PATHOLOGY

Medical Committee
The University of Jordan

SHEET

SIIDE

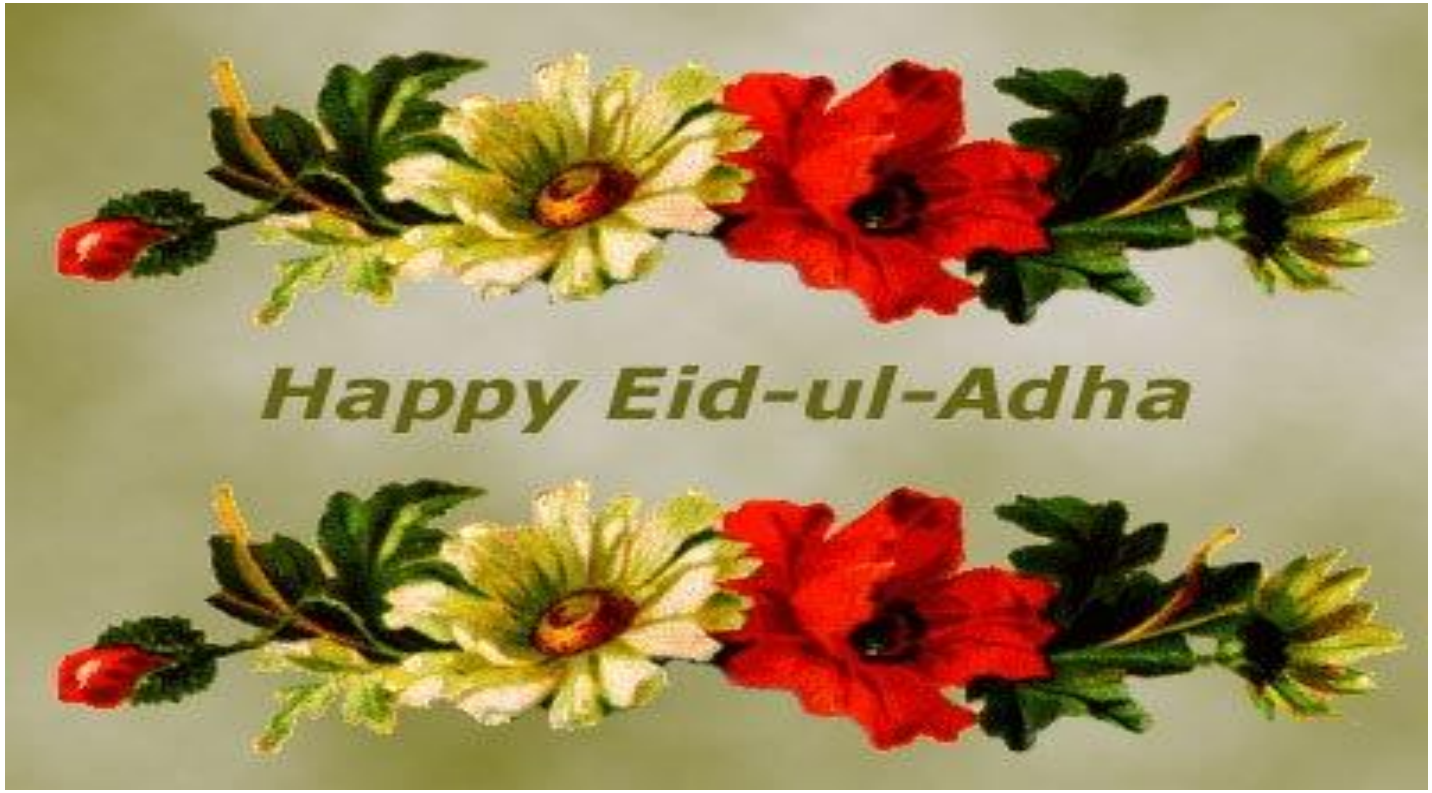
Slide : 6

Doctor: Heyam Awad

Designed by: Majida Al-Foqara'

