MICROBIOLOGY & IMMUNOLOGY

DOCTOR 2019 | MEDICINE | JU

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SCIENTIFIC CORRECTION :

GRAMMATICAL CORRECTION :

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lecture 5

✳ Functions of the immune system :- Recognise → Store → Remember.
　　　　　　　　　　　　　　　　　　　↓　　　　↓　　　　　↓
　　　　　　　　　　　　　| Patterns |　The pathogen info.　for a faster response
　　　　　　　　　　　① Not found in mammalian cells
　　　　　　　　　　　② Essential for the microbe
　　　　　　　　　　　③ Called (PAMPs) → Pathogen-associated molecular patterns.
✳ The innate sys. recognies 10^3 ↗, while the adaptive, recognises 10^7.
　　　↓　　　　　　　　　　　　　　　　　　↓
　　General　　　　　　　　　　　　　　Specific
✳ Examples on PAMPs :- ① (unique nucleic acid (dsRNA)
　　　　　　　　　　② Certain based in DNA unmethylated (CpG)
　　　　　　　　　　③ Microbial protein (N-formylmethionine)
　　　　　　　　　　④ Microbial lipids & carbohydrates (LPS,
　　　　　　　　　　　　PGN, Mannose-rich oligosaccharide)

✳ Clonal → adaptive imm. :- Clone for every certain antigen
✳ Non-clonal → innate imm. :- Same receptor [non-specific].
✳ Autoimmunity → adaptive immunity over-reacting

✳ DAMPS → Damag-associated molecular patterns.
　　↳ endogenous (normally found in the wrong place)
✳ Examples on DAMPs :- ① Stress-induced proteins (HSPs)
　　　　　　　　　　② Nuclear proteins (HMGB1) (supposed to be in
　　　　　　　　　　　　　　　　　　　　　　the nucleus)

✳ PRR → Pattern Ricognition Receptor, expressed by innate sys. cells to
　　　identify PAMPs & DAMPs → On the cell membrane ⎤
　　　　　　　　　　　　　　　→ endosomes　　　　　⎥ OR soluble in the fluid
　　　　　　　　　　　　　　　→ cytosol　　　　　　⎦

Examples on PRRs

- ==Bound==

① TLR [Toll like receptors] :- ==found on the cell surface on the endosome==
   (1-9 types)
   ==- Recognise PAMPs & DAMPs==

leucir-rich domains ———————> Signal to the cytoplasmic part ↙ dimers homo/hetero ⟳ w/ transcript ⟶

adapter proteins ==activate==> Transcription factor (NF-kB)

inflam antory genes (cytokines)

(EXAMPLE) ———>
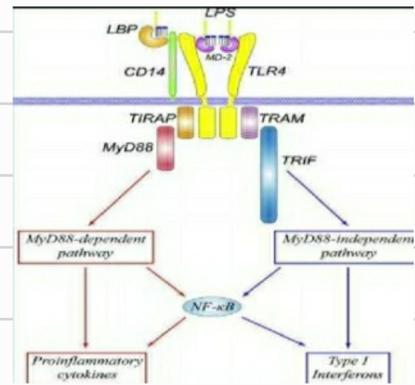
TLR on the cell surface differ from endosomes

② Receptor for carbohydrates : ==Recognise carbs on the surface of the microbe.==
==Belong to the c-type lectin family==

③ N-formyl (met-leu-phe) receptors : ==Expressed by macrophages and neutrophiles==
==Recognise bacteria peplides containing N formyl methionine.==

④ Scavenger receptors : ==Recognise lipids==
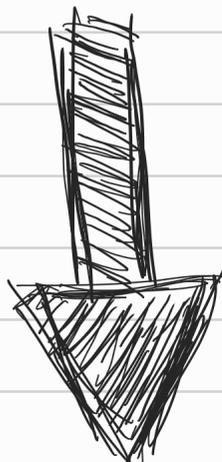
- In the cytoplasm

※ Usually detect nucleic acids ※

① NOD-like receptors (NLR) : Recognise PAMPs & DAMPs

Detect bacteria cell wall peptidoglycans.

Make inflammosomes (protein complex)

⑨ Cleaves cytokine & re-cytokine into activate form.

e.g → pro-interleukin into IL-1b activated

⑨ Used In drugs → for it plays an important role in the detiction of Ca^{2+} crystals.

② RIG-like receptors (RLR) : Detect viral RNA

Induce the production of interferon

___

※ Cytokines ⇒ Way of communication (e.g : TNF, IL-1 & IL-6)

mainly from macrophage & mast cells

- DAMPs /PAMPs <u>stimulate</u> TNF (tumor necrosis factor)
TLRs, NLRs & RLRs <u>induce</u> gene expression of

- Cytokines induce local inflammation, TF & IL-1 work on cells to produce adhesion molecules (to enter tissue in the site of infection)

$$IL-1 \left\{ \begin{array}{l} \to IL-1\alpha \\ \to IL-1\beta \end{array} \right.$$

IL-1β ⇒ (Main) , transcription induced by TLR & NOD

<u>activate</u> → NF-κB

pro-IL-1β cleaved by NLRP3 inflammosome

- Cytokines systematic effects ⟶ fever , increase the production of leukocytes in the bone marrow reach hepatocytes & heart causing systematic effects

lecture 6

ف نقاط سعي المناعة انكثر في معايير المناعة انكثر في اي انه واحد اعمق.

