I FAGOCITI. FENOTIPO E FUNZIONI

Prof Giovanni Bernardini 28-10-2026

Il materiale contenuto in questo documento e distribuito a uso interno e a puro scopo didattico

RIASSUMENDO…

L'antigene è una molecola microbica riconosciuta da recettori dell'immunità innata?

SI/NO?

How do the components of the innate immune system recognize pathogens?

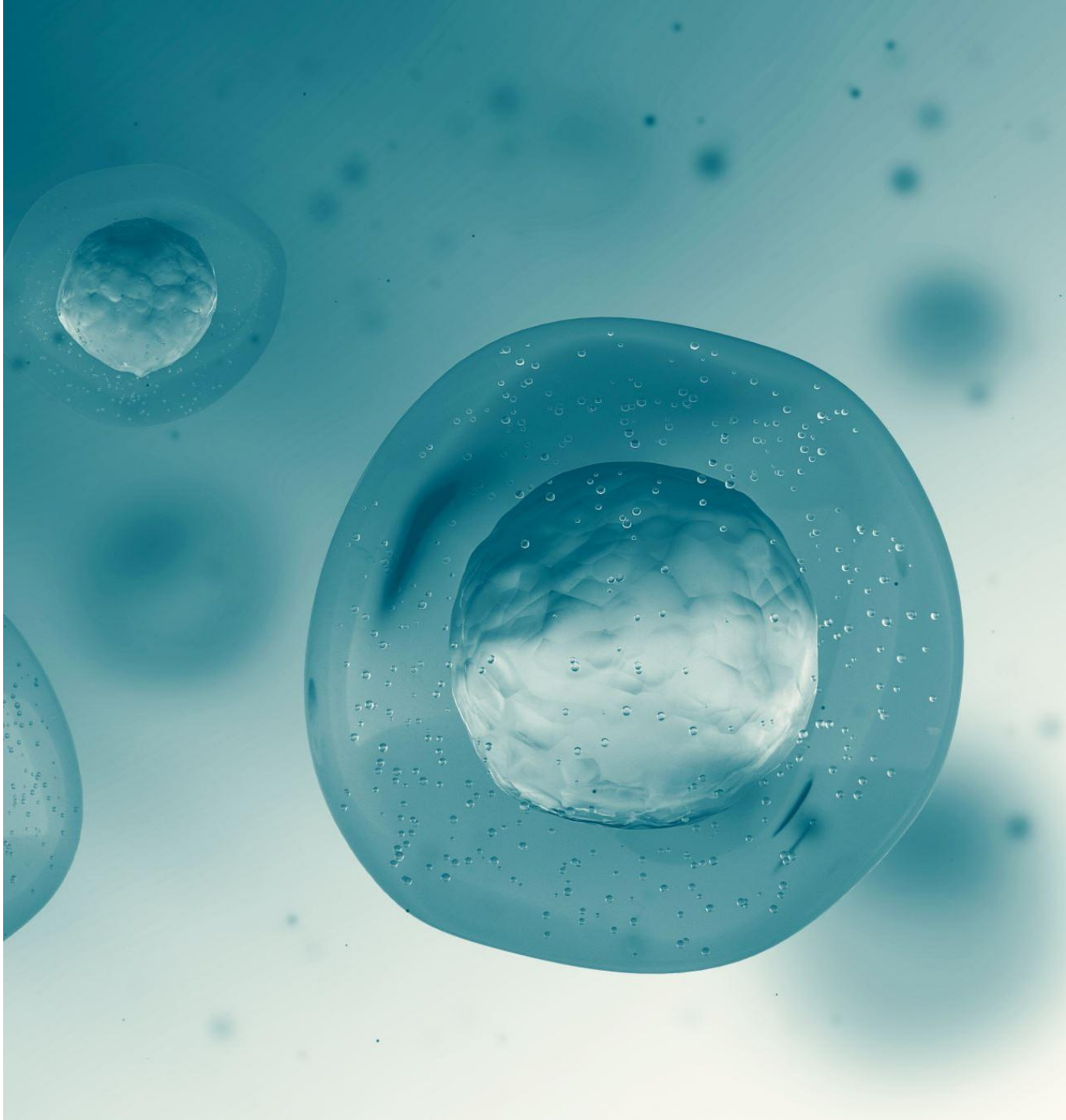
Which of these cellular components belong to the innate immune system?
Monocytes
T lymphocytes
Natural Killer cells
B lymphocytes

What is a DAMP?
A microbial molecule recognized by PRR
A host biomolecule that exert microbicidal activity
A host biomolecule released during tissue damage and is recognized by PRR
A host biomolecule that can be recognized by TCR

Which of the following statements about TLR is correct?
are expressed exclusively on the cell membrane
are expressed exclusively in the cytoplasm
are expressed both on the cell membrane and in the cytoplasm
are expressed at the nuclear level

Cells need intra-cellular pathogen recognition

In the cytoplasm



NOD-like receptors (NLR) constitute a family of more than 20 cytosolic proteins able to recognize PAMP and DAMP and assemble signal transduction complexes. containing a **nucleotide-binding oligomerization domain** (NOD)



At least three domains:

1- domain containing repeated leucine residues (LRR) for recognition

2- NOD domain responsible for oligomerization

3. Effector domain that recruits proteins involved in signal transduction and can be of three subfamilies: **CARD**, **Pyrin** and BIR

NOD1 e NOD2 (CARD family)

Recognize peptydoglycans on bacterial cell wall

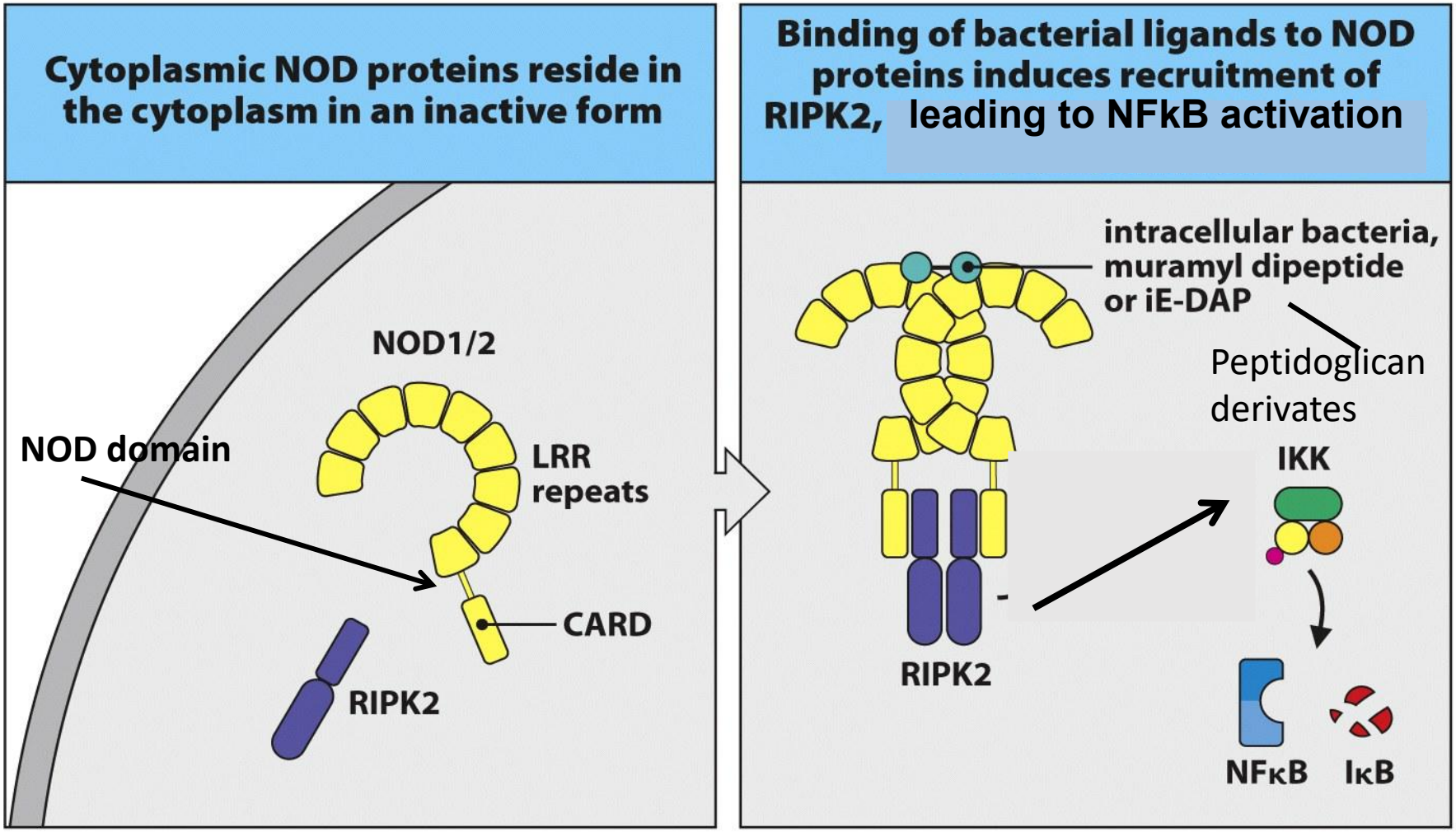


Figure 3.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

CARD:Caspase Activation and Recruitment Domain

RIPK2: Receptor-Interacting Protein (RIP) family of serine/threonine protein kinases type 2

Epithelial and phagocytic mucosal cells express NOD1/2

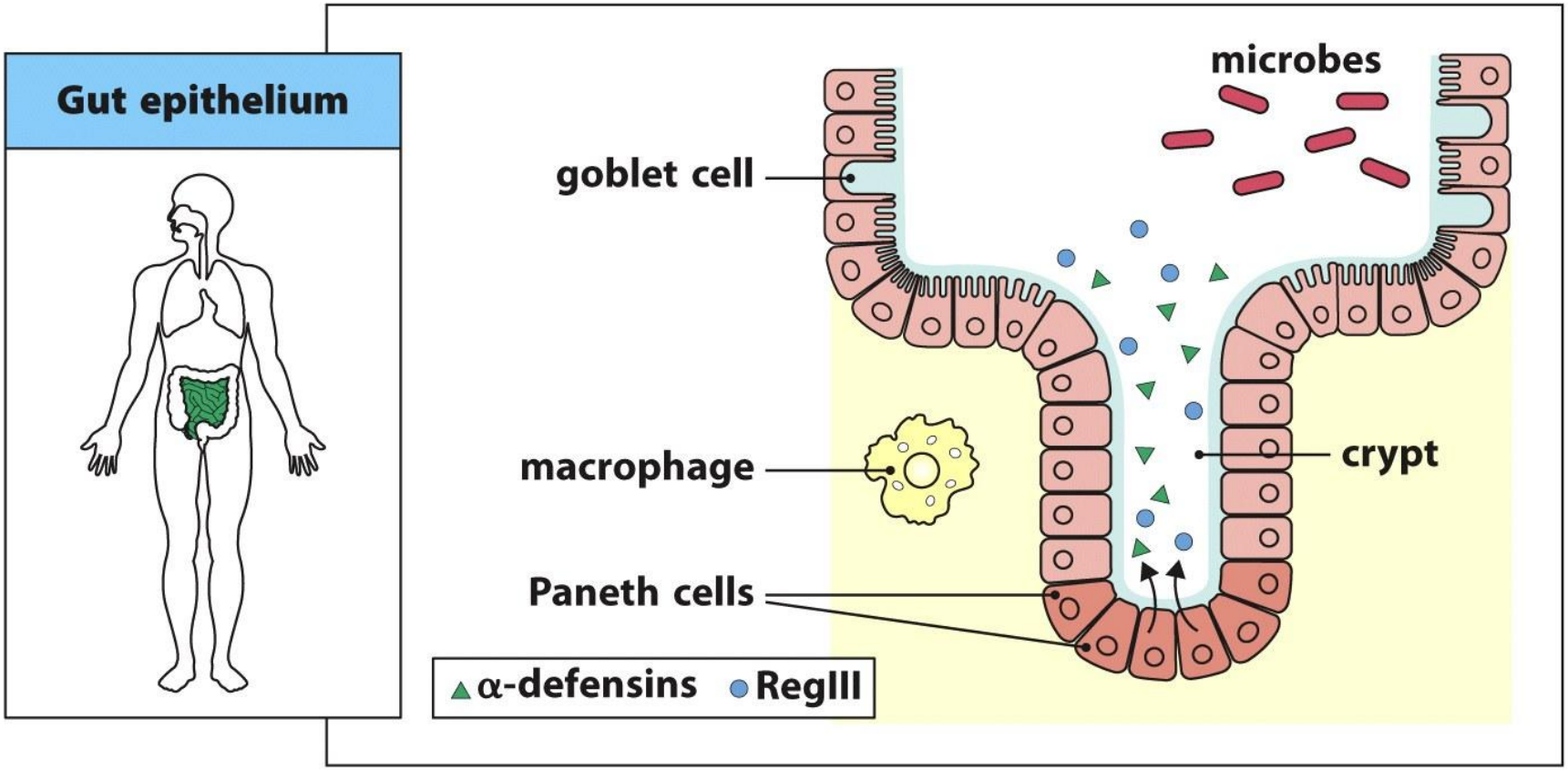


Figure 2.10 part 3 of 3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

NOD1 / 2 mediate the response to pathogenic bacteria of the gastrointestinal tract including *Helicobacter pylori* and *Listeria Monocytogens*

While NOD1 is expressed by many cell types, NOD2 seems to have a specialized and non redundant role, being strongly expressed in the gut (prevalently by Paneth cells and by goblet cells) where it regulates the expression of potent antimicrobial peptides such as the defensins and of mucus.

Loss-of-function variants in NOD2 in humans increase susceptibility to the inflammatory bowel condition known as **Crohn's disease** due to impaired bacterial clearence.

L'inflammasoma

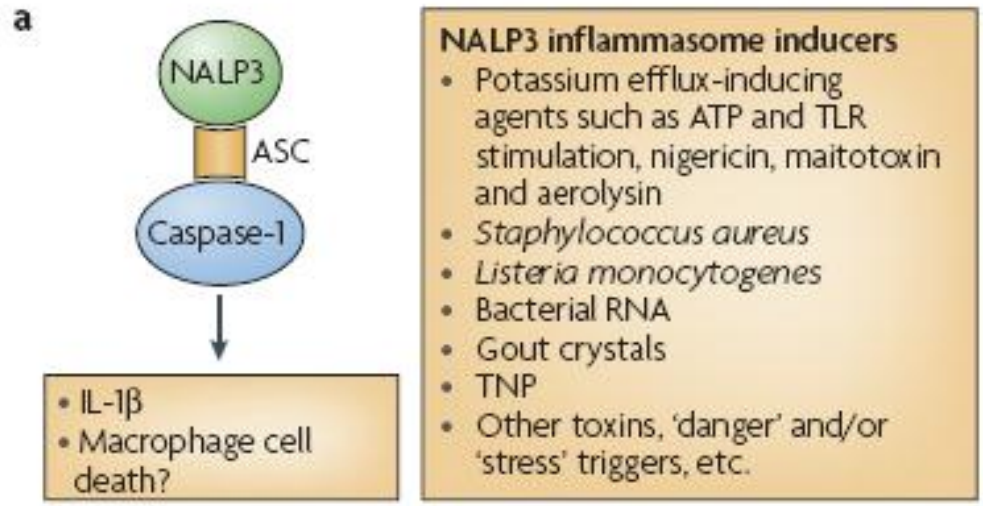
Famiglia dei recettori NOD-like Pyrin NLRP

Gli inflammasomi sono complessi multiproteici che si formano in seguito a presenza di DAMPS e PAMPS nel citosol.
Hanno la funzione di generare la forma matura di citochine pro-infiammatorie molto importanti chiamate IL-1beta e IL-18

In aggiunta possono indurre la morte delle cellule che producono queste citochine **(piroptosi)** per promuoverne il rilascio

L'inflammasoma e i suoi corecettori

Famiglia NLRP
NOD-like receptor contenente dominio Pyrin



Organizzazione generale:
1- sensore dell'inflammasoma (contenente i tre domini dei **NLR**)
2- un adattatore *ASC* codificato dal gene *PYCARD* comune a tutti gli inflammasomi
3- la caspasi-1 connessa al recettore tramite *ASC*

La diminuzione del K^+ citoplasmatico è un segnale che favorisce l'assemblaggio dell'inflammasoma NLRP3