INFLAMMATION LECTURE

DR HEYAM AWAD, FRCPATH

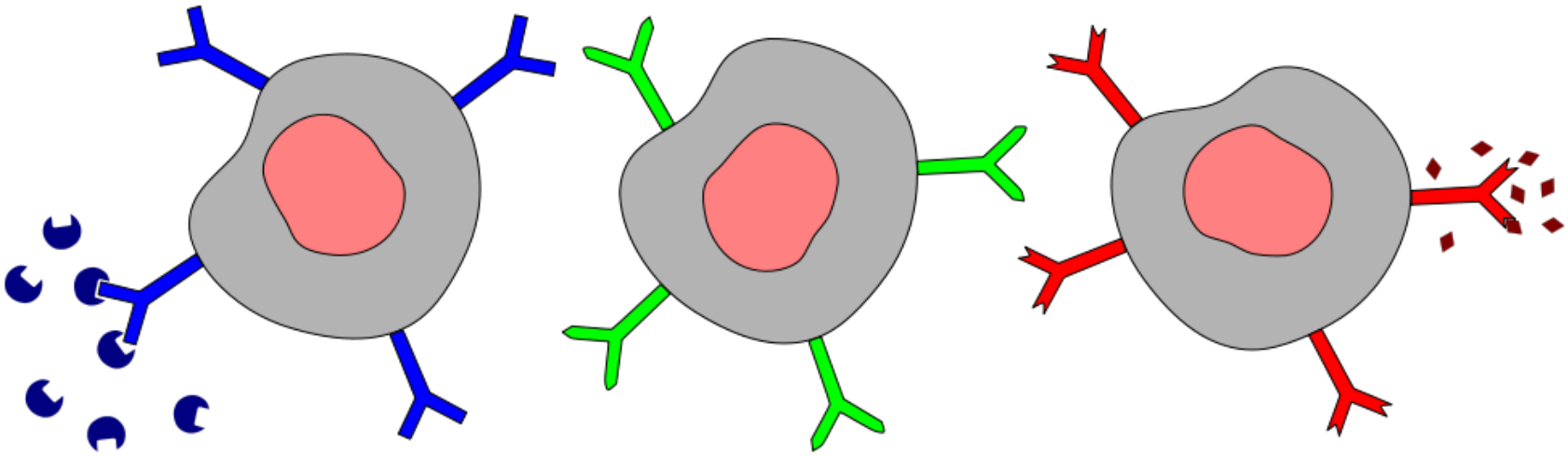

Happy Eid-ul-Adha

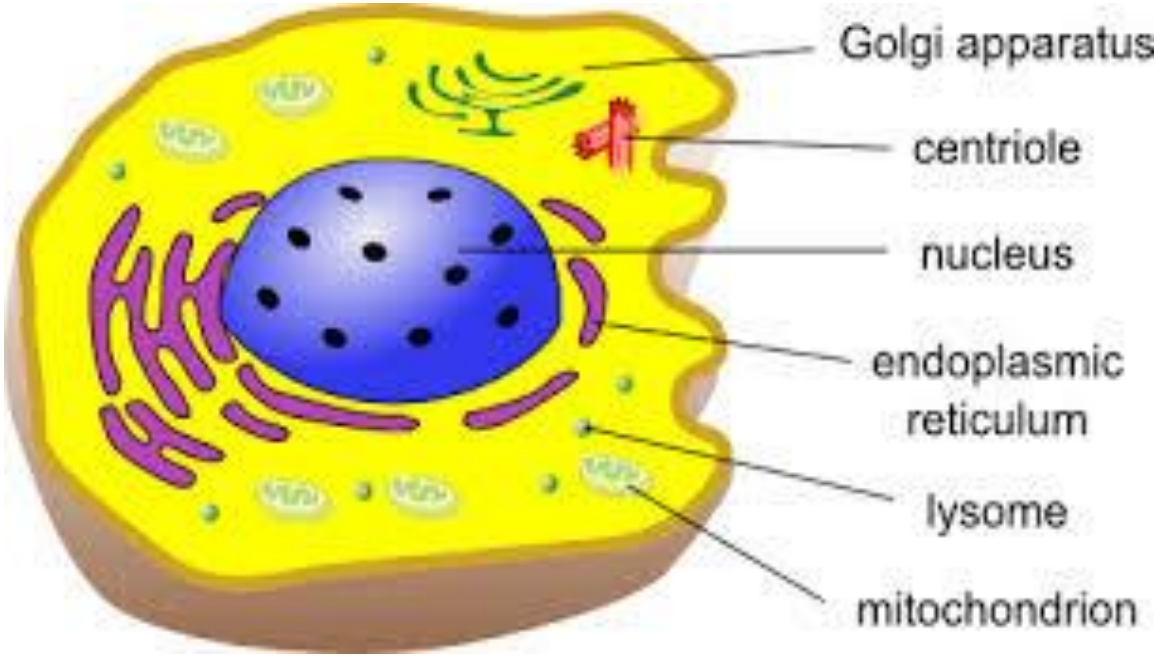
INFLAMMATORY REACTION

- RECOGNITION.
- RECRUITMENT.
- REMOVAL OF THE AGENT.
- REGULATION.
- RESOLUTION/ REPAIR.

