Done by: Muntaha Al-Khazalleh
Lecture: Reactions of Innate Immunity
Reactions of innate immunity

Ali Al Khader, MD
Faculty of Medicine
Al-Balqa’ Applied University
Email: ali.alkhader@bau.edu.jo
• Innate immune system

-Faster, but:
...less specific
...without memory

-Inflammation is one of its reactions

**recognition**: the process of binding Ligand with specific receptor

We will discuss:

1- Recognition (pathogen-associated molecular patterns and the receptors for them)

2- Soluble molecules...esp. interferons

3- Cellular defenses...responses of phagocytes and NK cells

4- Inflammation...briefly
Recognition

Pathogen-associated molecular patterns (PAMPs)

Pattern recognition receptors (PRRs)

- Epitope: part of antigen molecule to which an antibody attaches

By this, the innate system discriminates between self and non-self

*PRRs genes do not undergo somatic modification (they are conserved/germline)
...unlike the receptors of the adaptive immune system which are:
- Epitope-specific somatically generated
- Expressed by B and T lymphocytes
Pathogen-associated molecular patterns (PAMPS)

• Limited number----widely expressed

• May be: -sugars
  -proteins
  -lipids
  -nucleic acids

• Recognized mainly by phagocytic cells: -directly by PRRs or -indirectly by complement receptors,...etc.

• In phagocytosis:
  Binding ➔ immobilization of microbe ➔ phagocytosis ➔ phagocyte activation

That’s mean less specific
ممكن اكثر من ميكروب عندهم رح ترتبط على نفس المستقبل واحد
Indirectly by complement receptor:

- **PRR:**

  **بيعني المستقبل**

  **This process called opsonin** *(e.x for its molecule c3b,c4b,lectin,CRP,Igg)*
• **PAMPs on bacteria:**
  • Gram +....carbohydrates and proteins in peptidoglycan
  • Gram -....lipids and carbohydrates in LPS and to a lesser degree: also molecules of peptidoglycan

  ...**PRRs for the above:** -TLR2 (toll-like receptor 2) for peptidoglycan
  -TLR4 (toll-like receptor 4) for LPS

  *on phagocytes

*Phagocyte activation ➔ Production of: -microbicidal molecules
  -Enzymes
  -cytokines
  -Activation of inflammation
PRRs

*Membrane-bound or *Extracellular

• Examples:
  - Toll-like receptors
  - Scavenger receptors
  - Opsonins

*Signal transduction: synthesis of proteins:
  - Microbicidal
  - Cytokines
  - Chemokines...recruitment of WBCs to the site
  ...activation of inflammation

- Internalization of bacteria
- Phagocytosis of apoptotic host cells
  *Bind to: -modified LDL
  - polysaccharides
  - nucleic acids...etc.
Markers of abnormal self

• Viruses: MHC class I molecules on infected host cells

.........also expression of “stress signals” on cell surface

- HSPs (heat shock proteins)
  - MICA
  - MICB

..detected by: -TLR2
  - TLR4
  - KARs (killer activation receptors) of NK cells

this also happens to cells in cancerous transformation
**When occur inflammation in the cell formed abnormal self signal**

- normal cell has MHC-1(HLA):
  - **يختلف من شخص لآخر لهيك اله دور مهم بنجاح عمليات نقل الأعضاء والتبرع**
  - **Normal self**
  - **Abnormal self**
  - **Stress signal**

- NK cell has 2-receptor: KAR and KIR

- KAR: تزيد ال stress signal
- KIR: كل م كان عدد MHC كبير يكون ع السطح
Soluble mechanisms (by soluble molecules)

• Interferons type I

• Microbicidal molecules...we have discussed

• Complement...we will discuss later

• Cytokines: -by many cells
  -many functions
  -chemokines are cytokines with chemoattractant function (chemotaxis)
Type I interferons

• Produced by virus-infected cells (many cell types: dendritic cells, GI epithelial cells.....etc.), and also by injured cells
• The main producers: plasmacytoid dendritic cells...see next slide
• Produced within 5 minutes after interaction between certain PAMPs and PRRs
• Induce -production of antiviral molecules...RNA-dependent protein kinase (PKR)
  -apoptosis
  -activation of phagocytes, CD8, Th1, and NK cells
Plasmacytoid dendritic cells

• They represent a type of APCs (antigen-presenting cells)
• They have PRRs that bind to viral RNA

Toll-like receptor 3 (TLR-3)  
(PAMP)

this RNA is double stranded  
(not present in human)
Cellular actions...phagocytes

- Special areas in phagocyte membrane: clathrin-coated pits

- Different receptors are in these regions
  - PRRs
  - Complement receptors (CRs)
  - Fc receptors

1. Cellular extensions (pseudopodia)
2. Internalization (endocytosis)
3. Phagosome
4. Phagolysosome
5. Phagocyte activation
Cellular actions...phagocytes, cont’d

• What is macropinocytosis?

• **Phagocyte activation:**
  - Lysosomal destruction of microbe: -acid hydrolases (proteases, lipases, nuclease..etc)
    - oxygen free radicals
    - nitrous oxide (NO)
    - acidity
    - ...etc

**Remember the enzymes:**
1- NADPH oxidase
2- Myeloperoxidase
• **Oxidative burst**: is the rapid release of reactive oxygen species (superoxide radical and hydrogen peroxide) from different types of cells

• plays an important role in the immune system. It is a crucial reaction that occurs in phagocytes to degrade internalized particles and bacteria

• **NADPH oxidase**: produces superoxide

• $O_2 \rightarrow O_2^- \rightarrow OLC^{-}$
Cellular actions...phagocytes, cont’d

- Phagocyte activation...cont’d
  - Secretion of cytokines and chemokines:
    - IL-1 and IL-6: fever, also vascular permeability
    - TNF-alpha: vascular permeability, also fever
    - IL-8 and IL-12: chemotaxis of neutrophils and NK cells, respectively
Cellular actions...NK cells

Killer activation receptors (KARs) **VS** Killer inhibition receptors (KIRs)

- MICA
- MICB

- MHC I
How do NK cells kill the target cells?

- Perforin...creating pores (يخرب غشاء الخليه المهاجمه)
- Granzyme...proteolysis and apoptosis (يحطم بروتينات الخليه المهاجمه)
- Fas ligand...apoptosis
Thank You