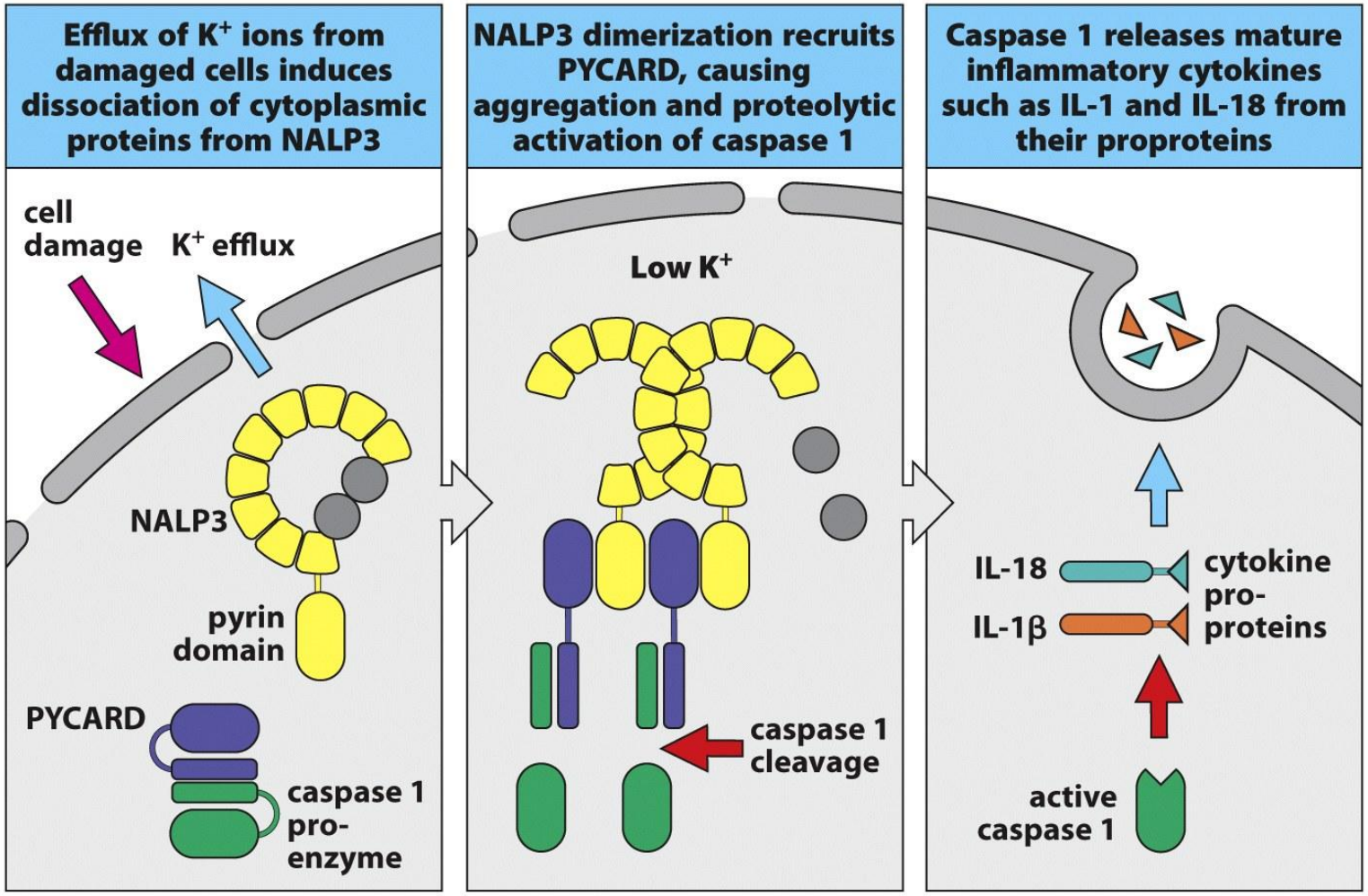


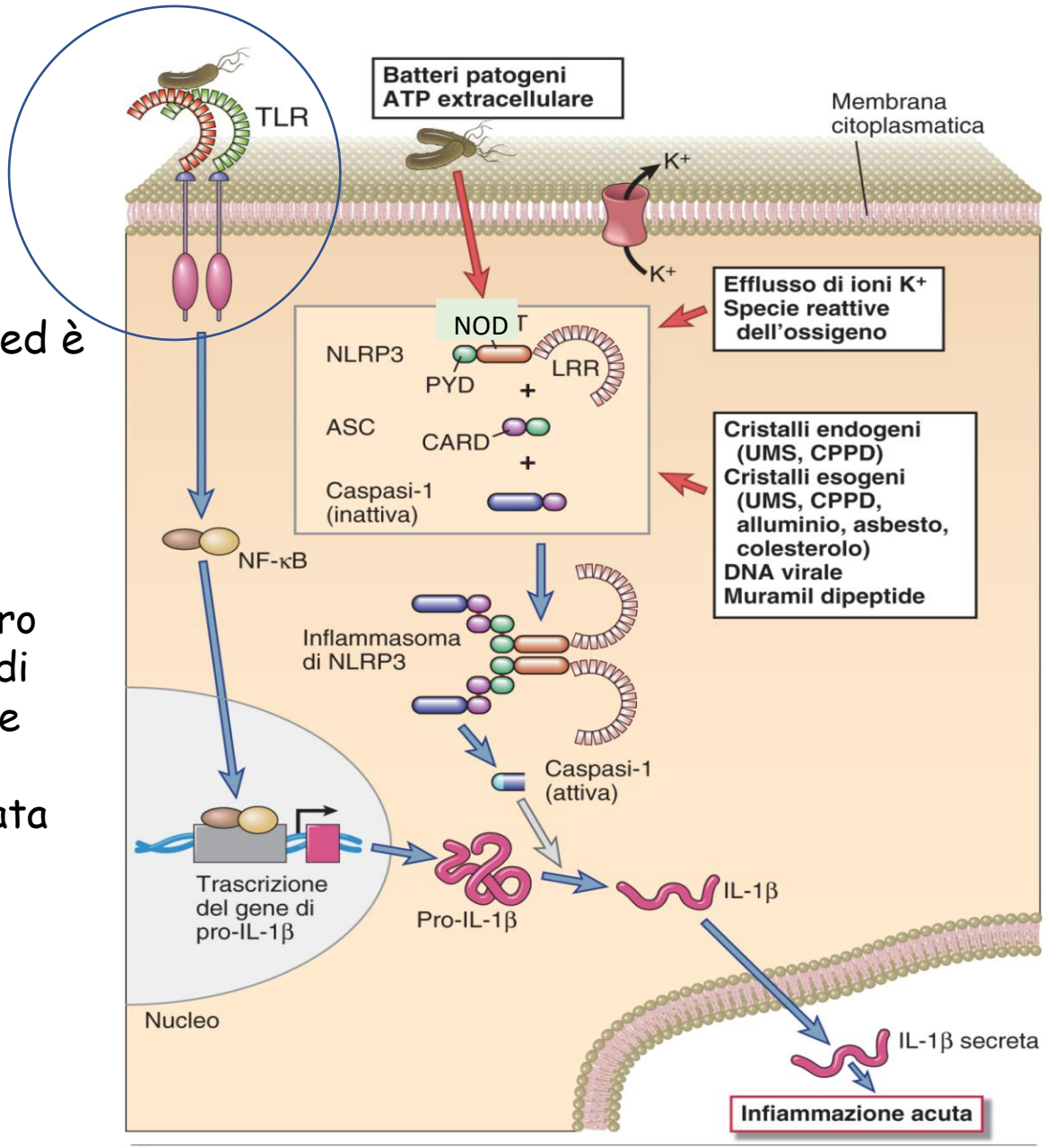
Figure 3.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

PYCARD è ASC **Casp**ase:**cysteine**-dependent aspartate-directed proteases

L'inflammasoma e i suoi corecettori (Pyrin family)

ASC serve da adattatore ed è composta da un dominio Pyrin e un dominio CARD

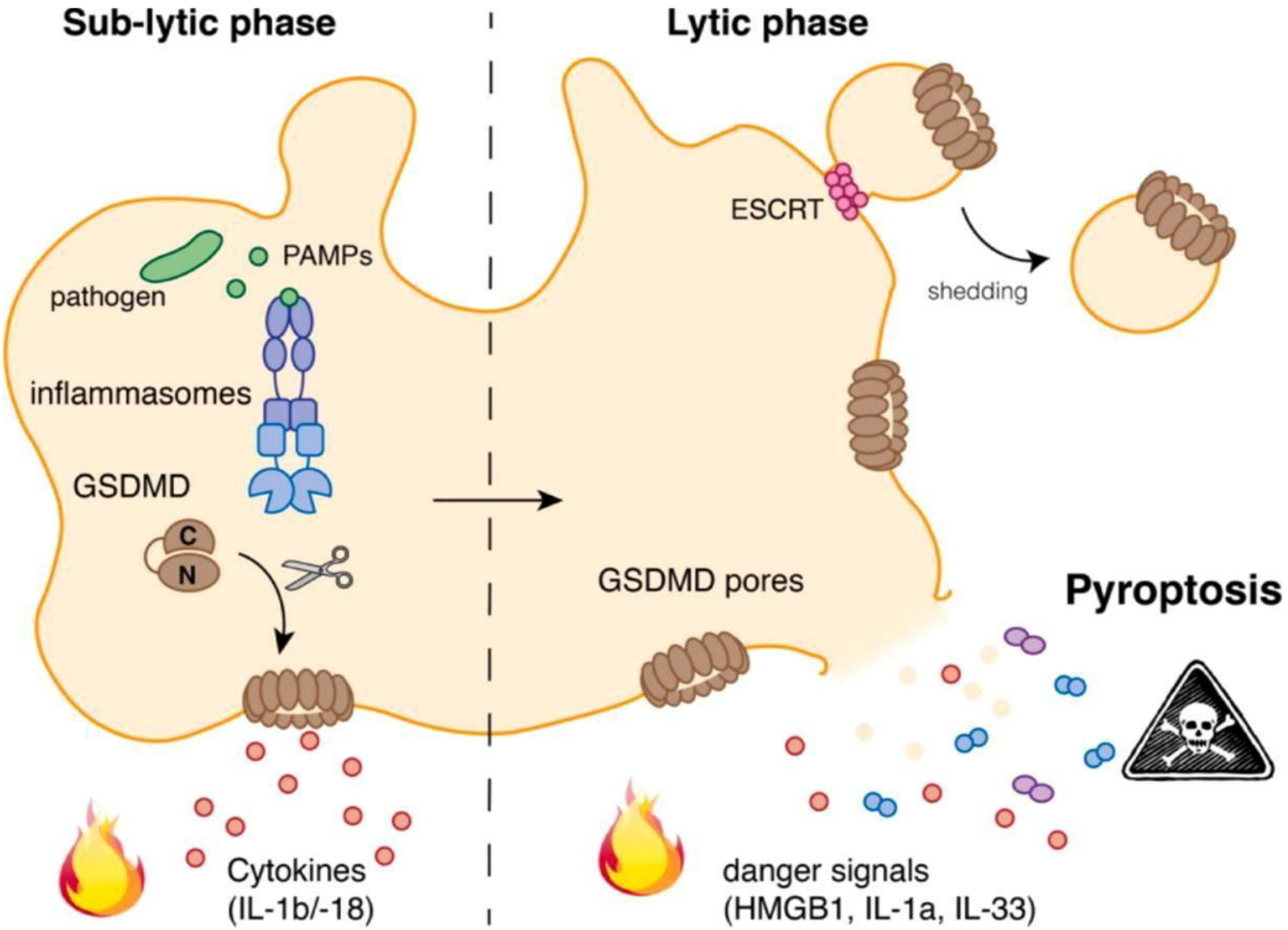
Queste citochine potrebbero essere rilasciate a seguito di una forma di morte cellulare programmata associata alle infezioni microbiche chiamata **Piroptosi**



Introducing GASDERMIN D..

the identity of the pyroptosis-inducing membrane pore remained unknown until 2015, when gasdermin D (GSDMD) was discovered as a pore-forming caspase-1 substrate and the single executor of inflammasome-associated pyroptosis

Lytic and sub-lytic functions of gasdermin D pores



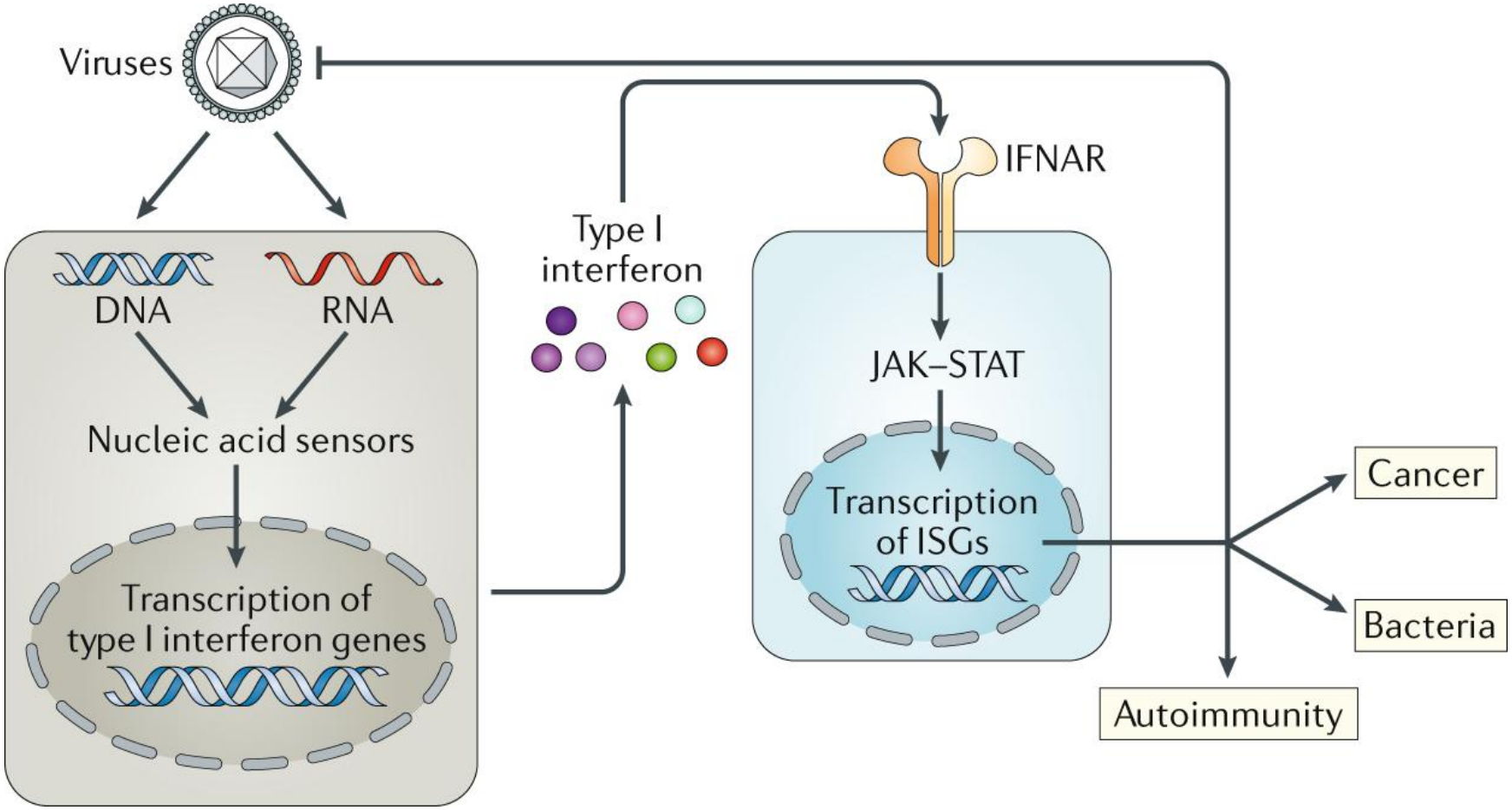
What happens when inappropriate activation of inflammasome occurs?

Gout has been known for many years to cause inflammation in the cartilaginous tissues by the deposition of monosodium urate crystals, Urate crystals are known to activate the NLRP3 inflammasome, which induces the inflammatory cytokines associated with the symptoms of gout.

Mutations in the NOD domain of NLRP2 and NLRP3 can activate inflammasomes inappropriately, and they are the cause of some inherited **autoinflammatory diseases**, in which inflammation occurs in the absence of infection.

Mutations in NLRP3 in humans are associated with hereditary periodic fever syndromes due to spontaneous production of IL1-beta by macrophages.

Intracellular Viral Sensing Pathways promote type I interferon expression



Outline of the lesson

What are phagocytes?

What is the origin of phagocytes?

Phagocyte heterogeneity. Diversification of macrophages into subpopulations.

Phagocytosis, what else? Functions of phagocytes.

Phagocytes are cells able to perform phagocytosis

Phagocytosis (from Ancient Greek «*phago*» , **meaning** 'to eat', and «*kytos*» , **meaning** 'cell') Greek *–ōsis* meaning a process (often associated to a disease)

In summary phagocytosis is the cell uptake of particulate material (leading to cell disruption)



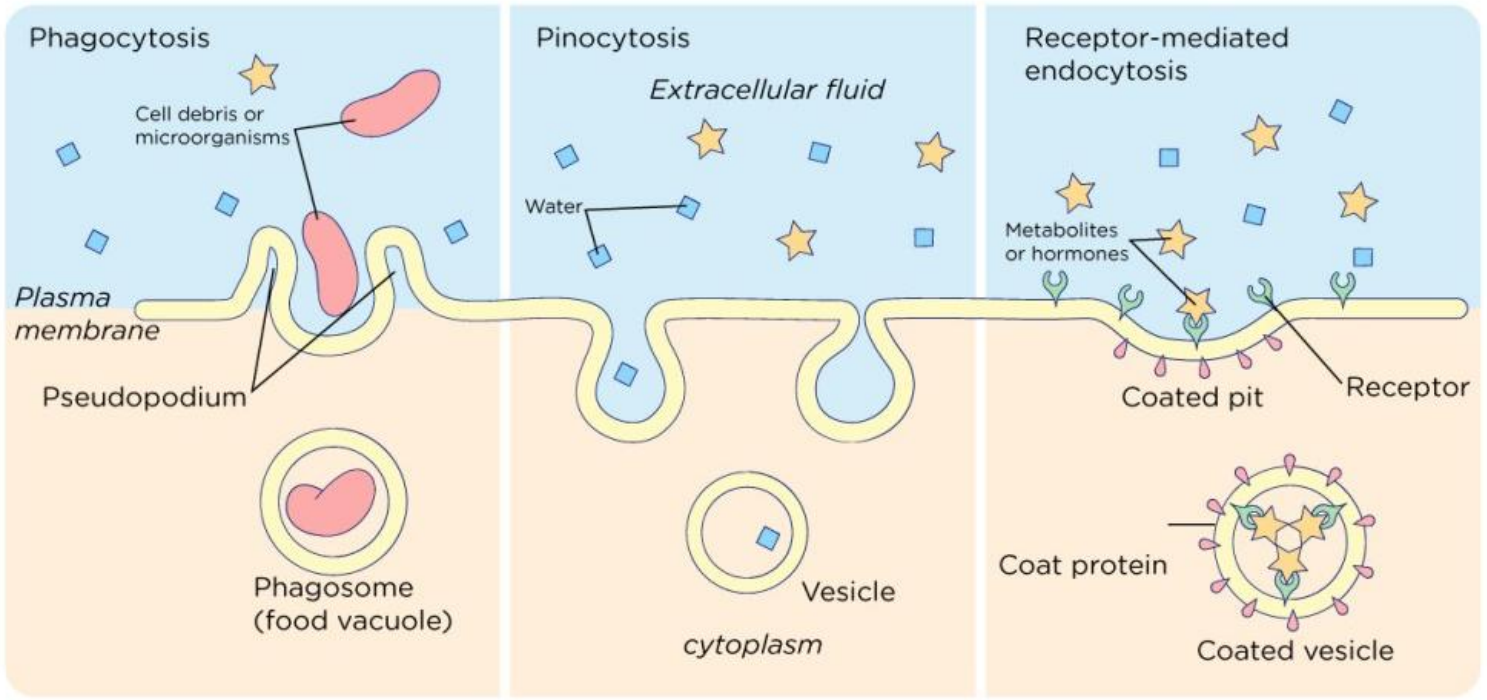
Phagocytosis

It is central to innate and adaptive immunity **against pathogens**

Phagocytosis contributes to the **physiological turnover** of erythrocytes and leukocytes by clearing senescent or dying cells

Overall, phagocytosis is the principal mechanism for **clearing dying and dead cells** in the mammalian body

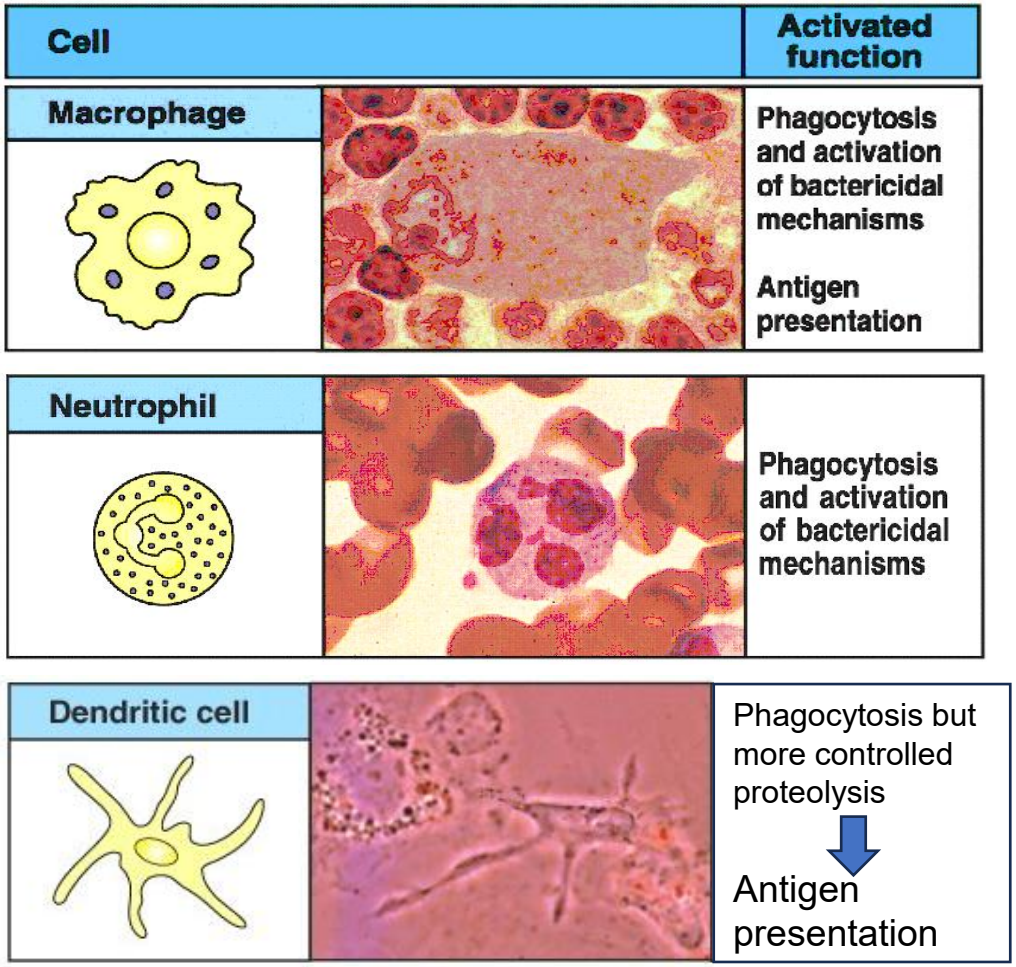
Phagocytosis is a type of receptor-mediated endocytosis



Phagocytosis is the engulfement of particulate material

L'INGLOBAMENTO E LA DISTRUZIONE DEI MICROBI E' MEDIATA DA FAGOCITI

Macrofagi, neutrofili e cellule dendritiche effettuano una efficace fagocitosi e per questo sono chiamati *fagociti professionisti*



Riconoscono il non-self (PAMPs) o il self modificato (DAMPs) e rispondono:

I **macrofagi e cellule dendritiche** tramite fagocitosi, o secrezione di citochine per partecipare alla **funzione 1**).
… ma nel frattempo interagiscono con linfociti T per promuovere la loro attivazione **(funzione 2)**.