RECOGNITION

RECEPTORS




Golgi apparatus
centriole
nucleus
endoplasmic reticulum
lysome
mitochondrion

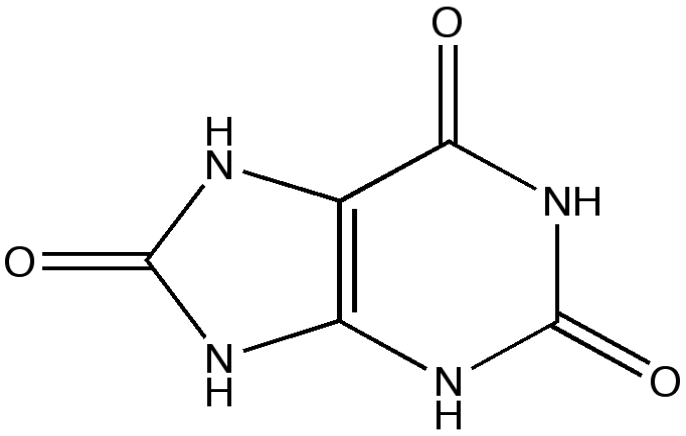
CELULAR RECEPTORS FOR MICROBES

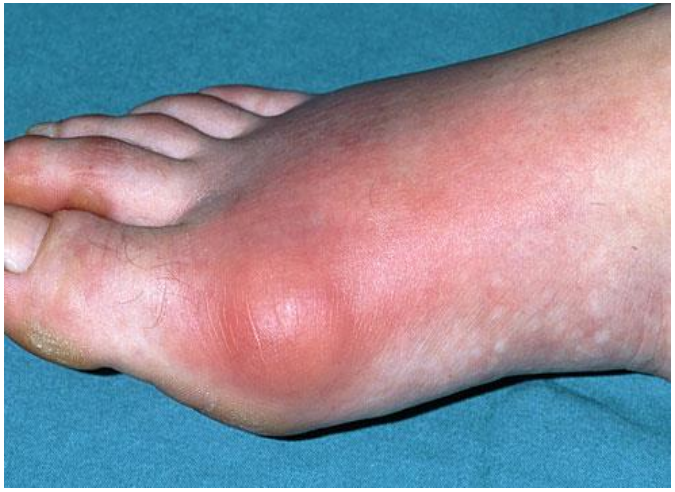
- TOLL-LIKE RECEPTORS (TLRs).

WHICH CELLS?

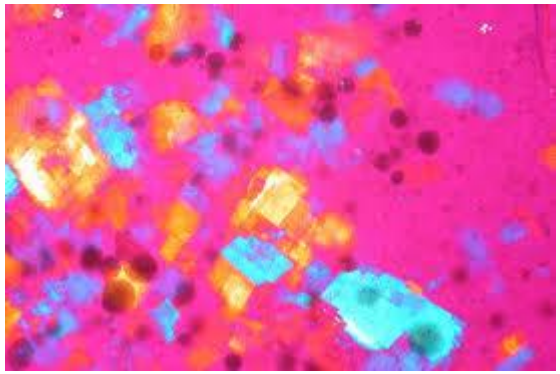
- EPITHELIAL.
- DENDRITIC CELLS.
- MACROPHAGES.
- WBCs.

SENSORS OF CELL DAMAGE.

