeeze through the endothelial junctions into the extravascular compartment.

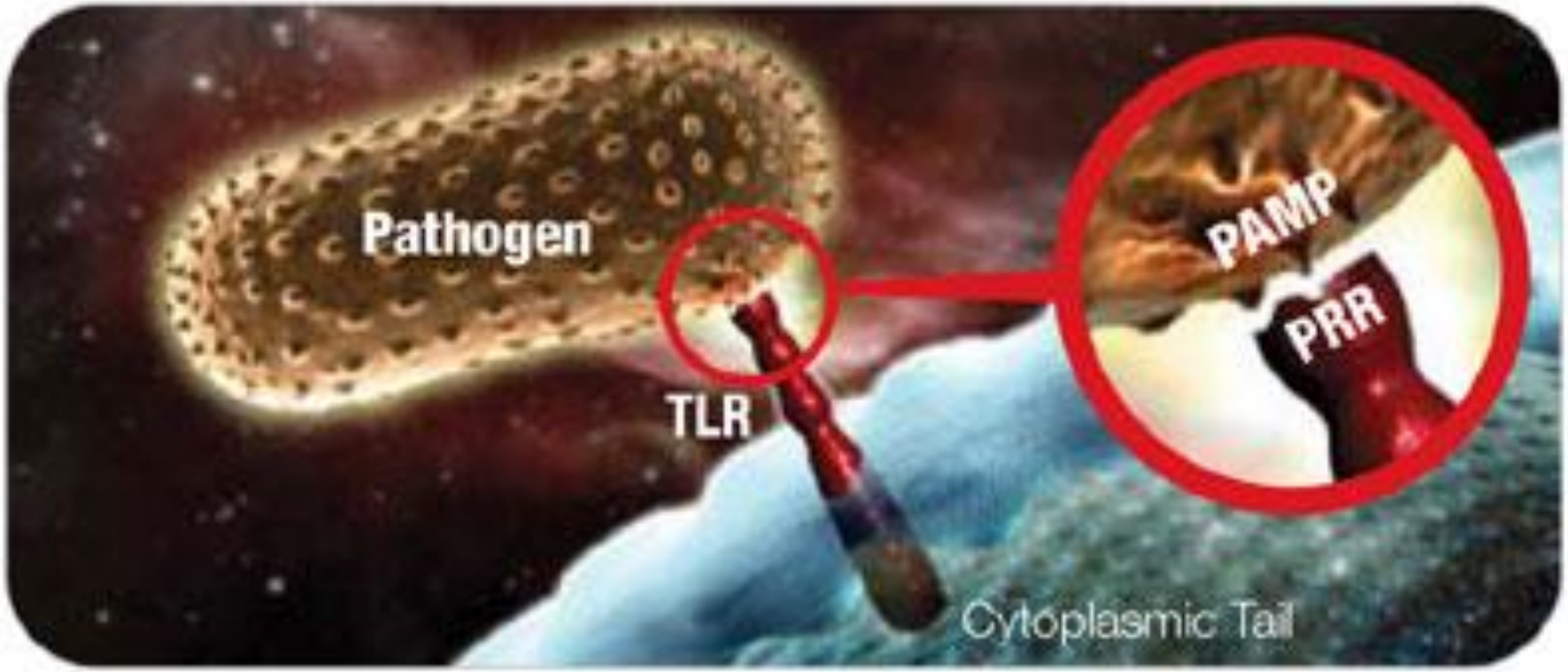
DIAPEDESIS


Selectins
Chemokines
Integrins
vessel lumen
1. Tethering and rolling
2. Activation
3. Firm Adhesion
4. Transmigration
endothelium
inflammatory stimuli


ISCHEMIA
REPERFUSION
ROS
Cytokines IL-1,6,8,10,…
TNF-α, PAF,LT,
Complement activation
Coagulation activation
Rec IL-8
CD11b/CD18
PSGL-1
O2 CO2
PECAM
L-selectin
ICAM-1
TNFα
Rolling adhesion
Tight binding
Diapedesis
P-selectin
Neutrophil
platelet
PECAM
TNFα
NO
IL-8
VasoC
Cytokines-ILs
ProteaseS
NADPH Oxydase +++
IL-1b, IL-8, IL-6,
TNF-α,…
O2 CO2