I neutrofili svolgono prevalentemente funzioni microbicide (fagocitosi, rilascio di granuli contenenti enzimi litici e nettosi)

Che tipo di recettori possono mediare la fagocitosi?

CRD: Carbohydrate recognition domain

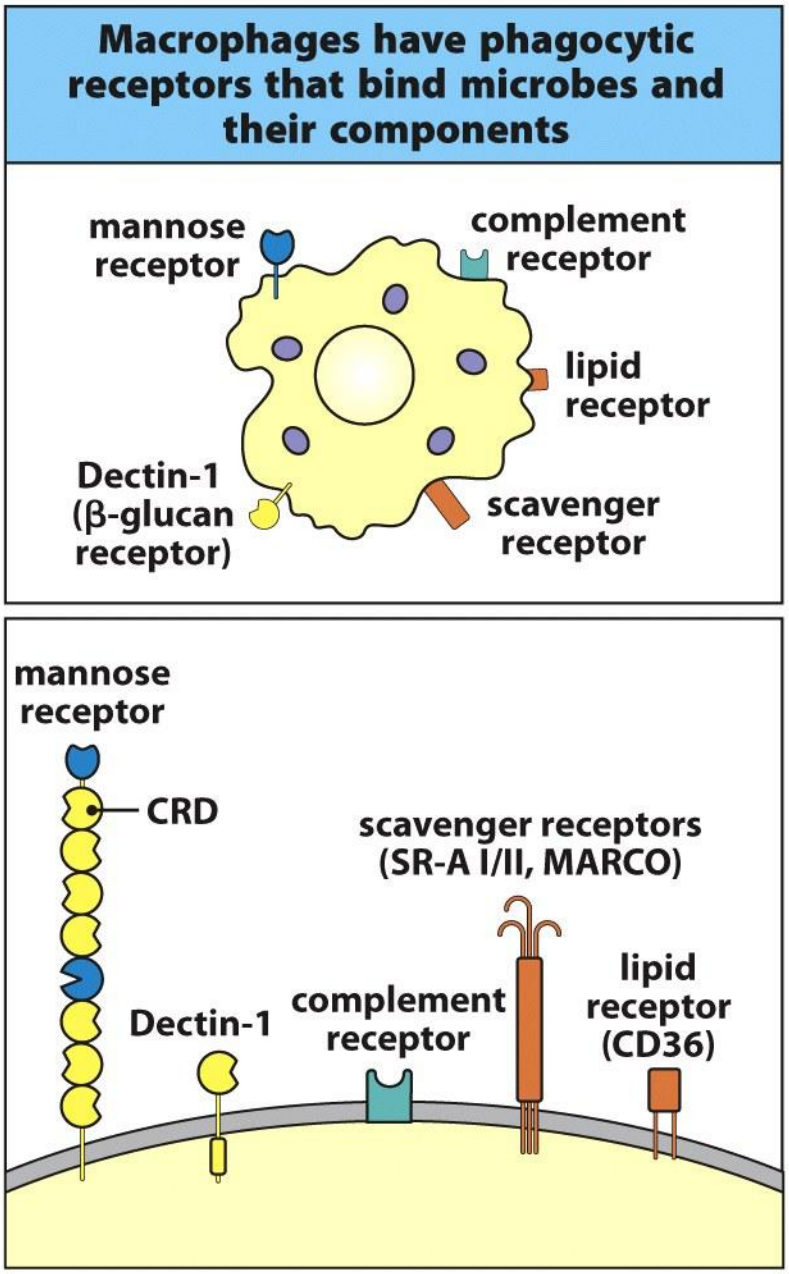


Figure 3.2 part 1 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Phagocytes take part to the innate immune response

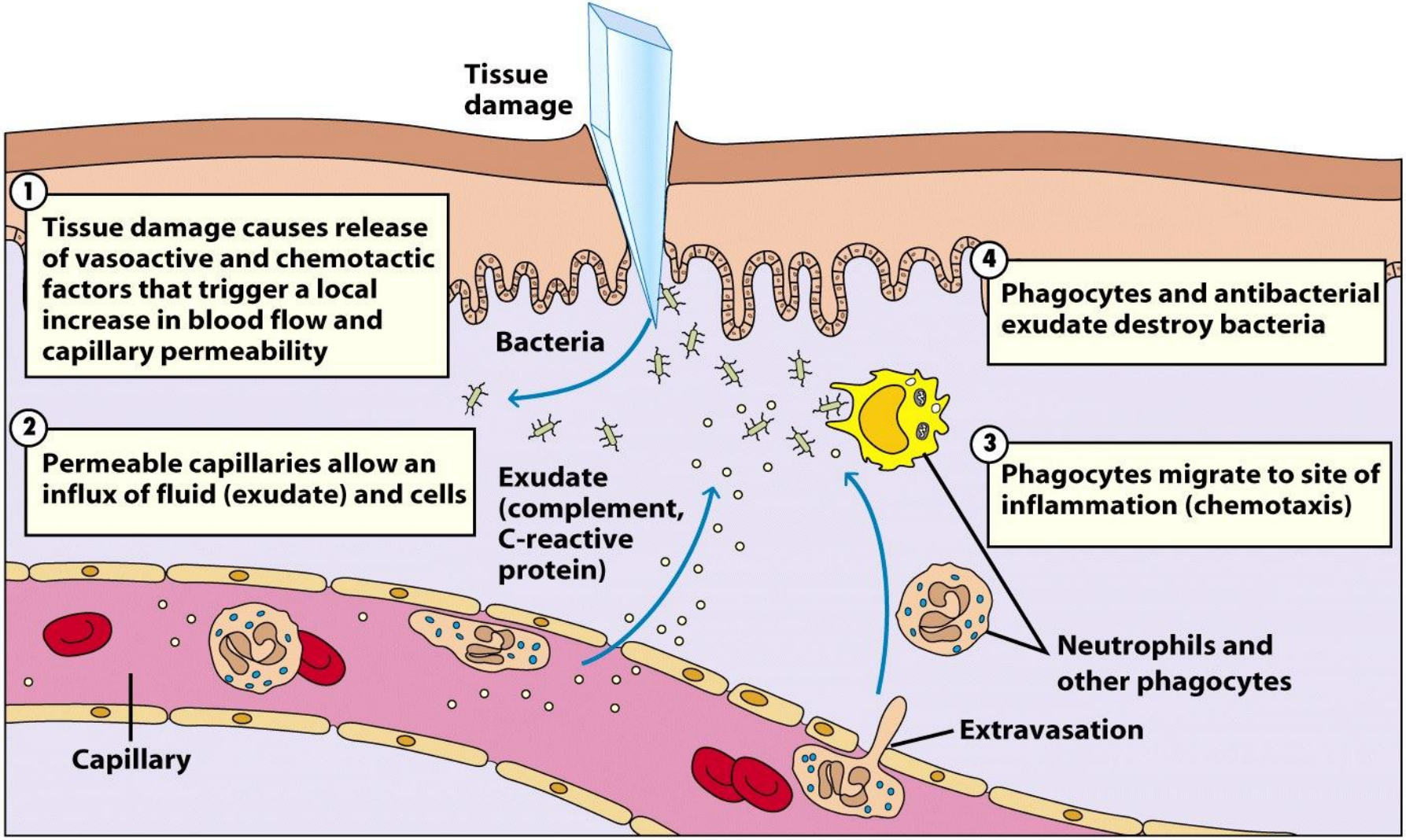


Figure 3-5
Kuby IMMUNOLOGY, Sixth Edition
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Phagocytes take part to the innate immune response

- Neutrophils are the most abundant population among the circulating white blood cells.
- Neutrophils are short-lived cells (1-2 days) and they die immediately after completing a phagocytosis cycle.
- Dead neutrophils are the main components of pus formed in certain infections caused by extracellular bacteria called pyogenic bacteria (or pus generators).
- Macrophages, on the contrary, are tissue cells which have a long life and the capacity to continuously generate new lysosomes.

Phagocyte-mediated immune response is fundamental for protection

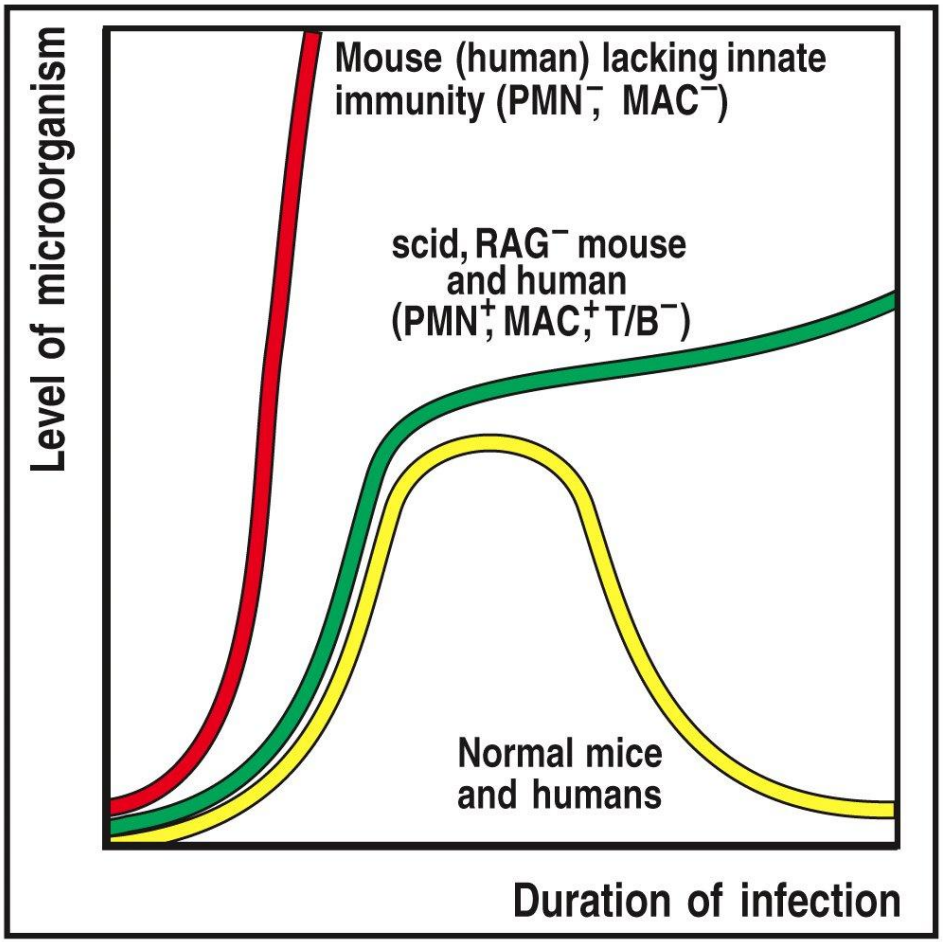


Figure 10-6 Immunobiology, 6/e. (© Garland Science 2005)

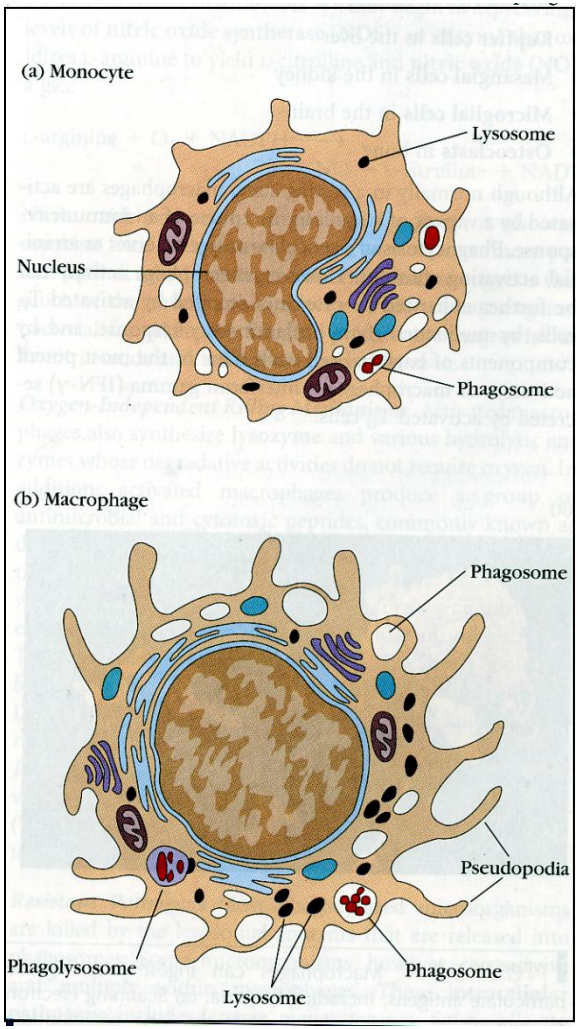
PMN: polymorphonuclear cells; MAC: Macrophages; T/B: T and B lymphocytes

ORIGINE DEI MACROFAGI e NEUTROFILI

Macrophages differentiate from circulating monocytes when these cells enter the tissues

Monocyte-macrophage differentiation:

- Increase in size of 5-10 times
- Increase in the number of organelles (lysosomes)
- Increased phagocytic capacity



ORIGINE DEI MACROFAGI
contributo dei monociti circolanti alla generazione di due tipi di macrofagi

MONOCITI INFIAMMATORI (MACROFAGI INFIAMMATORI O IMMUNOLOGICAMENTE STIMOLATI)

I monociti richiamati dal sangue durante la risposta infiammatoria differenziano in macrofagi dotati di proprietà fagocitiche citotossiche e capacità proinfiammatoria e di presentazione dell'antigene

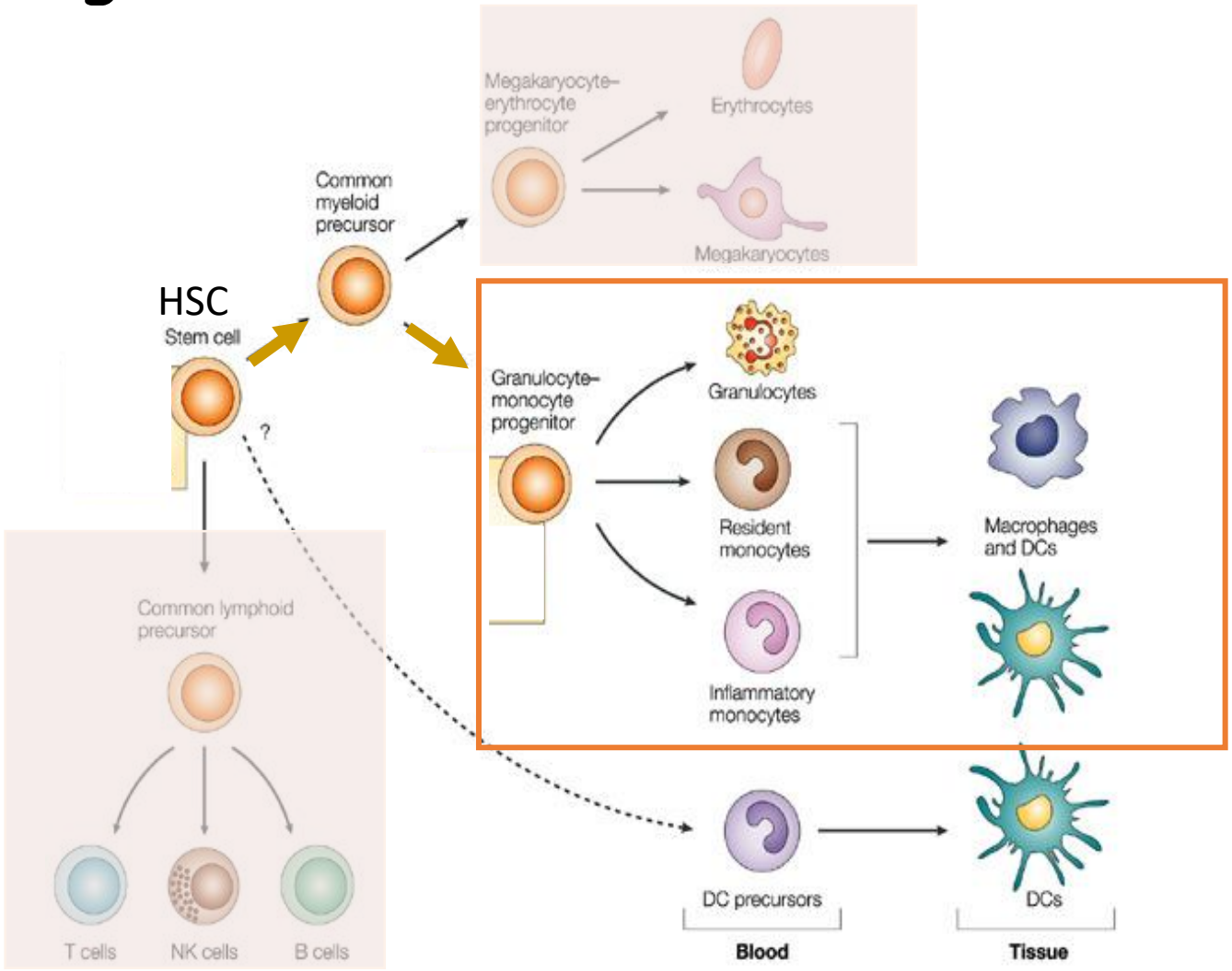
MONOCITI RESIDENTI (MACROFAGI RESIDENTI)

Hanno una funzione di sentinella e clearence e così facendo contribuiscono a mantenere le funzioni tissutali

Iniziano la risposta infiammatoria acuta e il rimodellamento vascolare

Importante: Per i neutrofili abbiamo solo la controparte circolante che, come detto, ha vita breve e non diventa residente una volta entrata in tessuti

After birth, myeloid phagocytes are generated in the bone marrow



Nature Reviews | Immunology

Phagocytes are cells of the hematopoietic system

Origine dei macrofagi:
i precursori dei macrofagi residenti e infiammatori possono essere identificati nel sangue