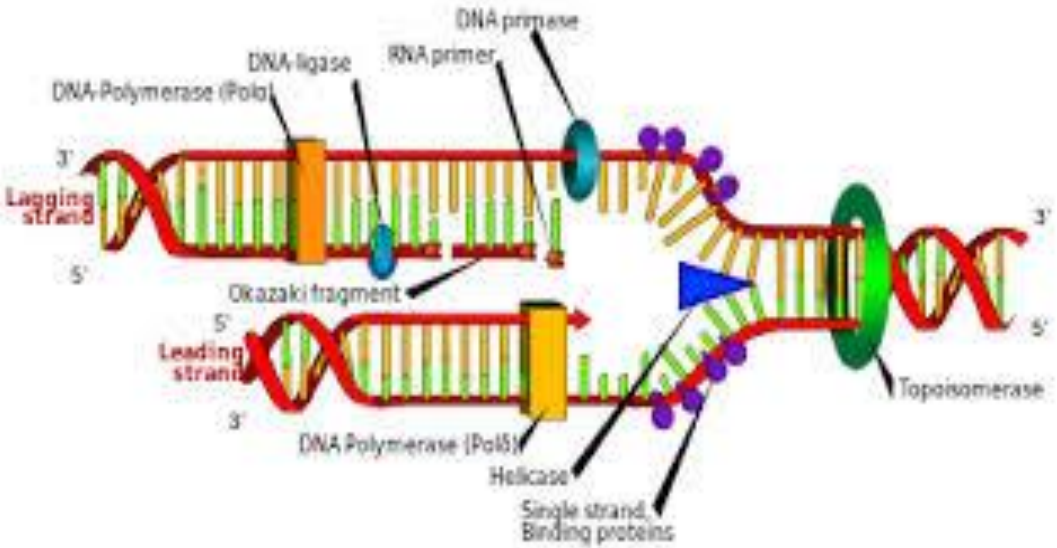




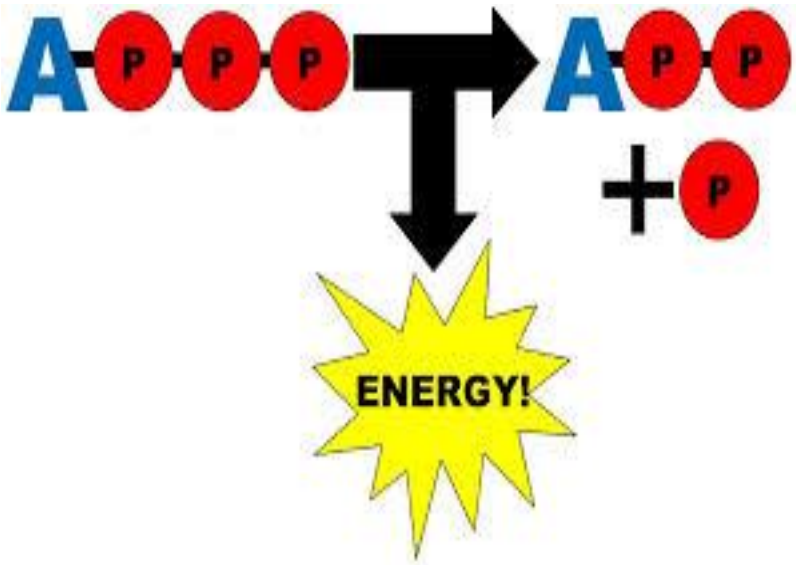
SENSORS OF CELL DAMAGE



SENSORS OF CELL DAMAGE



SENSORS OF CELL DAMAGE



- SENSORS OF CELL DAMAGE ACTIVATE A PROTEIN CYTOSOLIC COMPLEX CALLES INFLAMMASOME.
- INFLAMMASOME INDUCES PRODUCTION OF IL-1.
- IL-1 RECRUITS LEUKOCYTES.

- WHICH CELLS?
- WHERE IN THE CELLS?