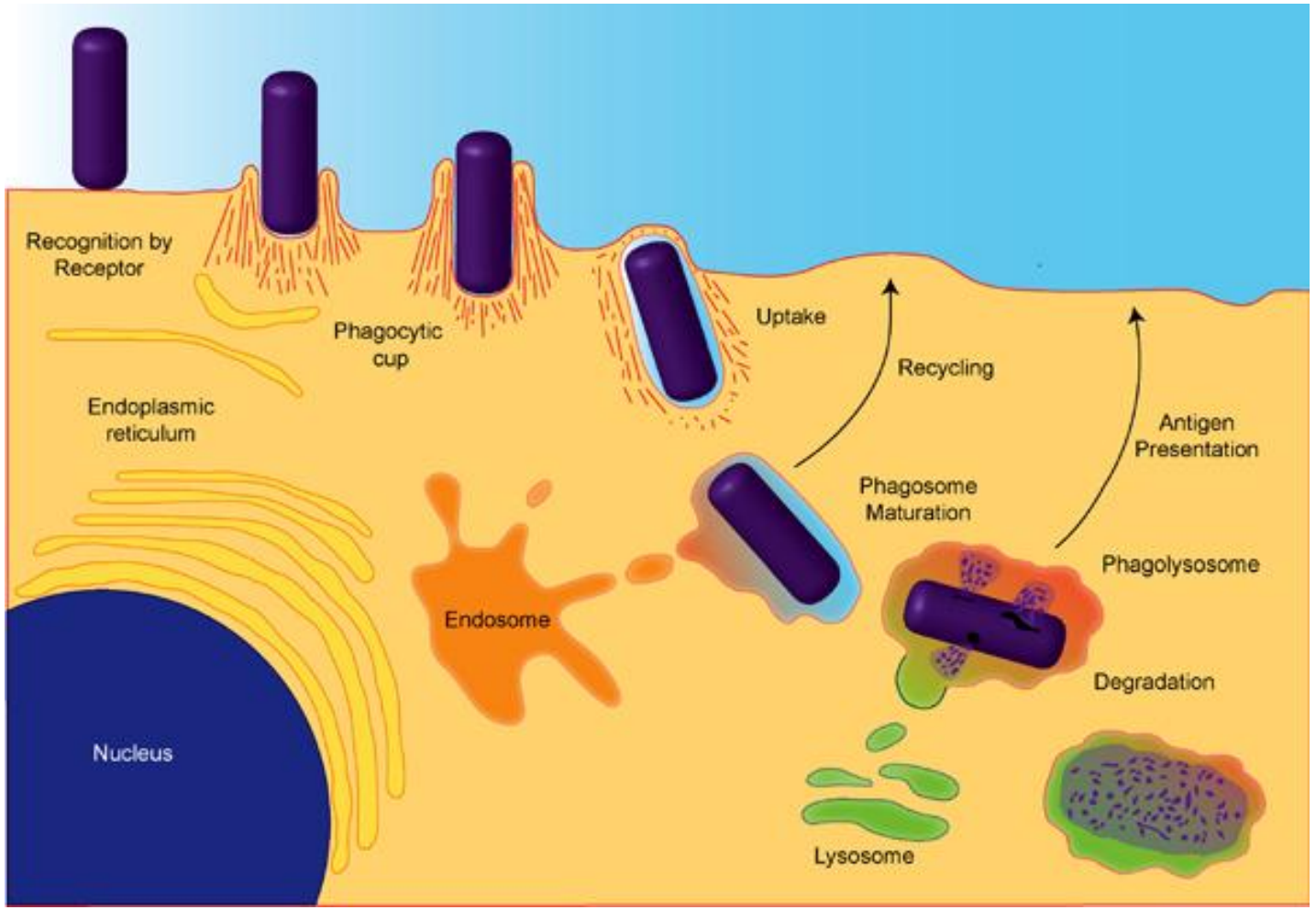
PATHOGEN RECOGNITION

- Phagocytes express on their surfaces a variety of receptors called **pattern recognition receptors (PRRs)**, some of which directly recognize specific conserved molecular components on the surfaces of microbes called **pathogen-associated molecular patterns (PAMPs) or (MAMPs)** such as mannans and - glucans, lipopolysaccharides (LPS), other lipid-containing molecules, peptidoglycans, and surface proteins. .
- Activation of phagocytosis can also occur indirectly, by phagocyte recognition of soluble proteins that have bound to microbial surfaces, thus enhancing phagocytosis, a process called **opsonization.**


Pathogen
TLR
PAMP
PRR
Cytoplasmic Tail

INTRACELLULAR KILLING

- The binding of microbes bacteria, fungi, protozoan parasites, and viruses to phagocytes via pattern recognition receptors or opsonins and opsonin receptors activates signaling pathways. These signaling pathways trigger actin polymerization, resulting in membrane extensions around the microbe particles and their internalization, forming phagosomes.
- The phagosomes then fuse with lysosomes and, in neutrophils. The resulting phagolysosomes contain an arsenal of antimicrobial agents that then kill and degrade the internalized microbes.
- These agents include antimicrobial proteins and peptides (including defensins and cathelicidins), low pH, acid-activated hydrolytic enzymes (including lysozyme and proteases), and specialized molecules that mediate oxidative attack.


Recognition by Receptor
Phagocytic cup
Uptake
Recycling
Antigen Presentation
Endoplasmic reticulum
Phagosome Maturation
Phagolysosome
Endosome
Degradation
Nucleus
Lysosome

OXIDATIVE ATTACK

- Oxidative attack on the phagocytosed microbes, which occurs in neutrophils, macrophages, and dendritic cells, employs highly toxic **reactive oxygen species (ROS)** and **reactive nitrogen species (RNS)**, which damage intracellular components. Collectively the ROS and RNS are highly toxic to phagocytosed microbes due to the alteration of microbial molecules through oxidation, hydroxylation, chlorination, nitration, and S-nitrosylation, along with formation of sulfonic acids and destruction of iron-sulfur clusters in proteins.


Unregistered HyperCam 2