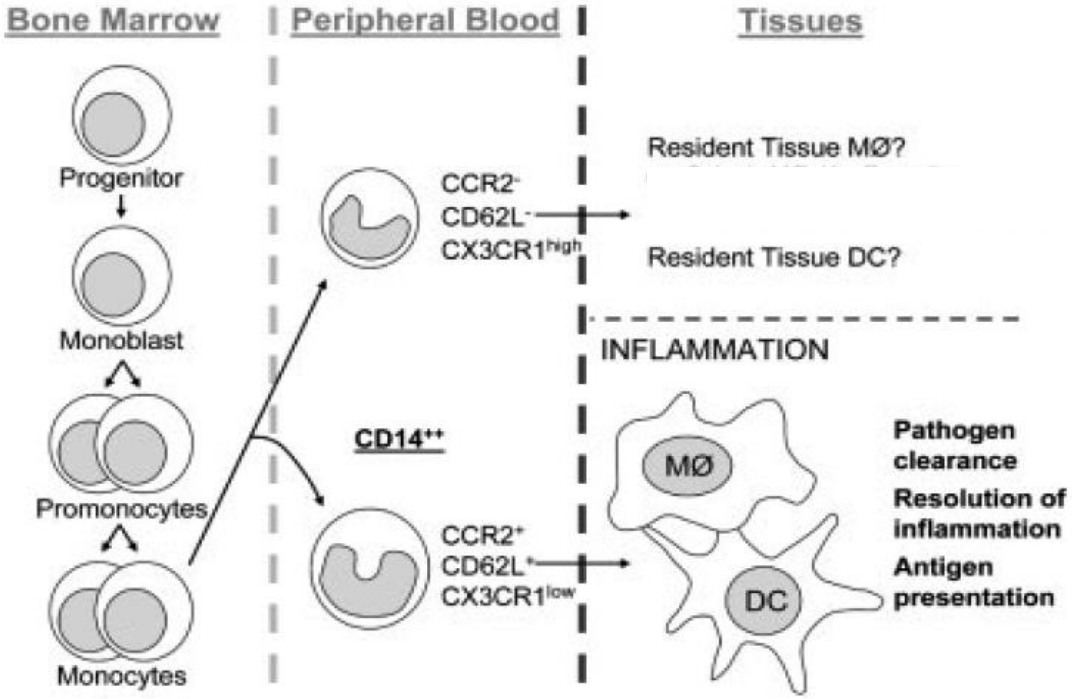
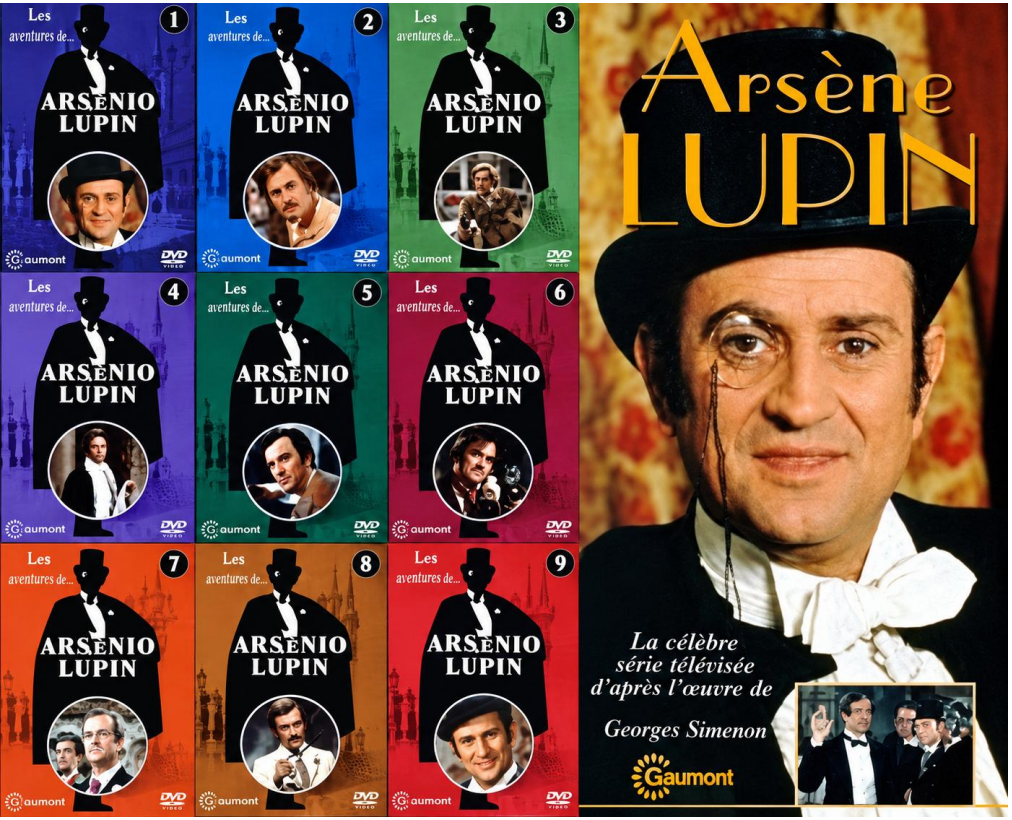


Figure 3. Differentiation and distribution of mononuclear phagocytes. Distinct subpopulations of circulating monocytes are thought to give rise to resident tissue macrophages, DC and osteoclasts compared with cells recruited by an inflammatory or immunologic stimulus. Further phenotypic heterogeneity

NELL'UOMO I MONOCITI INFIAMMATORI SONO CD14+CCR2+ E I MONOCITI RESIDENTI SONO CD16+CX3CR1+

Grazie alla loro versatilità (plasticità), i macrofagi sono abili trasformisti …come Arsenio lupin



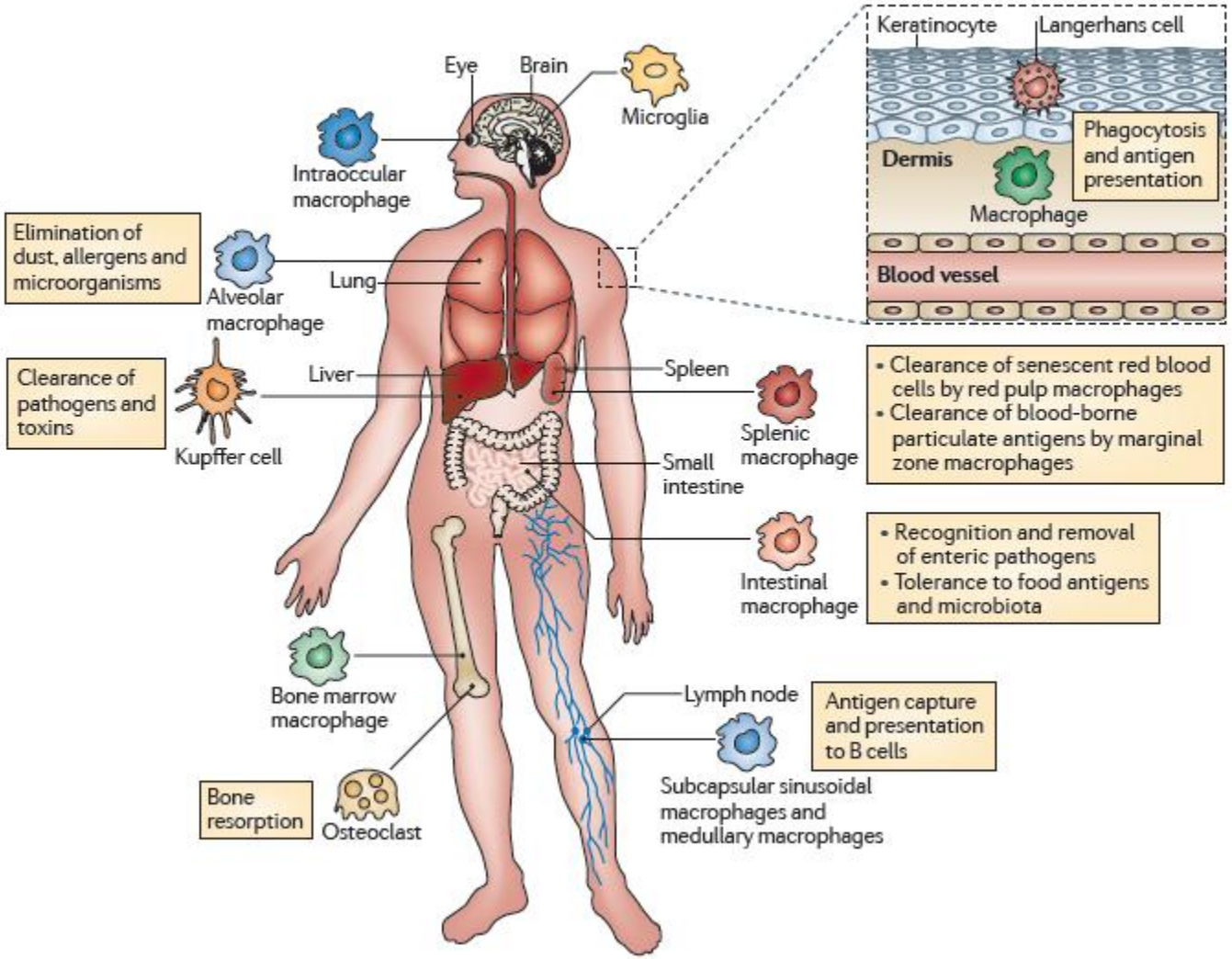
I **macrofagi residenti** si trovano in quasi tutti i tessuti per perlustrare l'ambiente e svolgere una serie di funzioni degradative e difensive **«housekeeping»**,

I monociti differenziano in macrofagi con **caratteristiche funzionali differenti a seconda dell'ambiente in cui si trovano**.

Vedremo poi che i macrofagi stessi possono acquisire un comportamento pro- o anti-infiammatorio se opportunamente stimolati

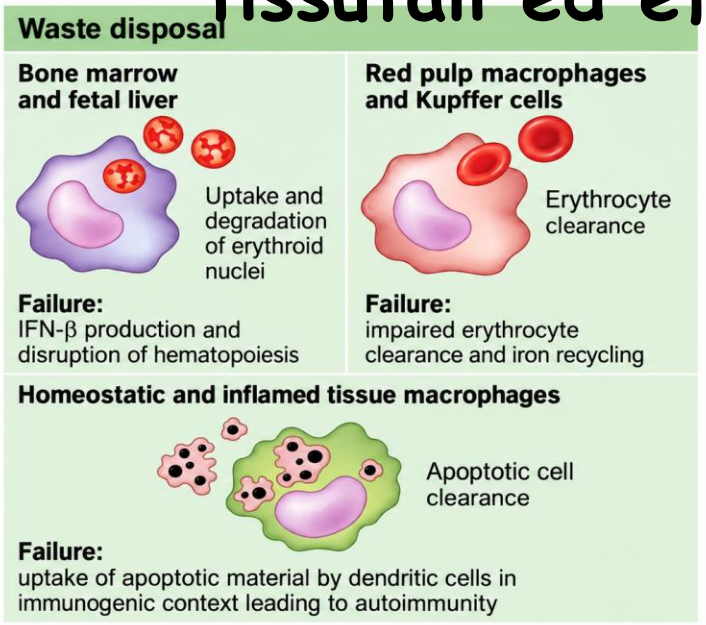
Funzioni fisiologiche dei macrofagi tissutali

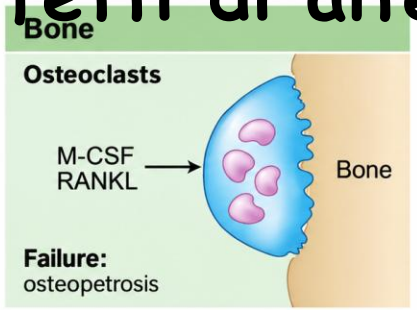
One of the major hallmarks of resident macrophages is their heterogeneity, which is reflected by their specialized function in a particular microenvironment.

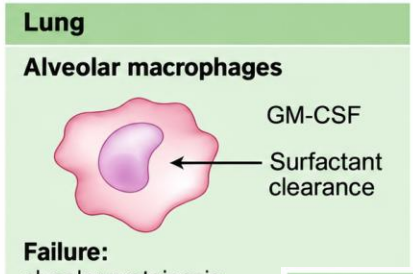


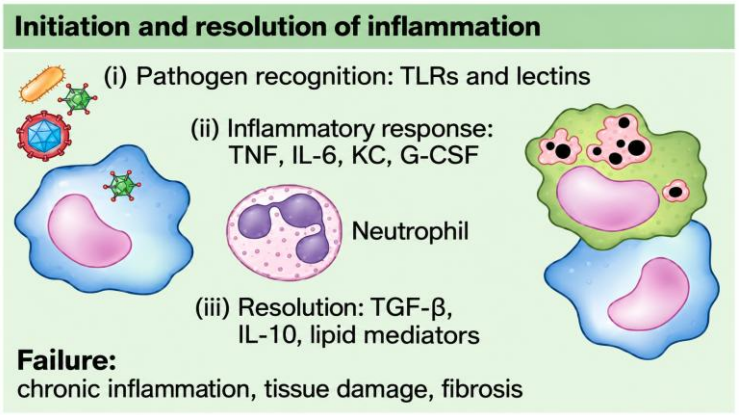
Transcriptional profiling of murine tissue macrophages isolated from the peritoneum, lung, spleen and the brain reveals that there is high diversity but some overlap in genes encoding molecules involved in phagocytosis of apopototic cells and PAMPS/DAMPS recognition

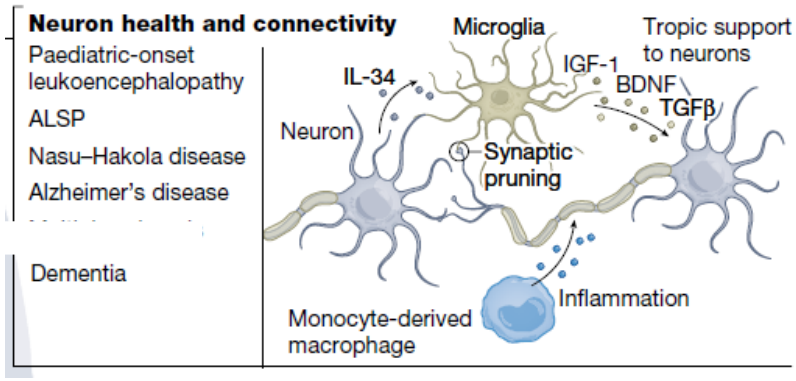
Funzioni fisiologiche e protettive dei macrofagi tissutali ed effetti di alterazioni funzionali











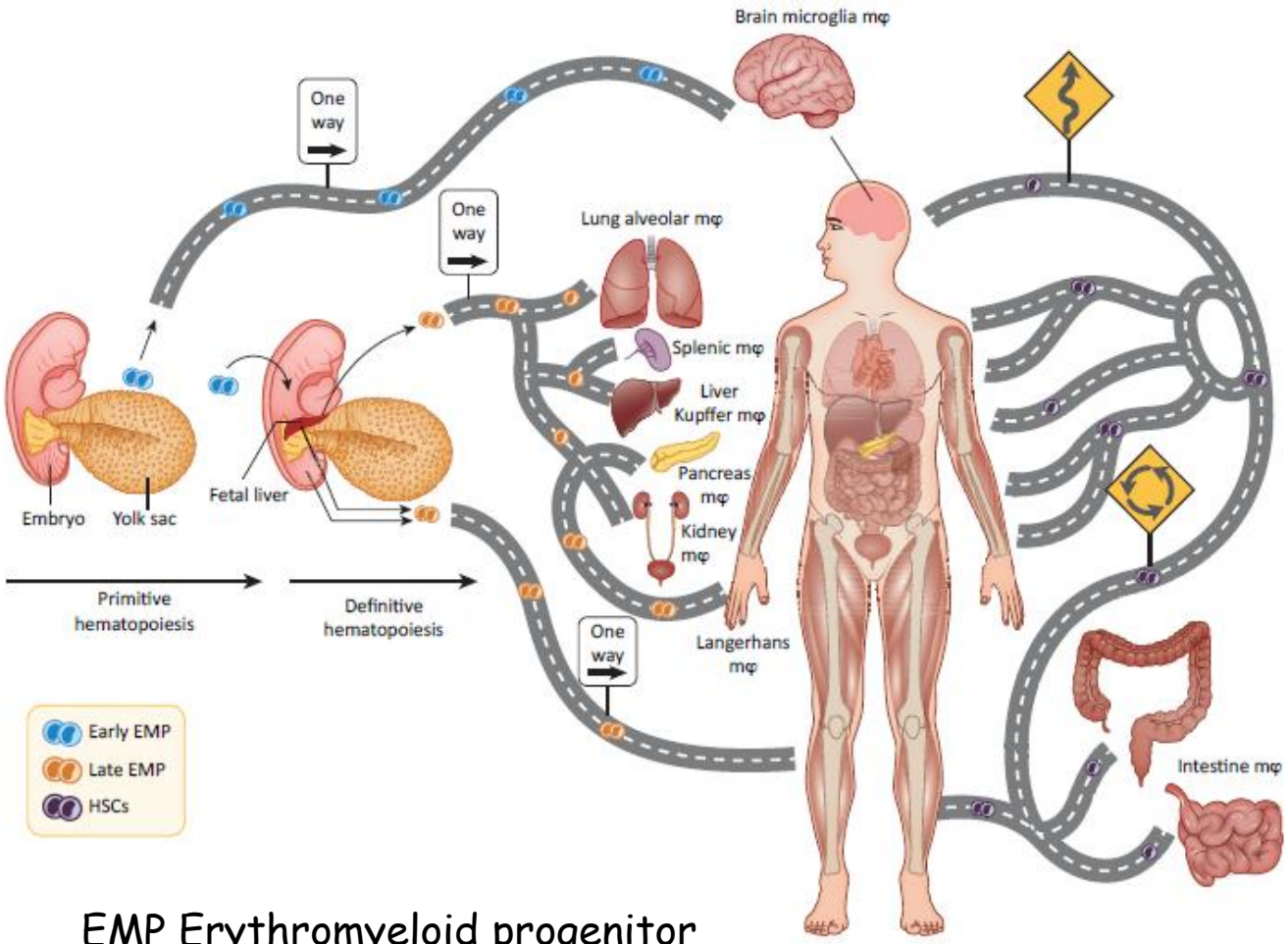
Davies et al. Nature Imm 2013

Lazarov et al. Nature Rev Imm 2023

- In contrast to the **classical model of macrophage development**, where macrophages differentiate from circulating monocytes…

….some type of tissue-resident macrophages **arise from yolk sac (sacco vitellino) or fetal liver-derived progenitors** and persist throughout life.