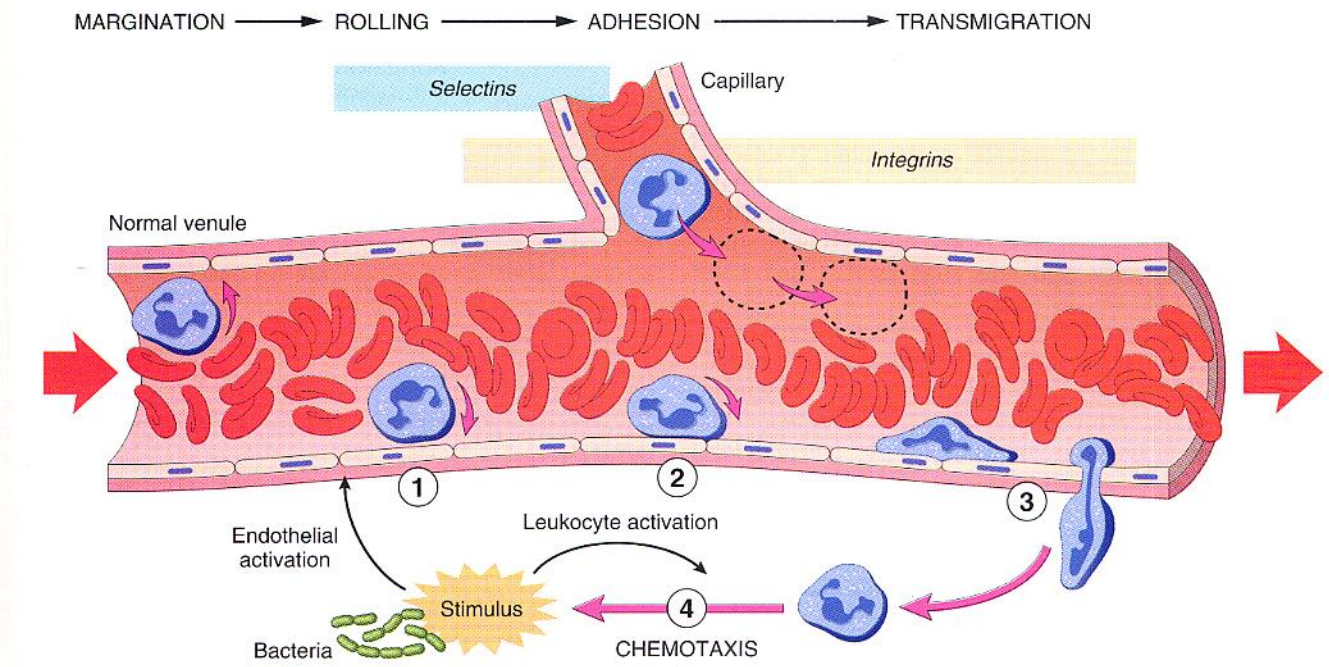
OTHER CELLULAR RECEPTORS

- WBCs EXPRESS RECEPTORS FOR Fc TAIL OF ANTIBODIES AND COMPLEMENT.....SO THEY RECOGNISE MICROBES COATED WITH ANTIBODIES AND COMPLEMENT

CIRCULATING PROTEINS

- COMPLEMENT SYSTEM REACTS AGAINST MICROBES.
- MANNOSE- BINDING LECTIN RECOGNISES MICROBIAL SUGARS.
- COLLECTINS BIND MICROBES.

