Harvard-MIT Division of Health Sciences and Technology HST.176: Cellular and Molecular Immunology Course Director: Dr. Shiv Pillai

Innate Immunity

Invertebrates and vertebrates

Responses in minutes and

Hours

Non-clonal pattern recognition Receptors

Limited diversity and specificity

Vertebrates

Responses in days and weeks

Adaptive Immunity

Clonal antigen receptors

Mind-boggling diversity and specificity

No Memory

Memory

"Non-Specific Protection"

- E p ith e lia l s u r fa c e s
- Mucus
- -Lysozym e
- -D e fe n s in s / o th e r a n tim ic ro b ia l p e p tid e s
- -Acid in stomach

-Commensalorganisms

Innate Immunity

- Secretions: mucus, lysozyme, defensins
- Cells: macrophages, granulocytes, Natural Killer cells; (also dendritic cells, B-1 and MZ B cells, and γδ T lymphocytes)
- Agglutinins: mannose binding lectin, Creactive protein (and natural IgM antibodies
- Complement: Alternative pathway, lectin pathway (and classical pathway for IgM)

Cells that mediate innate immune responses

- CELLS OF MYELOID ORIGIN
 - Macrophages
 - Granulocytes
 - Neutrophils (aka polymorphonuclear leukocytes)
 - Eosinophils
 - Basophils
 - Mast Cells
 - Dendritic cells
- CELLS OF LYMPHOID ORIGIN
 - Natural Killer (NK) Cells
 - $\gamma \delta T$ cells
 - B-1 B cells
 - Marginal Zone (MZ) B cells



NK cells



MAJOR CLASSES OF PATHOGENS

Viruses

Bacteria

Protozoa

Fungi

Worms

SURFACE STRUCTURES OF GRAM POSITIVE BACTERIA



SURFACE STRUCTURES OF GRAM NEGATIVE BACTERIA



For whom theTolls

- TLR2 peptidoglycans and bacterial lipoproteins (N-acyl Sdiacylglyceryl cysteine)
- TLR4 Lipopolysaccharide (endotoxin)
- TLR5 Flagellin
- TLR9 Unmethylated CpG DNA

Other PRRs

• F-Met-Leu -Phe receptor – (a serpentine GPCR) f-Met peptides

- Mannose receptor Mannans
- Receptor for Lipotechoic acid
 (scavenger receptor family)
- Lipotechoic acid



MBL BOUND TO MANNANS INITIATES THE LECTIN PATHWAY OF COMPLEMENT ACTIVATION





1. IN C R E A S E D K IL L IN G A B IL IT Y

2. SECRETION OF CYTOKINES AND

CHEMOKINES

3. EXPRESSION OF COSTIMULATORY LIGANDS



1. TNF, IL-1, IL-6 and IL-8 contribute to inflammation -increased vascular permeability, influx of phagocytes

2. "Acute Phase" response induced via hepatocytes by IL-6 Transcriptional induction of:

Fibrinogen

α -2 macroglobulin Complement proteins C-reactive protein

3. TNF and IL-1 can also reset the hypothalamic thermostat and contribute to an increase in body temperature





For more information and examples, see Immunobiology, by Janeway, C., Travers, P., Walport, M. and Capra, J., Garland Publishing, 5th edition, 2001 & Cellular and Molecular Immunology by Abbas, A., Pober, J., and Lichtman, A., W B Saunders; 4th edition, 2000.