Road of Macrophage Ontogeny into tissues

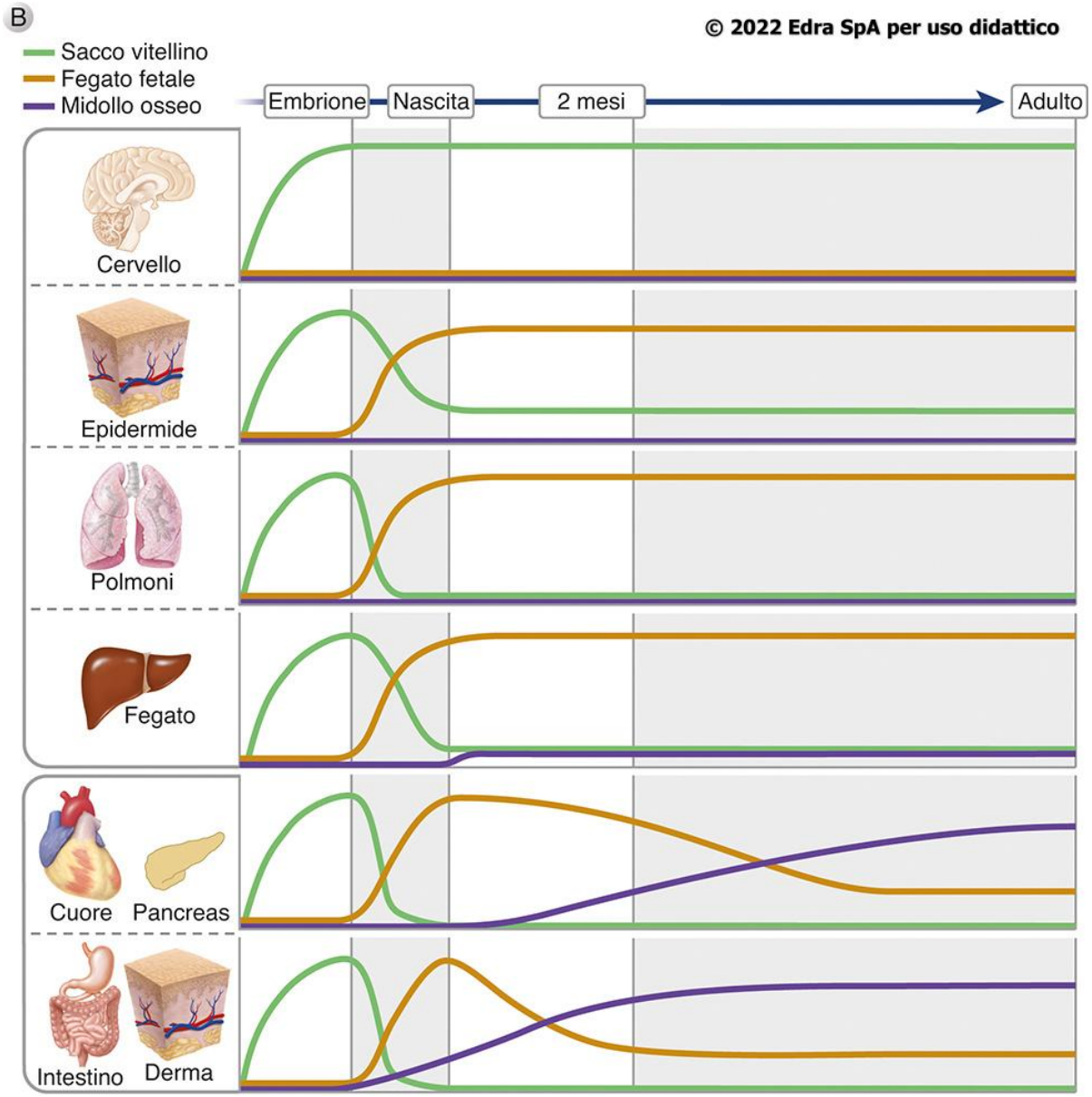


There are various types of macrophages in tissues, which arise from at least three distinct sources: the embryonic yolk sac (YS), the fetal liver (FL), and the **bone marrow (BM)**.

EMP Erythromyeloid progenitor

HSC Hematopoietic Stem Cell

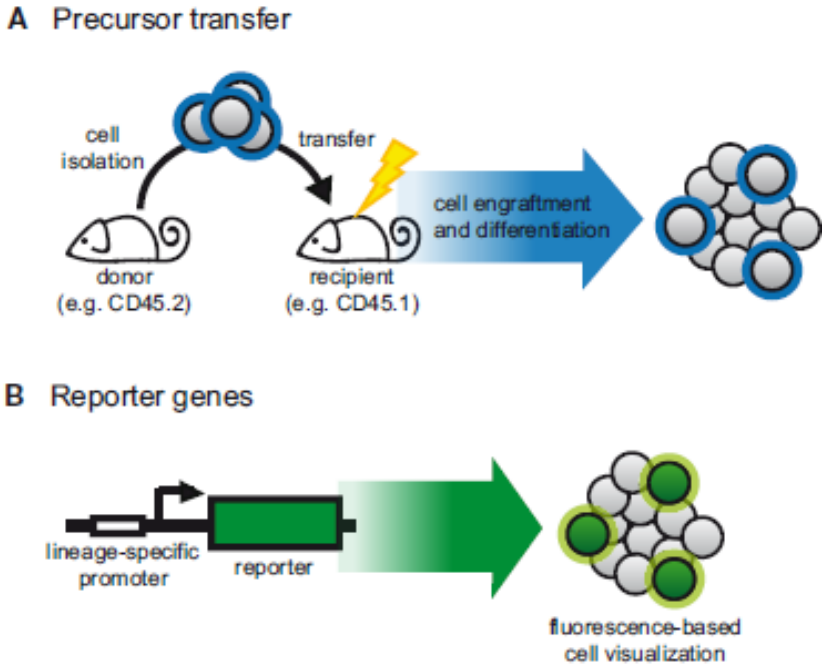
Macrophage Ontogeny into tissues



Certain tissues continue to recruit adult monocytes from the bone marrow to generate resident macrophages and **replace with time** the embryonic-derived macrophages.

How to track the developmental origin of tissue immune cells (fate mapping)

The transfer of purified and pre-marked precursor cells into congenic recipients is the most accessible form of fate mapping as a variety of labeling options can be used to distinguish between donor and host cells (A).

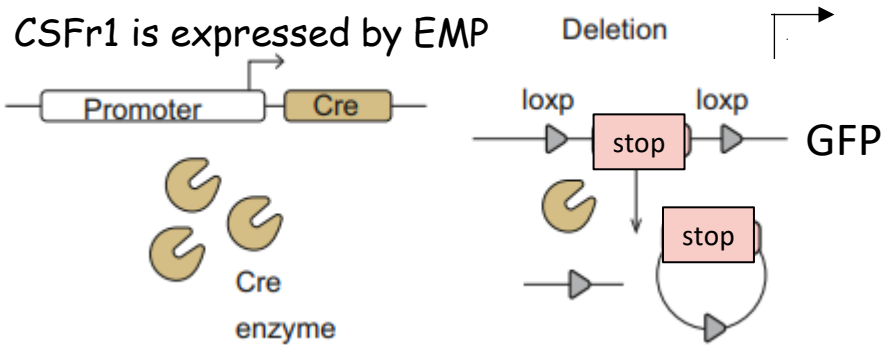


Lineage Restricted Reporters (lineage tracing) is used when the availability of isolatable progenitor cells is limiting and when populations are ontogenetically heterogeneous (B).

Fate Mapping studies

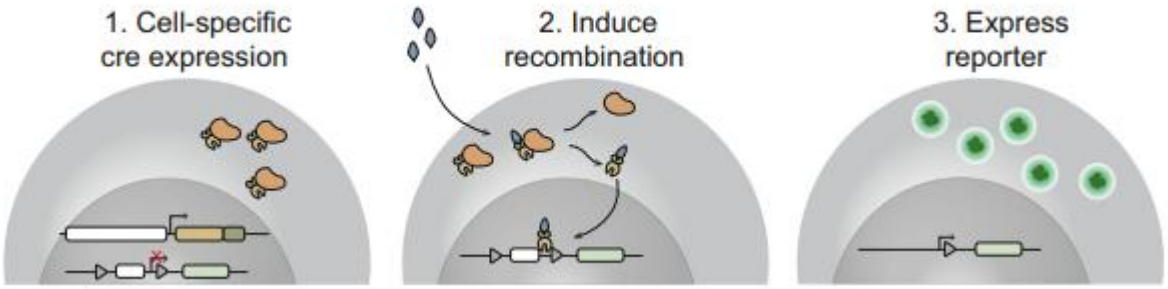
Fate-mapping mice are used to understand how cells of different developmental origins contributed to the assembly of organs and tissues.

In this system **Cre recombinase** drives a fluorescent protein that remains continually expressed UNDER THE CONTROL of a lineage-specific promoter



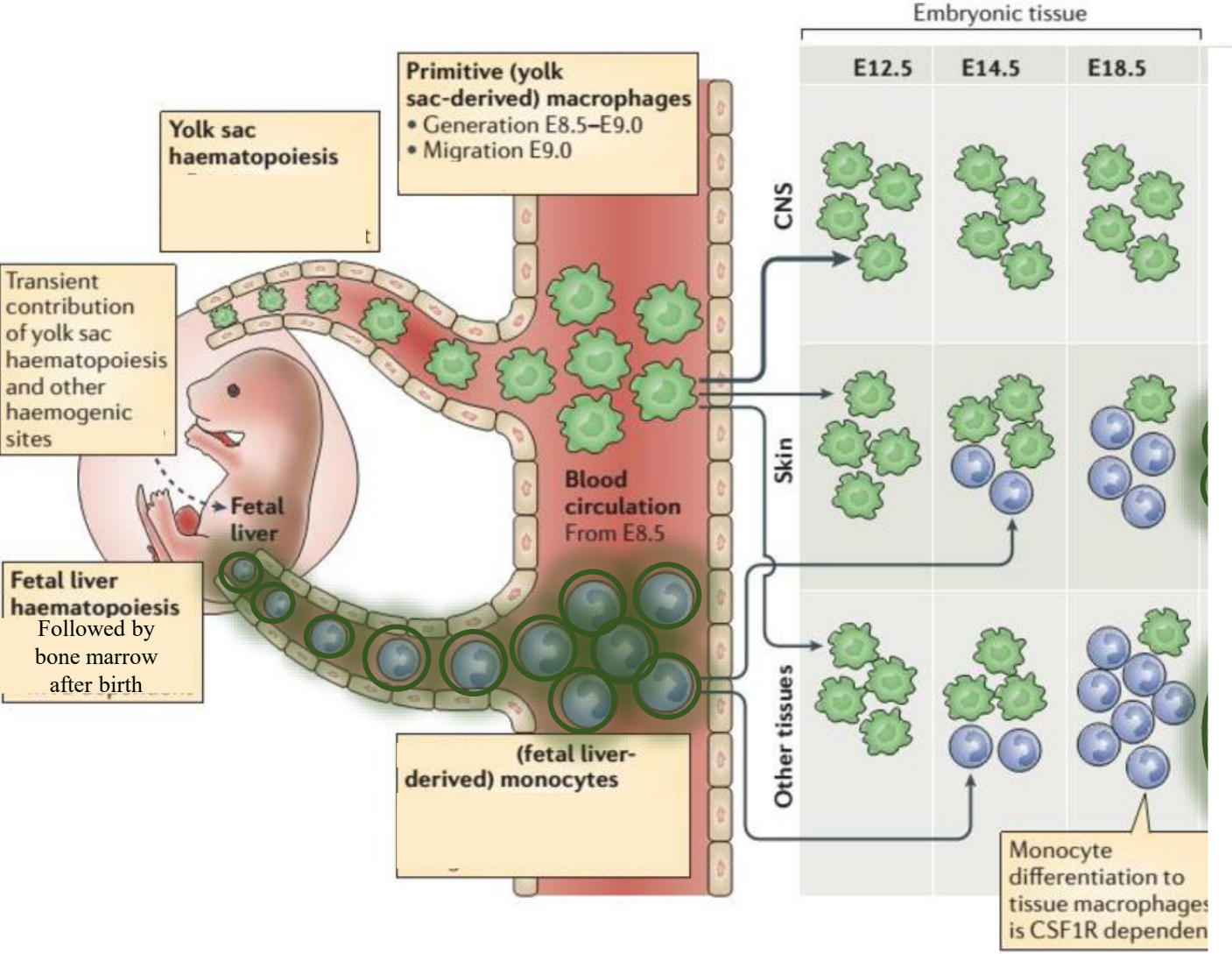
The selection of the promoter for lineage-defining genes is crucial to effective lineage tracing

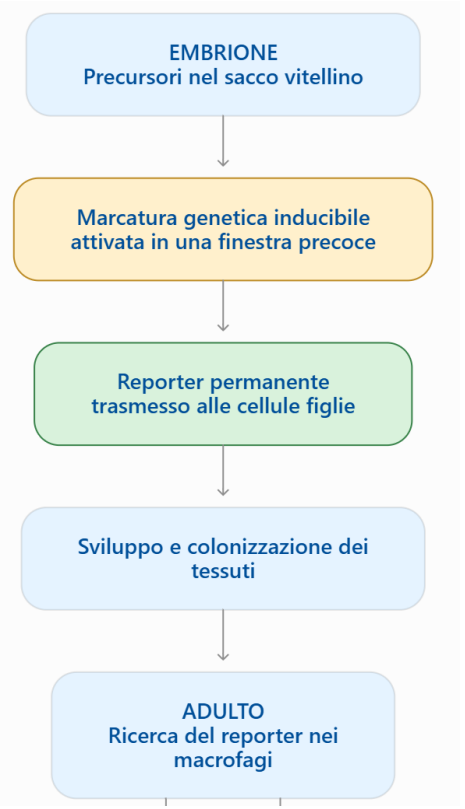
When the reporter is expressed, it becomes a permanent, heritable mark of the targeted cell population.



EMP progenitori eritromieloidi

How to track the developmental origin of tissue immune cells (fate mapping).

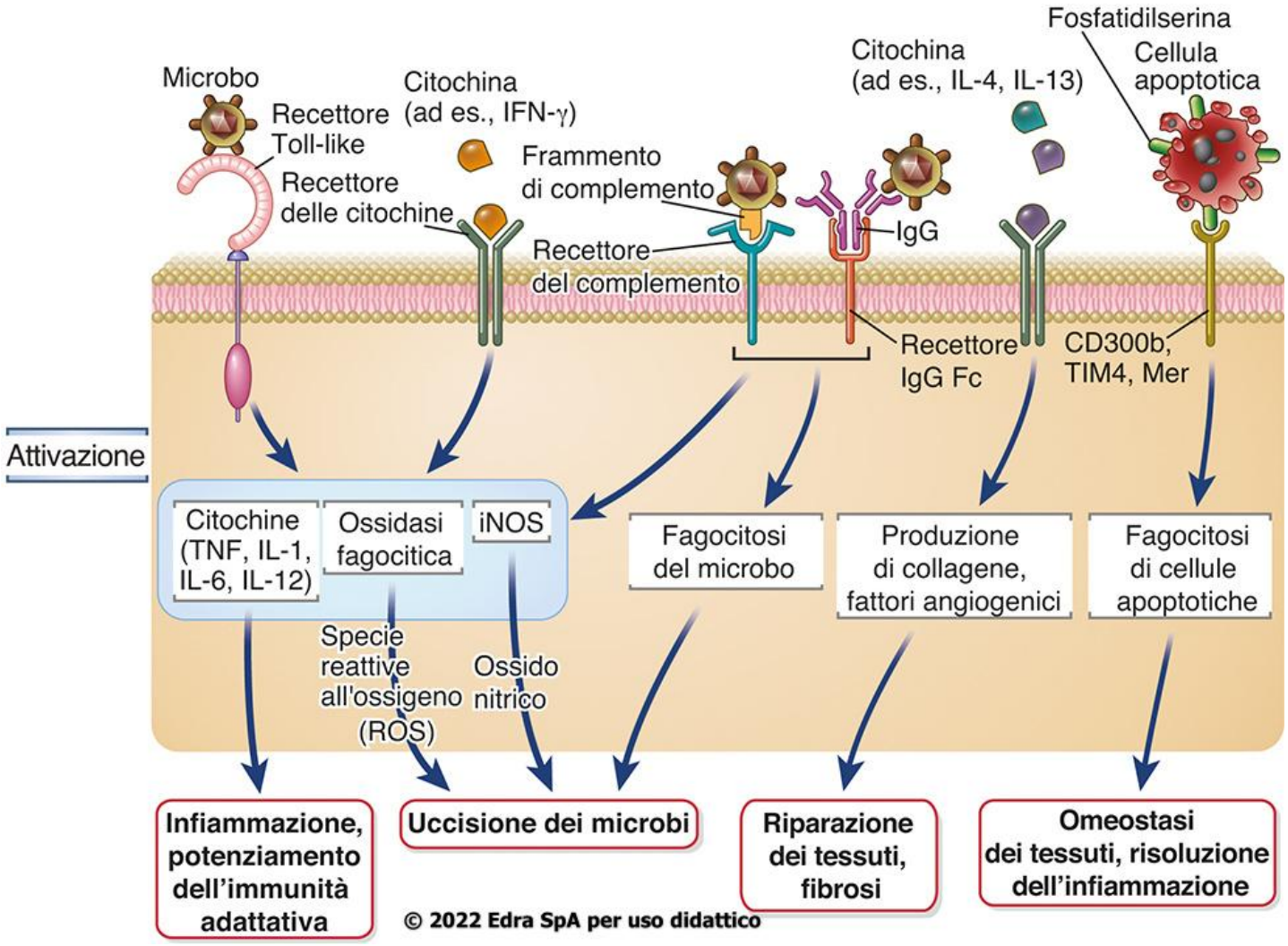




Fluorescent monocyte precursors (after birth)

Which MAIN functions do phagocytes accomplish?

Funzioni dei macrofagi



PHAGOCYTOSIS

RECEPTOR MEDIATED ENDOCYTOSIS

ENGULFEMENT OF PARTICULATE MATERIAL (CAN BE PATHOGENIC MICROORANISMS OR APOPTOTIC CELLS)

Tissue migration of leukocytes is mediated by chemotatic factors released during infection

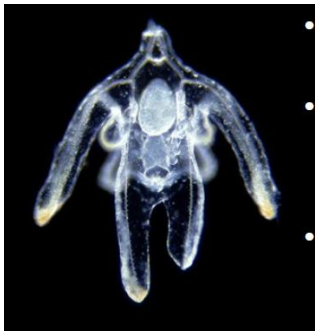


Phagocytosis was at first described by **Ilya Metchnicoff** at the end of 19th century



The key experiments was to inject carmine (carminio, un pigmento rosso) into starfish larvae





In 1908, Paul Ehrlich shared the Nobel Prize in Physiology or Medicine with Ilya Metchnikoff "in recognition of their work on immunity."

How do phagocytes recognize pathogens?

Functional classes of microbial recognition receptors capable of binding conserved portions of these molecules

1. **Endocytic pattern-recognition receptors**
   engulfment of pathogens

2. **Chemotactic pattern-recognition receptors**
   Migration to infection site

3. **Signaling pattern-recognition receptors**
   Production of effector molecules that participate to the immune response and affect the nature of adaptive response

Recettori per la fagocitosi

Type of phagocytosis	Receptors	Ligands
Non-opsonic phagocytosis	Dectin 1	β-glucan
	Macrophage receptor MARCO	Bacteria (undefined specific ligand)
	Scavenger receptor A	Bacteria (diverse charged molecules)
	αVβ5 integrin	Apoptotic cells
Triggered (nonspecific) phagocytosis	Toll-like receptors	Various, including lipopolysaccharides and lipopeptides

FcγR, Fc receptor for IgG.