RECRUITMENT

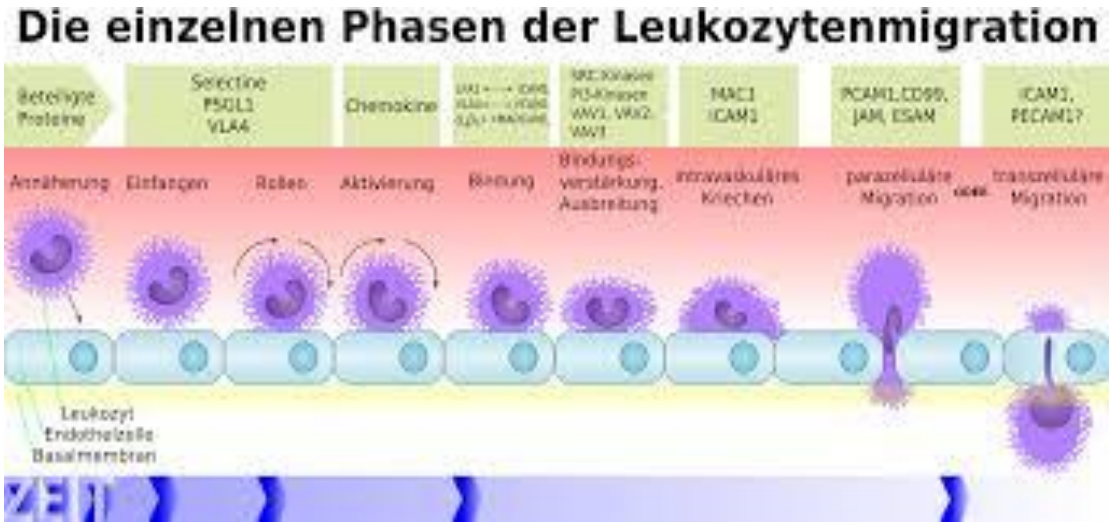


Sequence of events in leukocyte emigration in inflammation. Laminar blood flow and the presence of red blood cells tend to push leukocytes against the venular wall, increasing their contact with endothelial cells (see the capillary branch at the top with cells entering the venule flow). The leukocytes (1) roll, (2) arrest and adhere to endothelium, (3) transmigrate through an intercellular junction and pierce the basement membrane, and (4) migrate toward chemoattractants released from a source of injury. The roles of selectins, activating agents, and integrins are also indicated.

MARGINATION

- NORMALLY RBCs ARE CONFINED TO A CENTRAL COLUMN DISPLACING WBCs TO THE PERIPHERY.
- STASIS CAUSES DECREASE WALL SHEAR STRESS SO MORE WBCs TAKE A PERIPHERAL POSITION.

ROLLING


Die einzelnen Phasen der Leukozytenmigration
Beteiligte Proteine
Selectine
PSGL1
VLA4
Chemokine
MAC1
ICAM1
PCAM1,CD99,
JAM, ESAM
ICAM1,
PECAM1?
Annäherung
Einfangen
Rollen
Aktivierung
Bindung
Bindungs-
verstärkung,
Ausbreitung
intravaskuläres
Kriechen
parazelluläre
Migration
transzelluläre
Migration
Leukozyt
Endothelzelle
Basalmembran

- ROLLING IS FOLLOWED BY ADHESION.

- ROLLING AND ADHESION ARE CAUSED BY COMLEMENTARY ADHESION MOLECULES IN BOTH WBC AND ENDOTHELIAL CELLS.
- ADHESION MOLECULES: SELECTINS AND INTEGRINS.....A LONG STORY!!!

- SELECTINS CAUSE ROLLING....WEAK ADHESION.
- ROLLING SLAWS DOWN WBCs....CHANCE FOR FIRM ADHESION.
- FIRM ADHESION BY INTEGRING...VCAM AND ICAM

MIGRATION

- TRANSMIGRATION OR DIAPEDESIS.
- OCCURS MAINLY IN POSTCAPILLARY VENULES.
- ADHESION MOLECULES...PECAM (PLATELET ENDOTHELIAL CELL ASHESION MOLECULE).
- THROUGH THE BASEMENT MEMBRANE? COLLAGENASE.