Remember PRR? (Page 1) , Now

$\not\!\!\!p$ Soluble PRR [effector molecules]

① Opsonins

Opsonisation → Covering the pathogen w/ ⤸, to enhance phagocytosis

- Opsonins [antibodies!!] , have receptors on phagocytes
e.g C₃b protein

② Promoting inflammatory response [killing microbes]
e.g   a) Natural bodies ⇒ innate immun. , formed without
             being exposed to antigens (خلايا B [Anti- كزي مو]
                                                    cells   bodies
             Recognise PAMPs & DAMPs (IgM class)
       b) Pentraxins ⇒ 5 parts , one of them to ⌒increase during
             CRP [acute phase protein] ⌣inflammation
             Recognise PAMPs & DAMPs
       c) Collectins & ficolins ⇒ Recognise sugars &
                           activate complementary systems.
                                                    (C.S) ‎ال
                   — MBL: Mannose binding lectin
                           Not mammilian
                           activate (C.S)
   — Ficolin

* The complement system: Proteins circulating in the blood, defense against danger.
Recognize PRR. & start activation by cleaving proteins.

* Pathways ⟹ Goal : Cleavage of $\underline{C_3}$

↯ C_3 convertase cleaves ⟶ C_{3b} & C_{3a}

                                              heavy   light

                                              opsonin   attract WBCs

                                                          inflammation

(Classical Pathway)

C_{1q} $\xrightarrow{\text{activates}}$ C_{1rss} $\xrightarrow[\text{cleaves}]{C_{1rs}}$ $C_4 \& C_2$ $\xrightarrow{\text{forming}}$ C_3 convertase

MBL & Ficolin $\xrightarrow{\text{detect}}$ PAMPs & DAMPs $\xrightarrow{\text{activate}}$ MASPs $\xrightarrow{\text{forming}}$
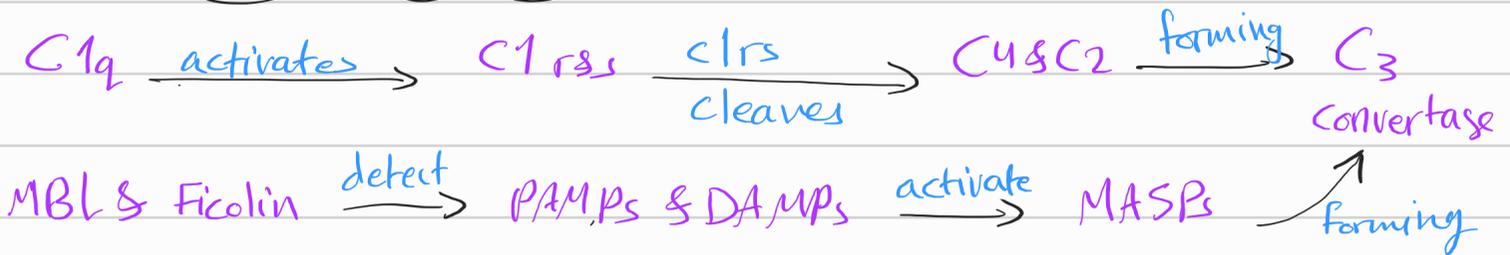
* if the pathway continued after C_3, C5 convertase will be formed generating ⟶ C_{5a} : light , inflammation
                                     ↳ C_{5b}-9 : heavy   form scaffold

                       ($C_{5,6,7,8}$) for C_9

                                         ↓

                                    form pore

                                         ↓

                                   Cell lysis

Alternative Pathway

- C_{3b} $\xrightarrow{\text{attach}}$ blood factor b $\xrightarrow{\text{forming}}$ C_3 convertase (differant)
- iC_{3b} : unstable form of C_3b (inactive form الشكل غير)

- C_3, C_4 $\longrightarrow$ acute phase proteins

* A Reference
  - PRR

  - Red circles :
    CD46 $\longrightarrow$ receptor for entry of
              certain viruses
    CD55 $\longrightarrow$ inhibit convertases
                regulation
    CD 59 $\longrightarrow$ cell bond
    Factor H $\longrightarrow$ inhibit convertases
                involved in some
                inflammantory
                diseases.
    C_5a, C_3a, C_3b $\longrightarrow$ opsonins.
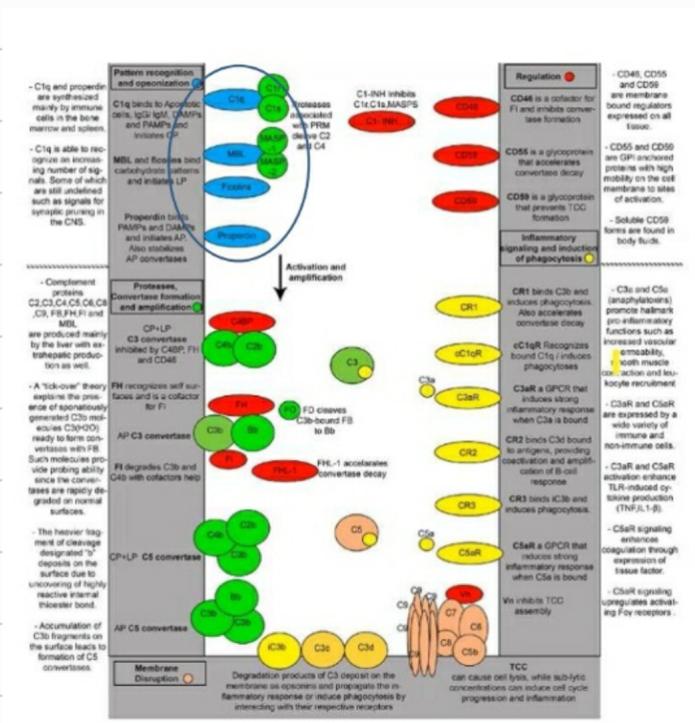
* Interferons (cytokines)
    Interfere w/ virsues $\longrightarrow$ sense the infection & block
          viral replication
    Increase toxicity of NKs & CD8+ CTLs & sequation of
lymphocytes in the lymph nodes.
    Upregulate the expression of class I MHCs