Type of phagocytosis	Receptors	Ligands
Opsonic phagocytosis	Fc receptor family (FcγRI, FcγRIIA and FcγRIIA)	Antibody-opsonized targets
	Complement receptors (CR1, CR3 and CR4)	Complement-opsonized targets

Opsonins facilitate recognition, binding, ingestion, and killing of microorganisms by phagocytes

Destruction of antibody-coated pathogens via Fc receptors

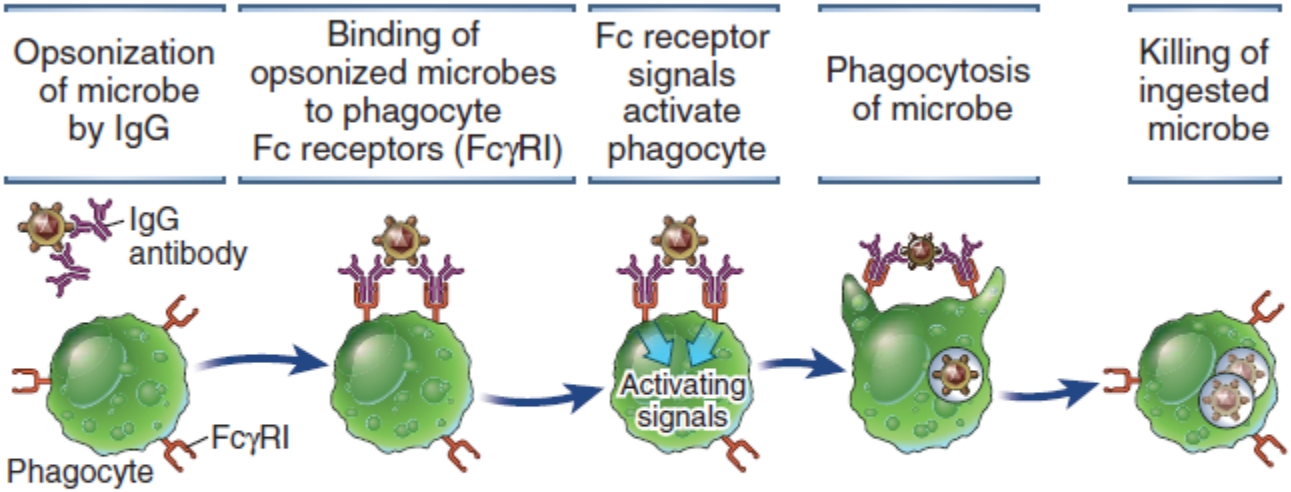
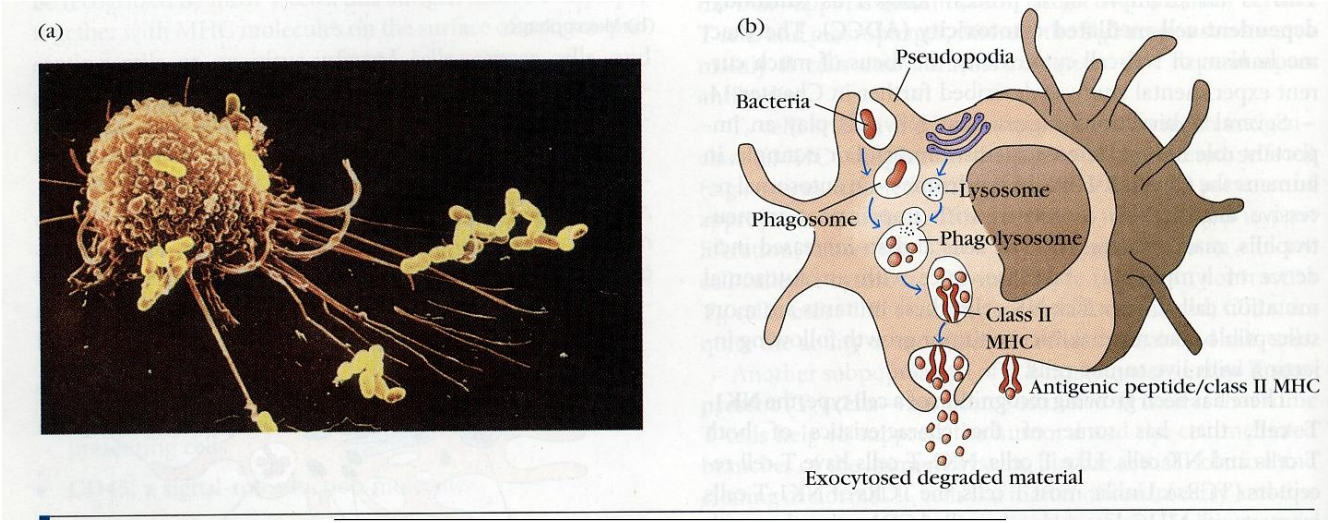


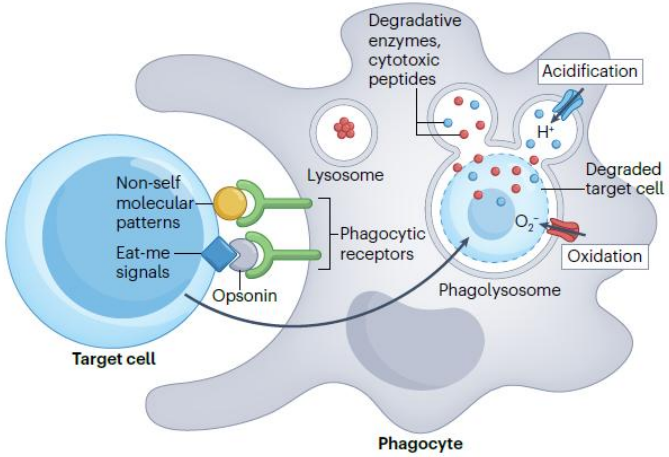
FIGURE 13.4 Antibody-mediated opsonization and phagocytosis of microbes. Antibodies of certain IgG subclasses bind to microbes and are then recognized by Fc receptors on phagocytes. Signals from the Fc receptors promote the phagocytosis of the opsonized microbes and activate the phagocytes to destroy these microbes. The microbicidal mechanisms of phagocytes are described in Chapters 4 (see Fig. 4.13) and 10 (see Fig. 10.7).

The process of coating particles to promote their phagocytosis is called opsonization

dal greco antico *ópson*, cibo

Phagocytosis





Zipper-like mechanism of injestion

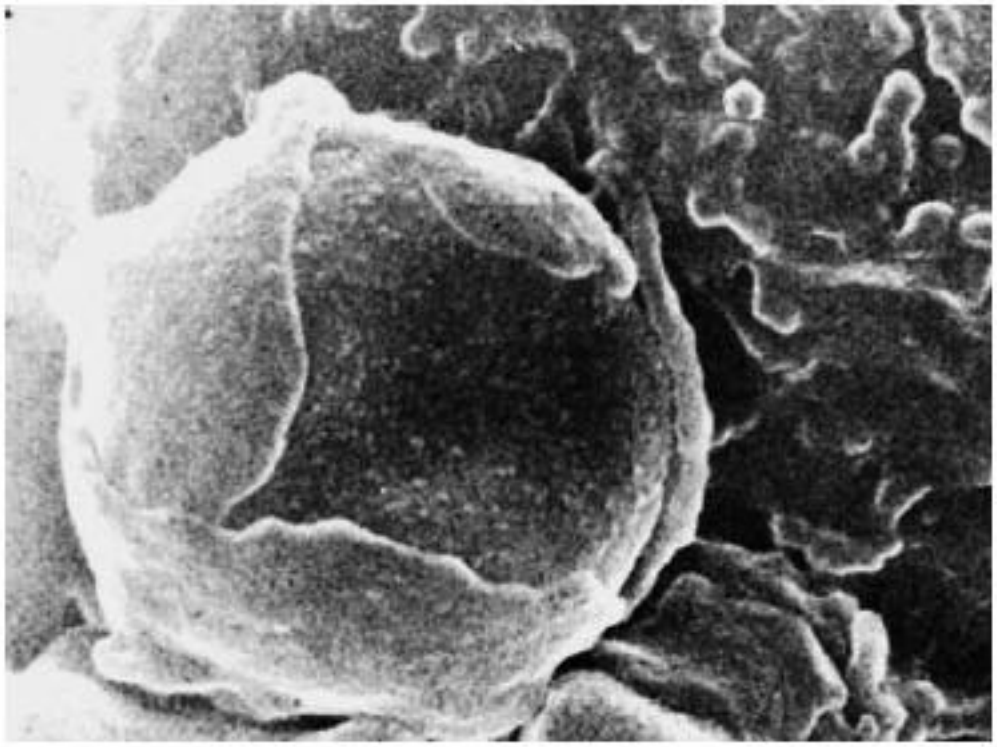


Figure 2. Electron micrograph to illustrate extension of macrophage pseudopodia during engulfment of an IgG-opsonised sheep erythrocyte, by a zipper-type mechanism.

Phagocytosis is a multi-phase event that requires:

Chemotaxis

Adhesion

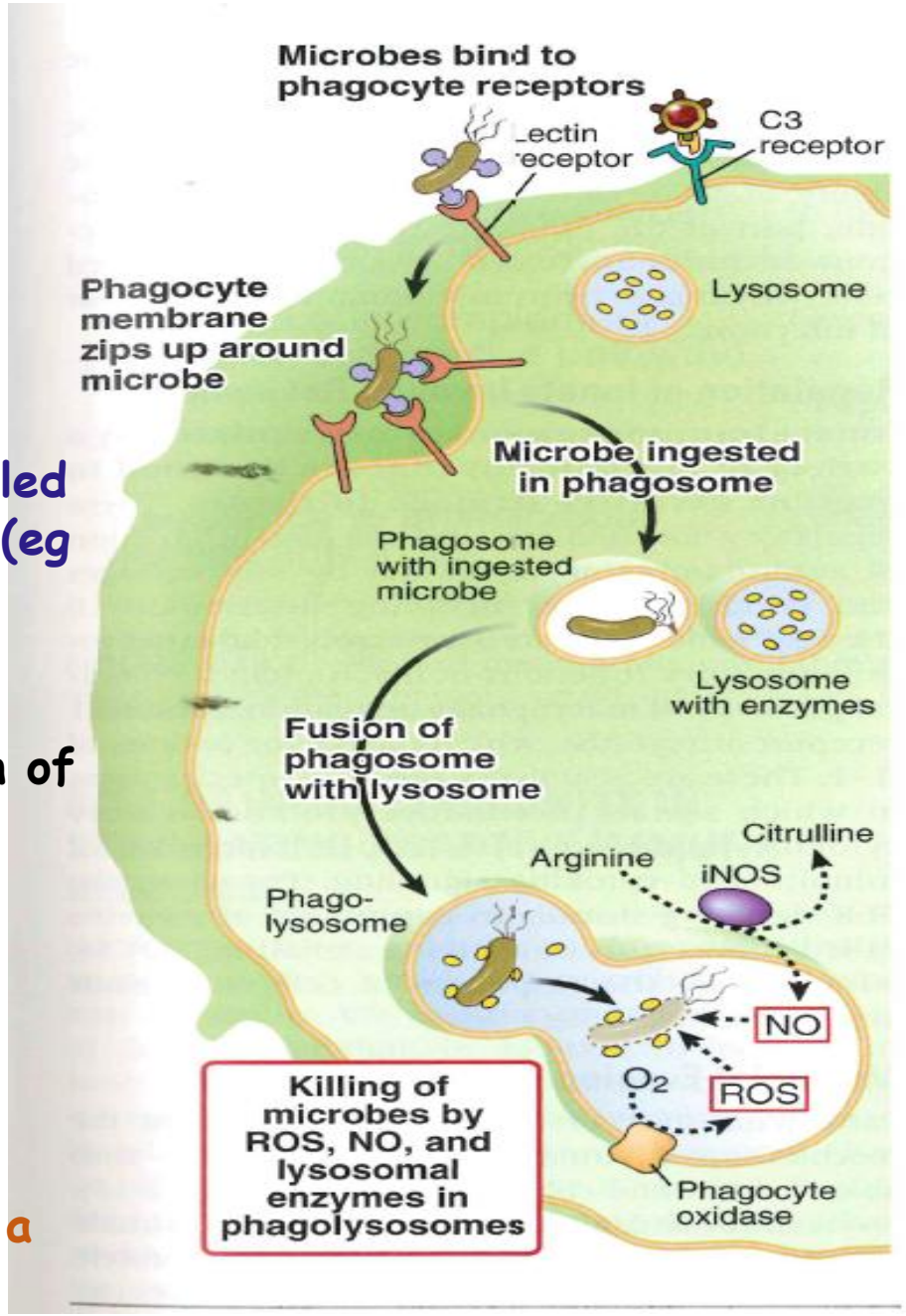
Recognition

Induction of membrane protrusions called pseudopodia that envelop the microbe (eg the zipper-like mechanism of the Fc receptor)

Pseudopodia fusion allows incorporation of the microbe in a structure called a phagosome

Fusion of the phagosome with the lysosome and formation of a phagolysosome

The digested content is eliminated by a process of exocytosis



Phagocytosis is a multi-phase event



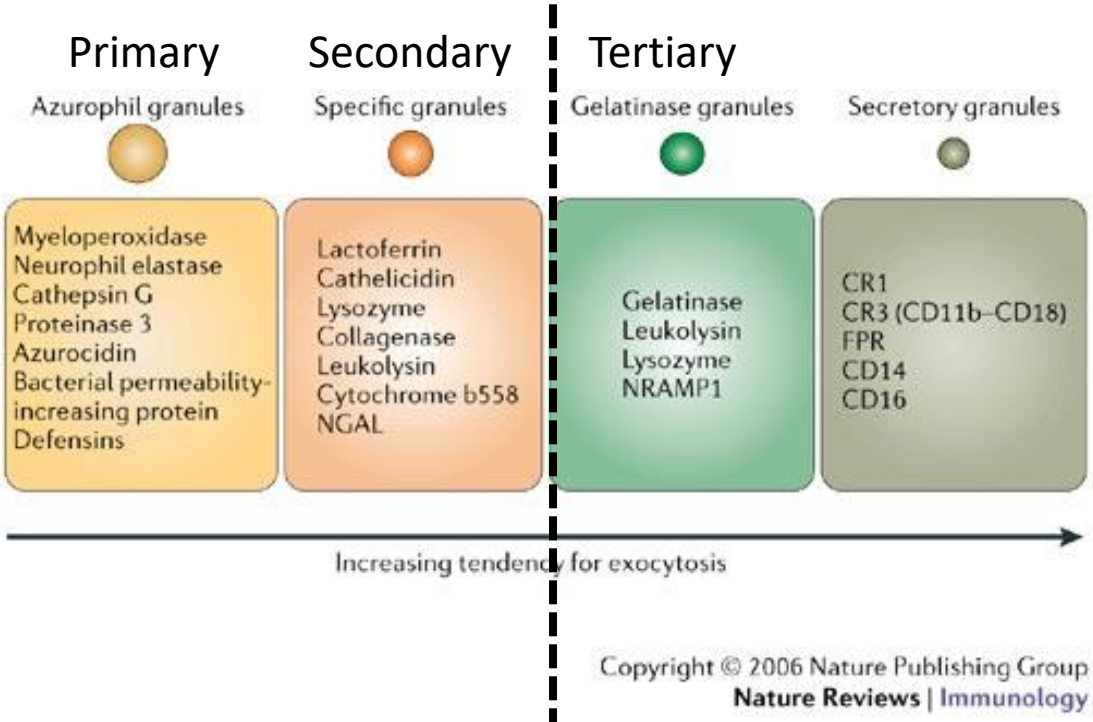
Activated neutrophils and macrophages kill phagocytosed microbes by the action of microbicidal molecules in phagolysosomes

Factors that help destroy microorganisms within a phagolysosome

Class of mechanism	Specific products
Acidification	pH=~3.5–4.0, bacteriostatic or bactericidal
Toxic oxygen-derived products	Superoxide O_2^-, hydrogen peroxide H_2O_2, singlet oxygen $^1O_2^*$, hydroxyl radical OH^*, hypohalite OCl^-
Toxic nitrogen oxides	Nitric oxide NO
Antimicrobial peptides	Defensins and cathelicidin
Enzymes	Lysozyme—dissolves cell walls of some Gram-positive bacteria. Acid hydrolases—further digest bacteria
Competitors	Lactoferrin (binds Fe) and vitamin B_{12}-binding protein

Figure 2-6 Immunobiology, 6/e. (© Garland Science 2005)

Neutrophil granules (in addition to lysosomes)



I granuli vengono esocitati precocemente durante il processo di extravasazione

NADPH oxidase is central to the microbicidal process

The activation of NADPH oxidase, which occurs when neutrophils or macrophages 'sense' a pathogen via pattern-recognition receptors, entails the phosphorylation and translocation of preformed cytosolic components to the membrane-bound catalytic core of the enzyme

Il processo di esplosione respiratoria è un meccanismo per produrre metaboliti estremamente tossici

Phagocyte oxidase reduces molecular oxygen into reactive oxygen species (ROS) such as superoxide radicals, with the reduced form of nicotinamide adenine dinucleotide phosphate (NADPH) acting as a cofactor

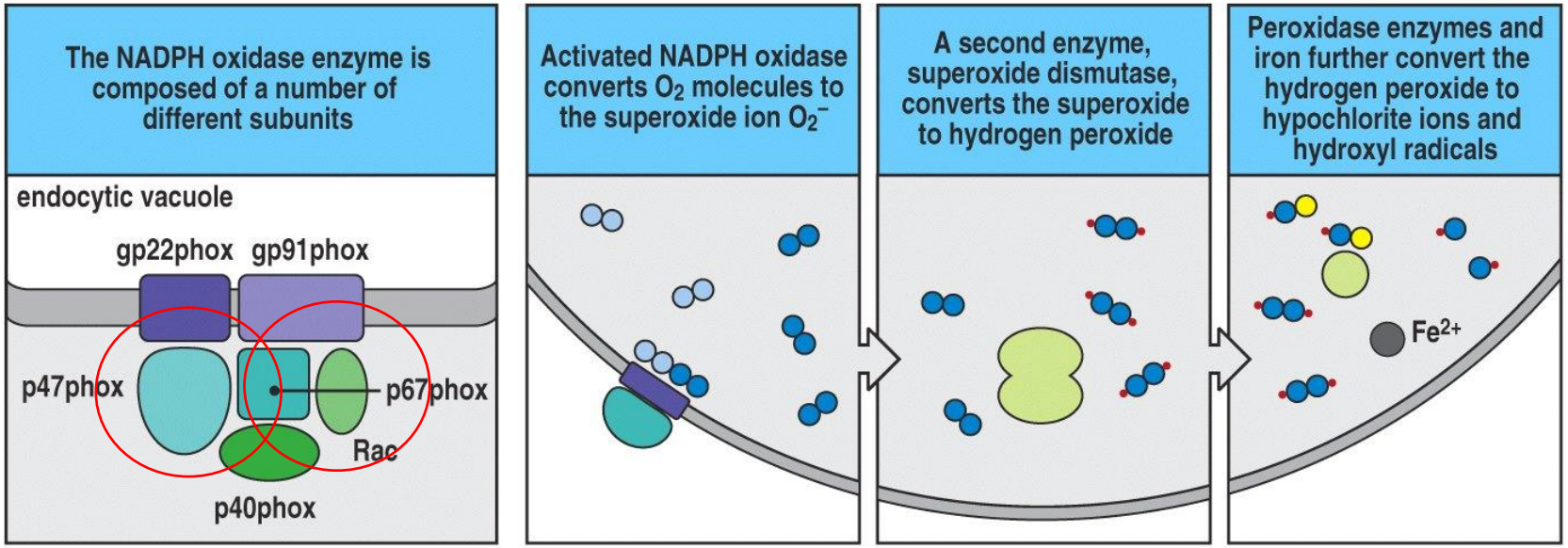
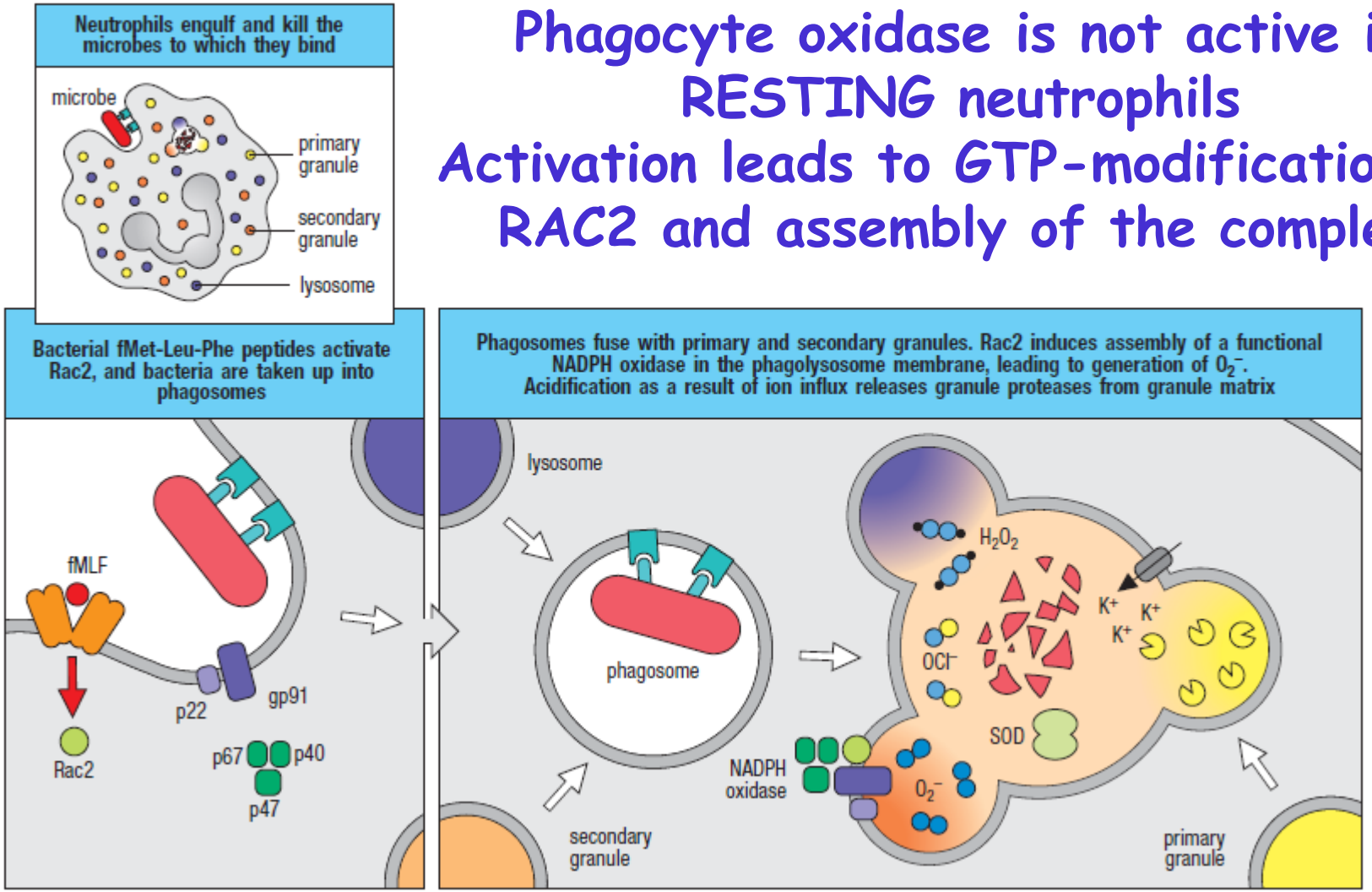