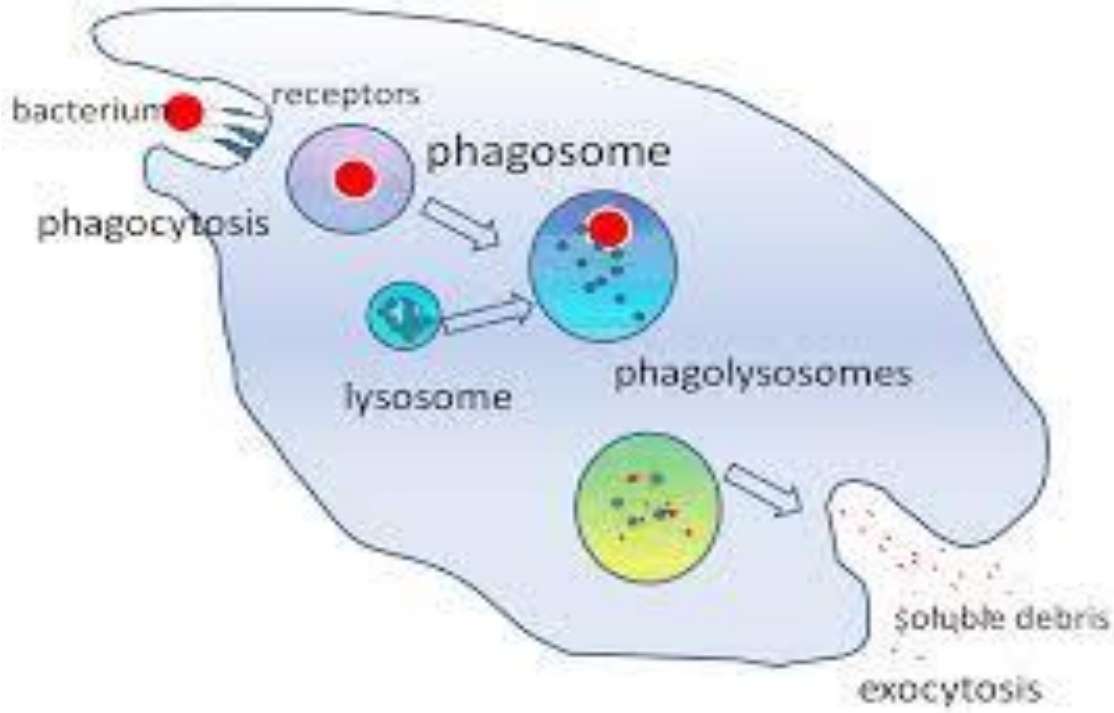
CHEMOTAXIS

CHEMOATTRACTANTS:

- BACTERIAL PRODUCTS; PEPTIDES AND LIPIDS.
- CYTOKINES, ESPECIALLY CHEMOKINES(IL8).
- COMPLEMENT C5a.
- ARACHIDONIC ACID METABOLITES, LEUKOTRIENE B4.

REMOVAL OF INSULT

- PHAGOCYTOSIS AND INTRACELLULAR KILLING.
- THREE STEPS : RECOGNITION AND ATTACHMENT, ENGULFMENT, KILLING OR DERGRADATION.


bacterium
receptors
phagosome
phagocytosis
lysosome
phagolysosomes
soluble debris
exocytosis

RECEPTORS FOR RECOGNITION

- MANNOSE RECEPTORS.
- RECOGNISE MANNOSE AND FUCOSE ON GLYCOPROTEINS AND GLYCOLIPIDS .

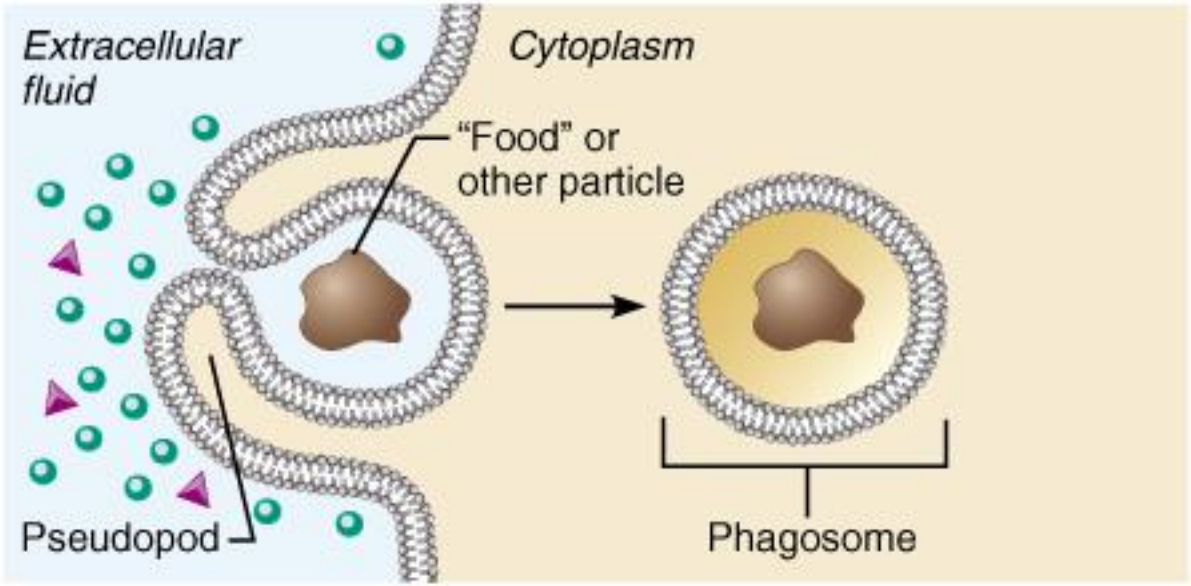
RECEPTORS

- SCAVENGER RECEPTOR.
- RECOGNISE MODIFIED LDL....OXIDISED OR ACETYLATED.

RECEPTORS

- RECEPTORS FOR OPSONINS.
- OPSONINS ARE PROTEINS THAT BIND MICROBES.
- OPSONINS: IgG, C3b, LECTINS.