Figure 2-7 Immunobiology, 6/e. (© Garland Science 2005)

Superoxide anion is enzymatically dismutated into hydrogen peroxide, which is used by the enzyme (myelo)peroxidase to produce microbicidal oxidized halogens and reactive oxygen species (ROS) that are toxic for bacteria.

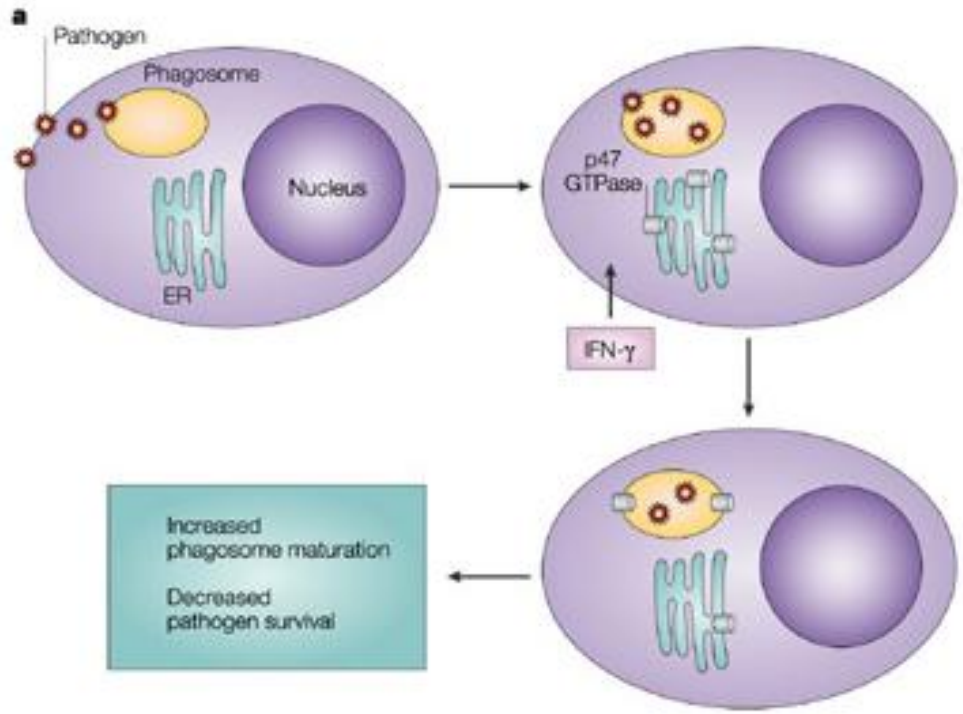
The process by which ROS are produced is called the **respiratory burst**, because it requires oxygen consumption (cellular respiration).

Phagocyte oxidase is not active in RESTING neutrophils
Activation leads to GTP-modification of RAC2 and assembly of the complex



Furthermore, phagosome acidification dissociates granule enzymes (such as cathepsin G and elastase (yellow) from their proteoglycan matrix, leading to their cleavage and activation by lysosomal proteases

Phagocyte oxidase is not active in RESTING macrophages as it cannot be assembled



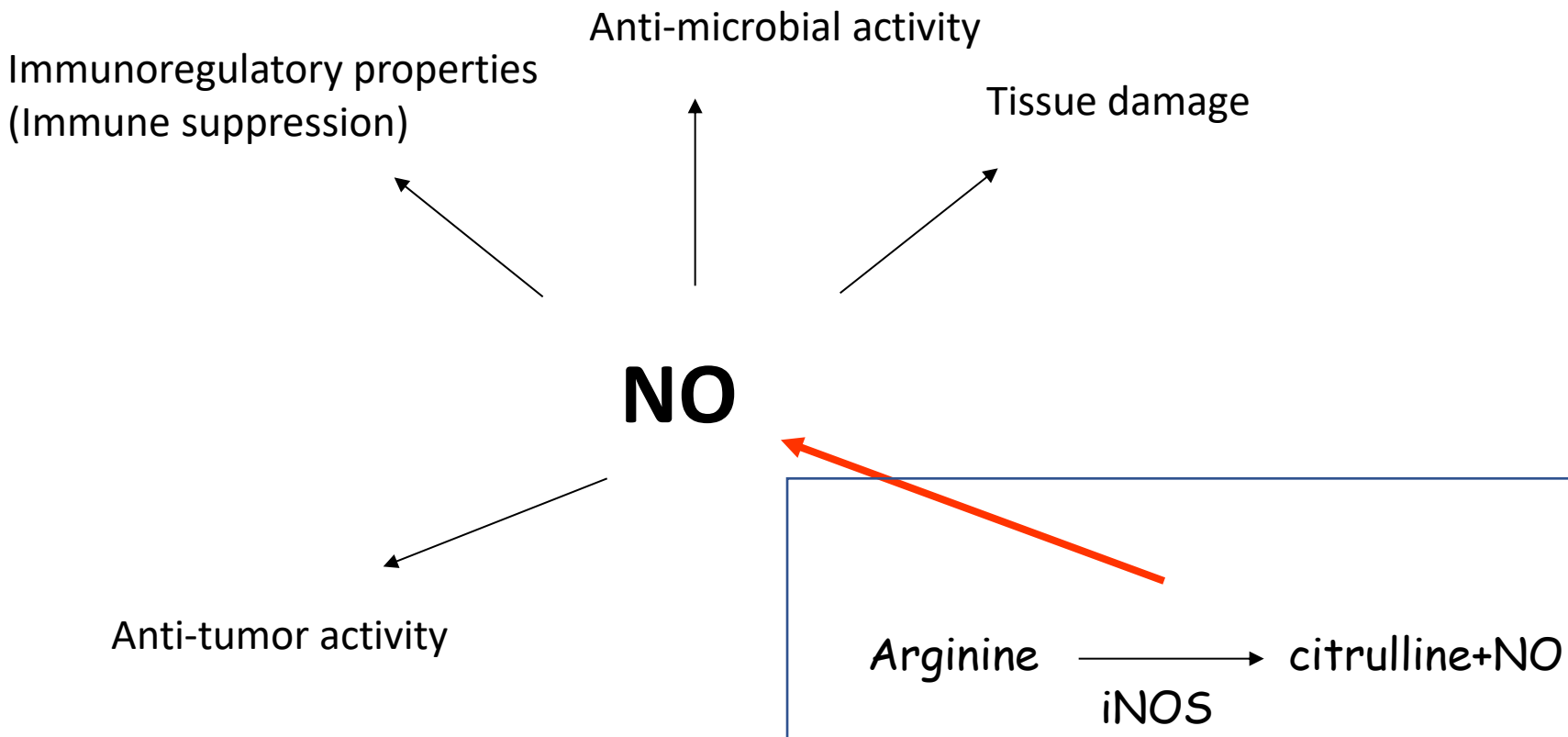
IFN gamma activated macrophages induce production of the oxidase subunit GTPase p47

Factors that help destroy microorganisms within a phagolysosome

Class of mechanism	Specific products
Acidification	pH=~3.5–4.0, bacteriostatic or bactericidal
Toxic oxygen-derived products	Superoxide O_2^-, hydrogen peroxide H_2O_2, singlet oxygen $^1O_2^*$, hydroxyl radical OH^*, hypohalite OCl^-
Toxic nitrogen oxides	Nitric oxide NO
Antimicrobial peptides	Defensins and cationic proteins
Enzymes	Lysozyme—dissolves cell walls of some Gram-positive bacteria. Acid hydrolases—further digest bacteria
Competitors	Lactoferrin (binds Fe) and vitamin B_{12}-binding protein

Figure 2-6 Immunobiology, 6/e. (© Garland Science 2005)

Nitric oxide is ha powerful anti-microbial compound but have also other activities



Nitric oxide synthase (NOS) synthesizes nitric oxide but is only expressed upon activation (**iNOS, also called NOS2**, stands for inducible NOS)

MECCANISMI COINVOLTI NEL KILLING DEI BATTERI

Class of mechanism	Specific products
Acidification	pH=~3.5–4.0, bacteriostatic or bactericidal
Toxic oxygen-derived products	Superoxide O_2^-, hydrogen peroxide H_2O_2, singlet oxygen $^1O_2^*$, hydroxyl radical OH^*, hypohalite OCl^-
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Figure 2-6 Immunobiology, 6/e. (© Garland Science 2005)

Killing mechanisms

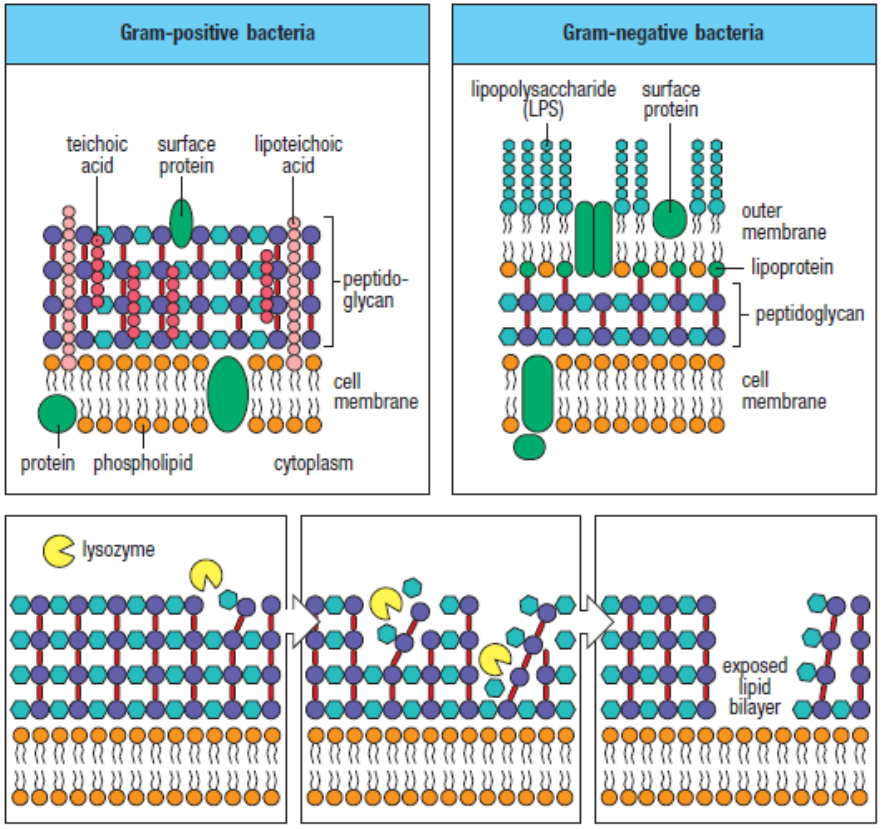
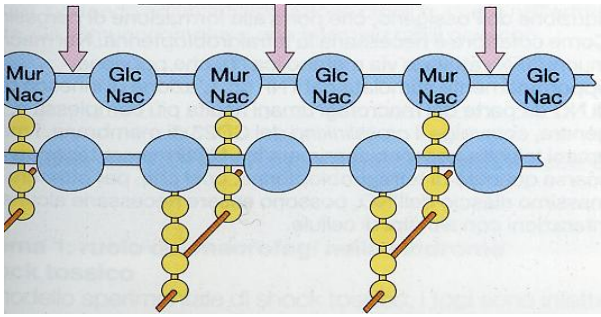


Fig. 2.9 Lysozyme digests the cell walls of Gram-positive and Gram-negative bacteria. Upper panels: the peptidoglycan of bacterial cell walls is a polymer of alternating residues of β-(1,4)-linked *N*-acetylglucosamine (GlcNAc) (large turquoise hexagons) and *N*-acetylmuramic acid (MurNAc) (purple circles) that are cross-linked by peptide bridges (red bars) into a dense three-dimensional network. In Gram-positive bacteria (upper left panel), peptidoglycan forms the outer layer in which other molecules are embedded such as teichoic acid and the lipoteichoic acids that link the peptidoglycan layer to the bacterial cell membrane itself. In Gram-negative bacteria (upper right panel), a thin inner wall of peptidoglycan is covered by an outer lipid membrane that contains proteins and lipopolysaccharide (LPS). Lipopolysaccharide is composed of a lipid, lipid A (turquoise circles), to which is attached a polysaccharide core (small turquoise hexagons). Lysozyme (lower panels) cleaves β-(1,4) linkages between GlcNAc and MurNAc, creating a defect in the peptidoglycan layer and exposing the underlying cell membrane to other antimicrobial agents. Lysozyme is more effective against Gram-positive bacteria because of the relatively greater accessibility of the peptidoglycan.

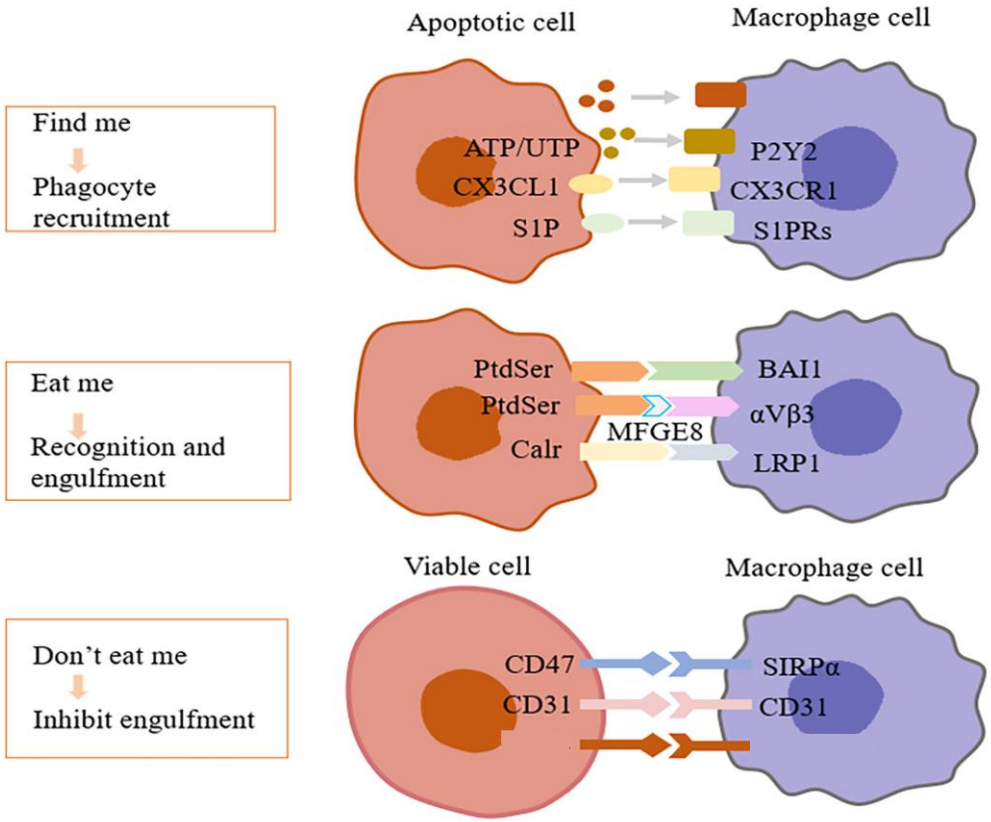
Lysozyme action



La fagocitosi ha anche un ruolo in processi fisiologici promuovendo l'eliminazione di cellule apoptotiche

Fagocitosi di cellule apoptotiche

The human body turns over 100 billion cells every day to maintain normal development, tissue homeostasis, or physiological function by clearing unwanted (damaged, dysfunctional, aged, or harmful) cells.



Efferocytosis is a highly conservative physiological process, involving **phagocytes** and **apoptotic cells (ACs)**. Effective clearance of ACs should be the ultimate destination of apoptosis, and it is also a key link to prevent inflammation and maintain tissue homeostasis under physiological conditions

An alternaive killing mechanism in neutrophils: Neutrophil extracellular trap (NET)

Neutrophil extracellular trap (NET)

Cell Death Differ. 2011 Apr;18(4):581-8. Epub 2011 Feb 4.

Dying for a cause: NETosis, mechanisms behind an antimicrobial cell death modality.

Remijsen Q, Kuijpers TW

J Parasitol Res. 2012;2012:929743. Epub 2012 Feb 26.

ETosis: A Microbicidal Mechanism beyond Cell Death.

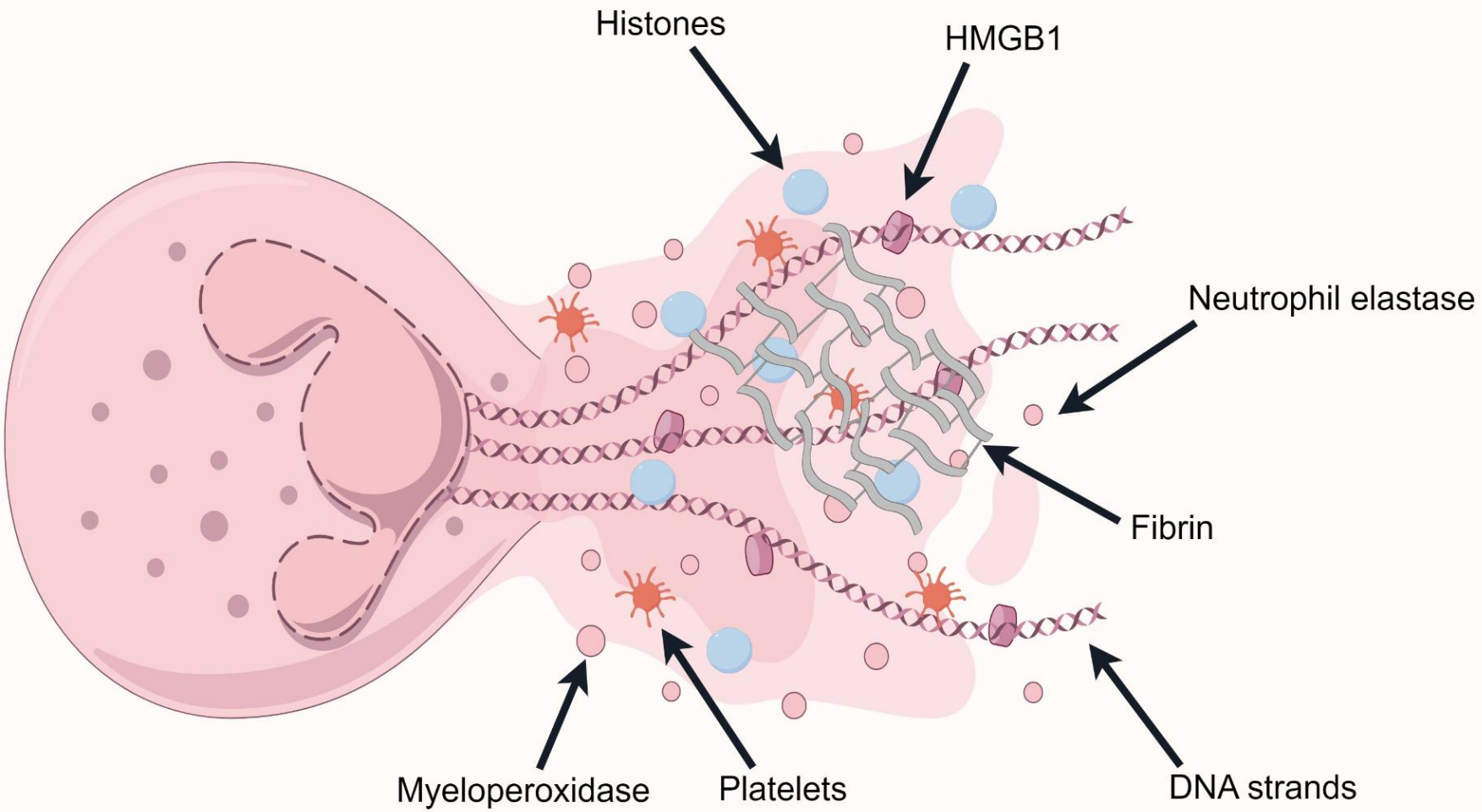
Guimarães-Costa AB, Nascimento MT, Wardini AB, Pinto-da-Silva LH, Saraiva EM.
Instituto de Microbiologia Paulo de Góes, Universidade Federal do Rio de Janeiro (UFRJ), 21941-901 Rio de Janeiro, RJ, Brazil.

Abstract

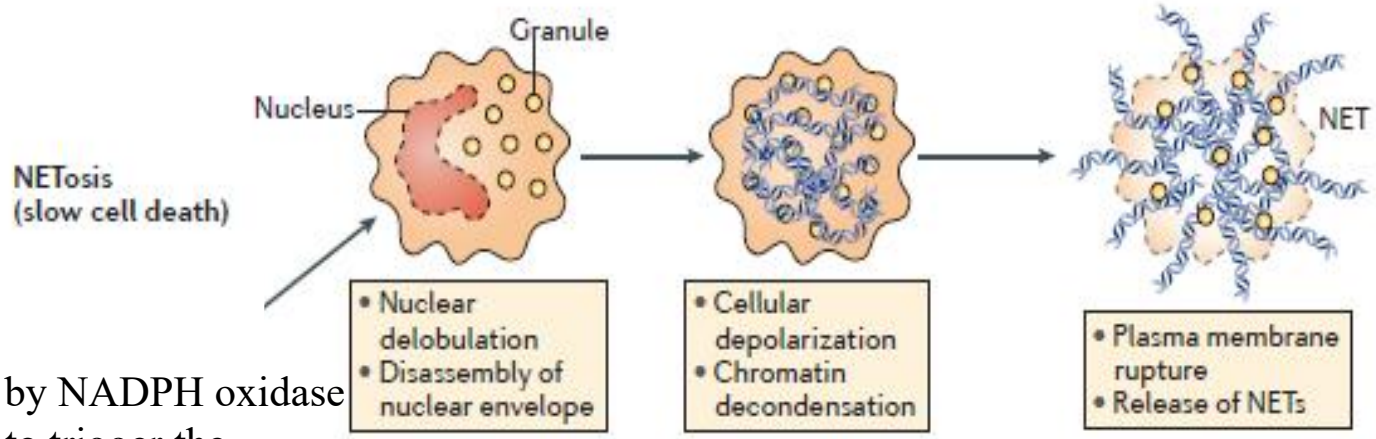
Netosis is a recently described type of neutrophil death occurring with the release to the extracellular milieu of a lattice composed of DNA associated with histones and granular and cytoplasmic proteins. **These webs, initially named neutrophil extracellular traps (NETs), ensnare and kill microorganisms.**

DNA and granule content extrusion, which form extracellular networks on which bacteria and fungi are trapped and killed.

NETs are large, extracellular, web-like structures composed of cytosolic and granule proteins that are assembled on a scaffold of decondensed chromatin

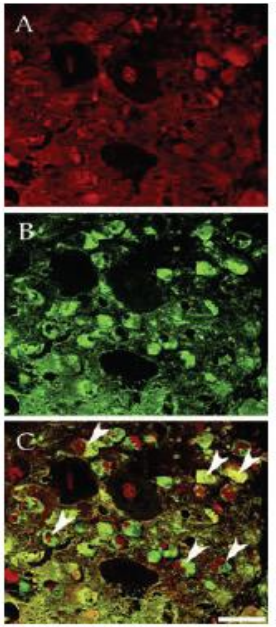

Histones
HMGB1
Neutrophil elastase
Fibrin
Myeloperoxidase
Platelets
DNA strands

Formazione dei NET mediante NETosi



ROS generated by NADPH oxidase stimulate MPO to trigger the activation and translocation of neutrophil elastase (NE) from azurophilic granules to the nucleus, where NE proteolytically processes histones to disrupt chromatin packaging

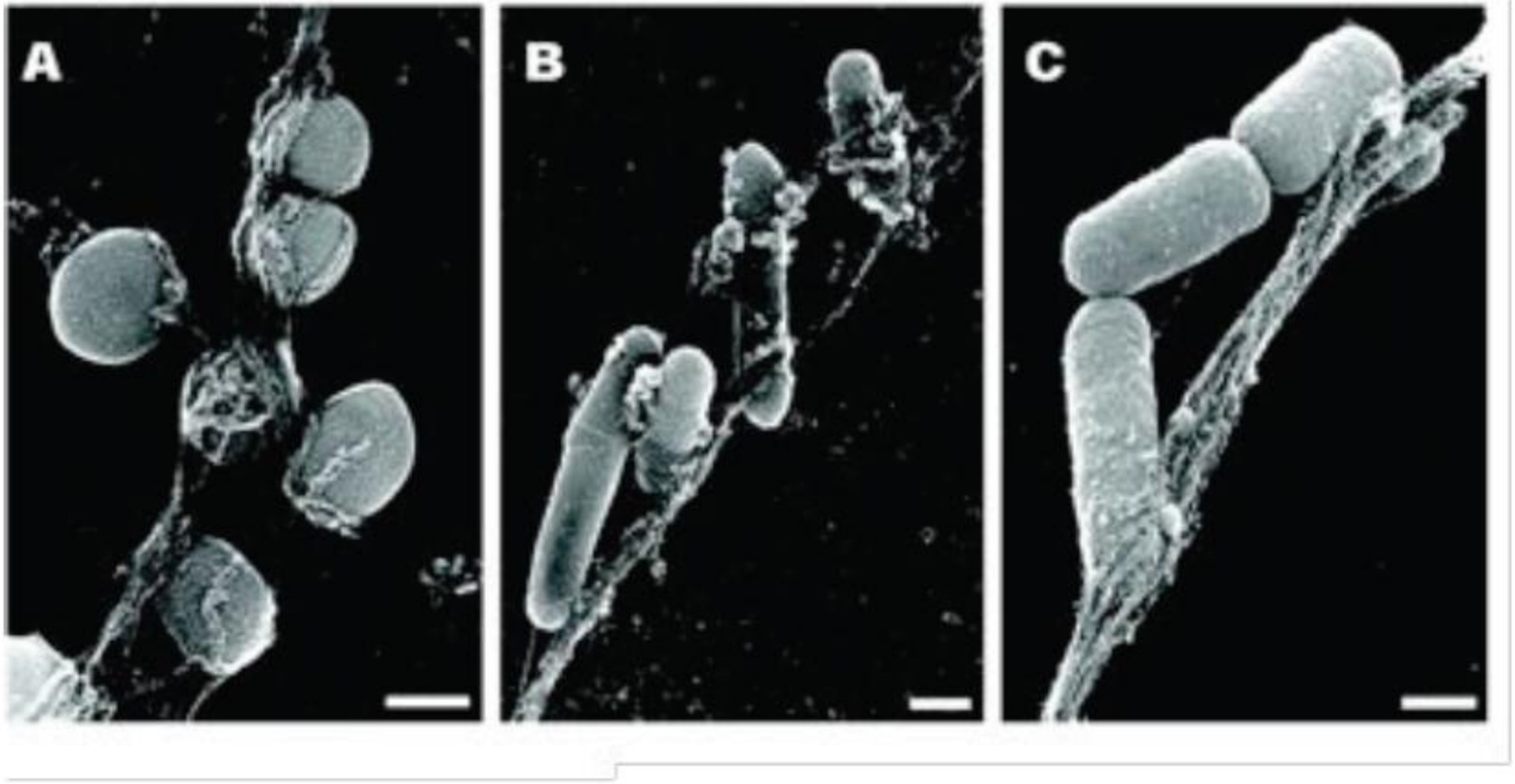
Pus consists of numerous neutrophils in various stages of NETosis surrounded by NETs. Semithin cryosection of pus from a Molluscum contagiosum lesion stained for NE (green) and chromatin (red). Bar, 20 µm.



Brinkmann V , Zychlinsky A J Cell Biol 2012;198:773-783

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NEUTROPHIL EXTRACELLULAR TRAPS ARE COMPOSED OF CHROMATIN AND GRANULE ENZYMES



What else? Macrophages produce cytokines

How do the cytokines of innate immunity work?

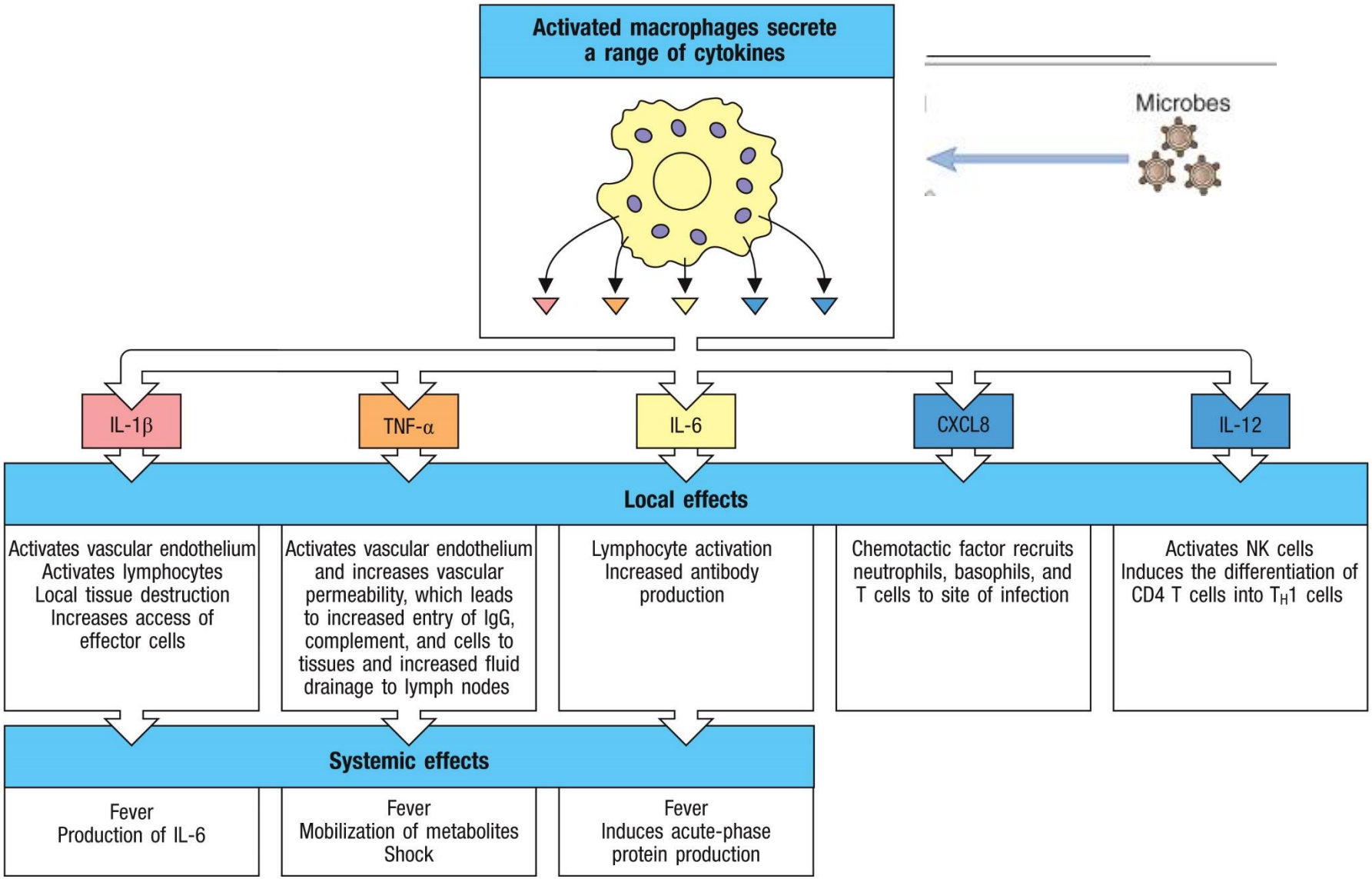
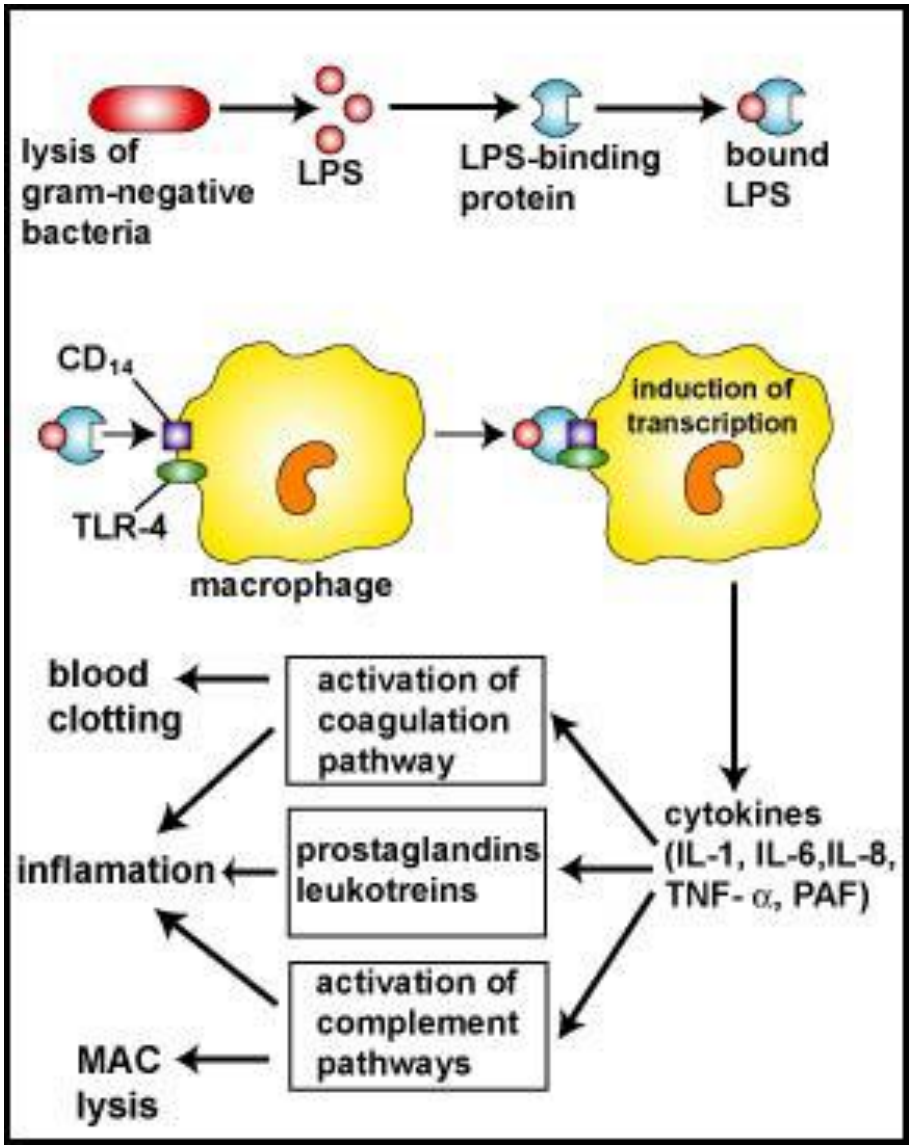


Figure 3.27 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Lypopolysaccharid (LPS) recognition and cell activation



The activation of the resulting macrophage leads to the release of chemicals involved in the defensive response called cytokines, including IL-1, IL-6, IL-8, TNF-alpha and PAF.

The cytokines then bind to cytokine receptors on target cells and begin the inflammatory process

TABLE 2.2 Distinguishing Properties of Neutrophils and Macrophages

	Neutrophils	Macrophages
Origin	HSCs in bone marrow	HSCs in bone marrow (in inflammatory reactions) Many tissue-resident macrophages: stem cells in yolk sac or fetal liver (early in development)
Life span in tissues	1-2 days	Inflammatory macrophages: days or weeks Tissue-resident macrophages: years
Responses to activating stimuli	Rapid, short lived, enzymatic activity	More prolonged, slower, often dependent on new gene transcription
Phagocytosis	Rapid ingestion of microbes	Prolonged ability to ingest microbes, apoptotic cells, tissue debris, foreign material
Reactive oxygen species	Rapidly induced by assembly of phagocyte oxidase (respiratory burst)	Less prominent
Nitric oxide	Low levels or none	Induced following transcriptional activation of iNOS
Degranulation	Major response; induced by cytoskeletal rearrangement	Not prominent
Cytokine production	Low levels per cell	Major functional activity, large amounts per cell, requires transcriptional activation of cytokine genes
NET formation	Rapidly induced, by extrusion of nuclear contents	No
Secretion of lysosomal enzymes	Prominent	Less