ENGULFMENT



(a) Phagocytosis

INTRACELLULAR DESTRUCTION

- LYSOSOMAL ENZYMES.
- REACTIVE OXYGEN SPECIES.
- REACTIVE NITROGEN SPECIES.

LYSOSOMAL ENZYMES

- WHICH CELLS?

NEUTROPHIL GRANULES

- 1. PRIMARY, LARGE, AZUROPHIL GRANULES.

  MYLOPEROXIDASE, BACTERIOCIDAL FACTORS, HYDROLASES.

2. SECONDARY, SMALL, SPECIFIC GRANULES.

  LYSOZYME, COLLAGENASE, GELATINASE, ALKALINE PHOSPHATASE, HISTAMINASE.

PROTEASES.

- ACID PROTEASES....DEGRADE ACIDIFIED DEBRIS .
- NEUTRAL PROTEASES... CAN DEGRADE COLLAGEN, ELASTIN, FIBRIN, CARTILAGE, BASEMENT MEMBRANE
- NEUTRAL PROTEASES CAN CAUSE TISSUE DESTRUCTION.

MACROPHAGES

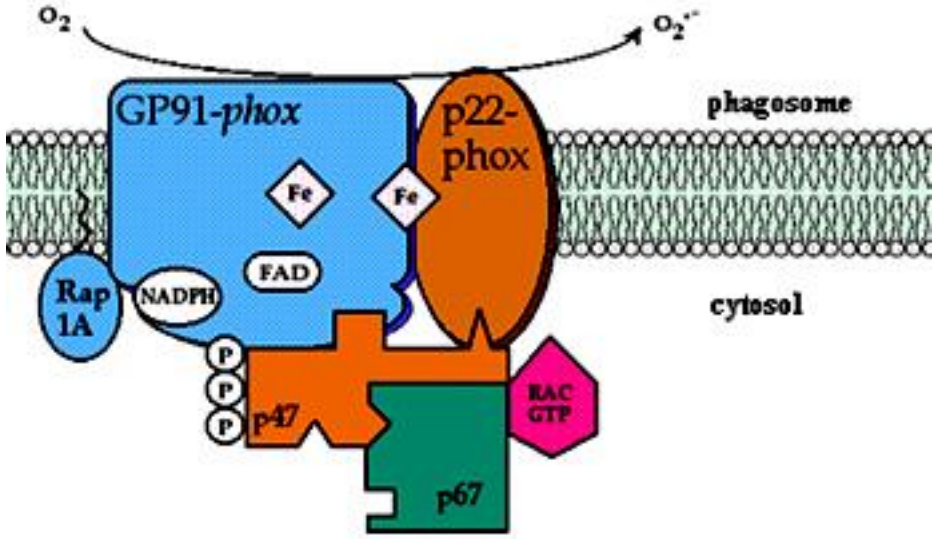
- CONTAIN: HYDROLASES, COLLAGENASE, ELASTASE, PHOSPHOLIPASE.

ANTIPROTEASES

- LYSOSOMAL PROTEASES ARE HARMFUL TO OUR TISSUE.
- CONTROLLED BY ANTIPROTEASES.
- ALPHA 1 ANTITRYPSIN INHIBITS NEUTROPHIL ELASTASE.

REACTIVE OXYGEN SPECIES

- OXIDASES CAN PRODUCE ROS, e.g: SUPEROXIDE ANION.
- OXIDASE CONSISTS OF 7 PROTEINS!!
- COMPONENTS IN PLASMA MEMBRANE AND CYTOPLASM.
- ROS PRODUCED IN PHAGOLYSOSOMES.



Subunits of the NADPH-oxidase complex

- SUPEROXIDE IS CONVERTED TO HYDROGEN PEROXIDE (H2O2)
- H2O2 CONVERTED BY MYELOPEROXIDASE TO HYPOCHLORITE (OCL2-)
- HYPOCHLORITE DESTROYS MICROBES BY HALOGENATION OR OXIDATION.

NITROGEN RADICALS

- NITRIC OXIDE (NO) PRODUCED BY NITRIC OXIDE SYNTHASE (NOS)
- NOS...eNOS, nNOS,iNOS.
- NO RECTS WITH SUPEROXIDE TO FORM PEROXINITRITE(ONOO-)