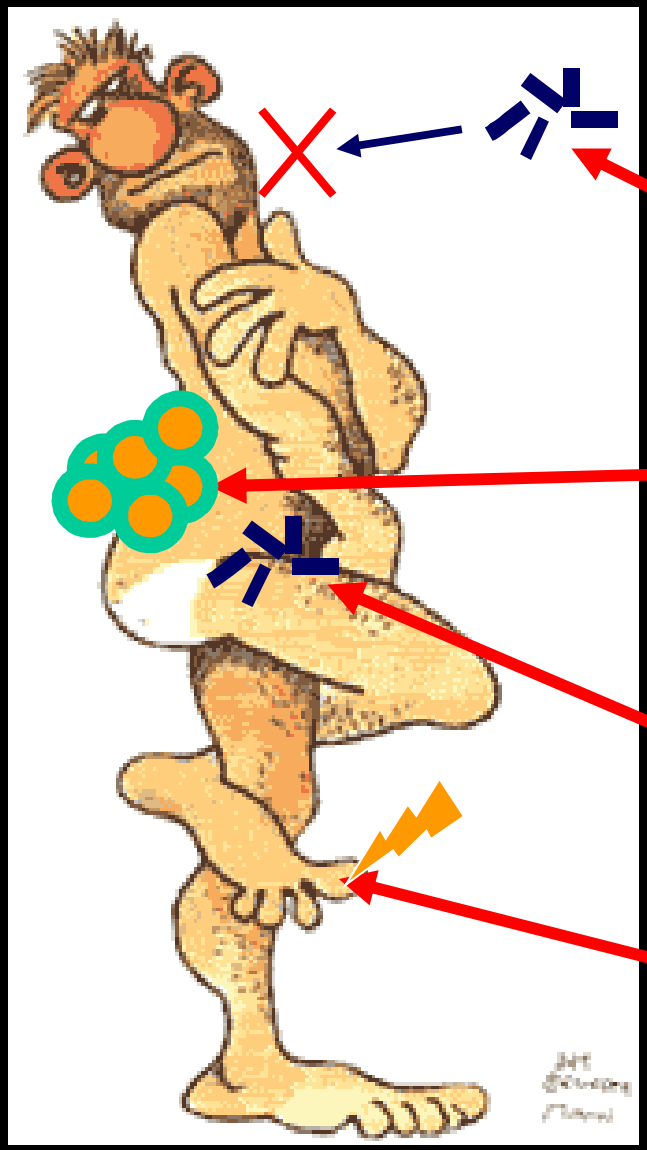
Mammalian innate immunity

Immunity



- colonization
- tissue overgrow
- pathogens
- wound infection

First barriers

- skin
- epithelia
- body liquids

  (enzymes and antimicrobial substances in tears, sweat, …)
- increased production of tissue liquids when sick (runny nose, diarrhea, …)

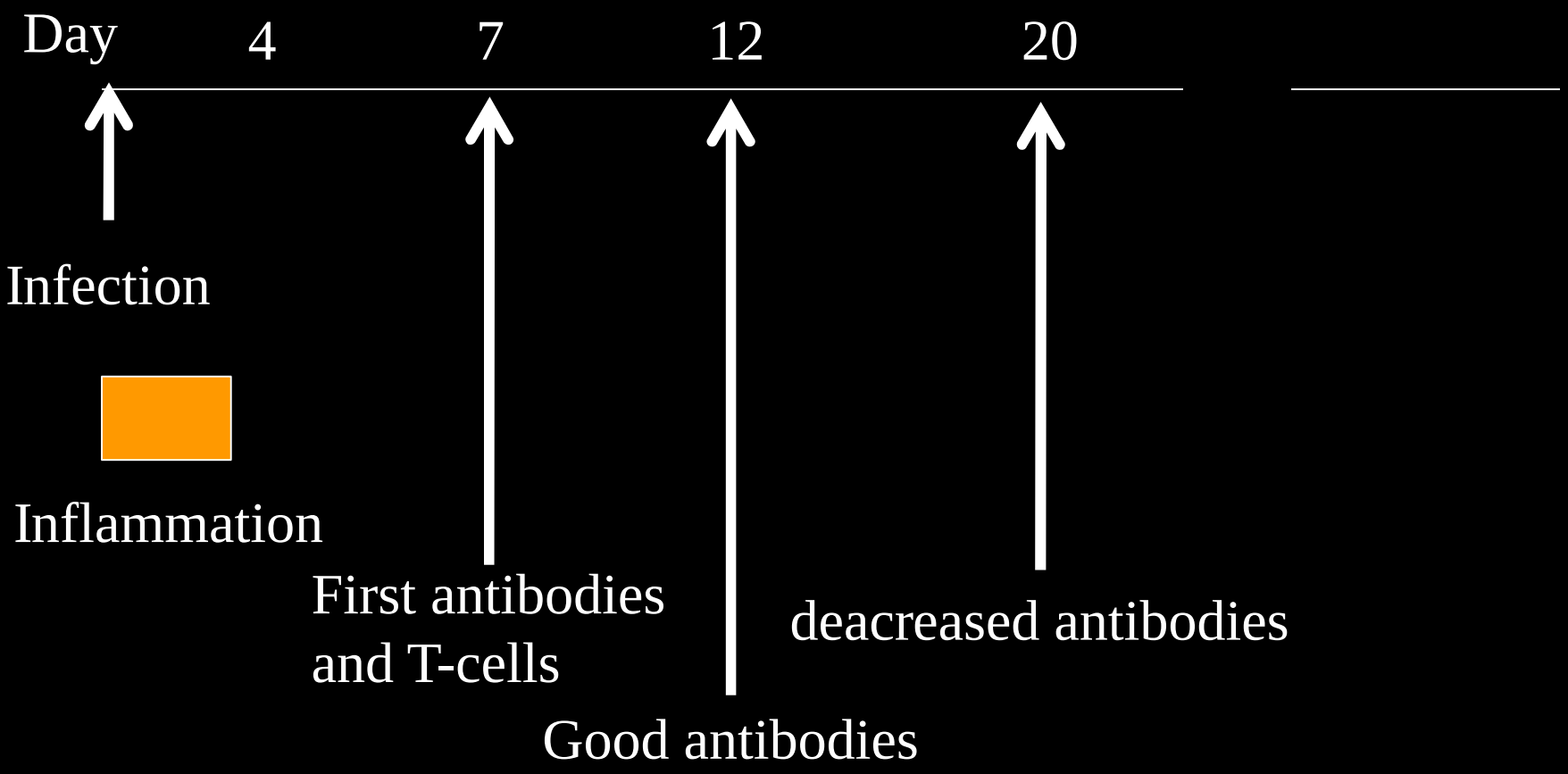
Immunity

self and non-self

What is non-self?

Non-self is very diverse.

Infection and Immunity



Innate vs acquired immunity

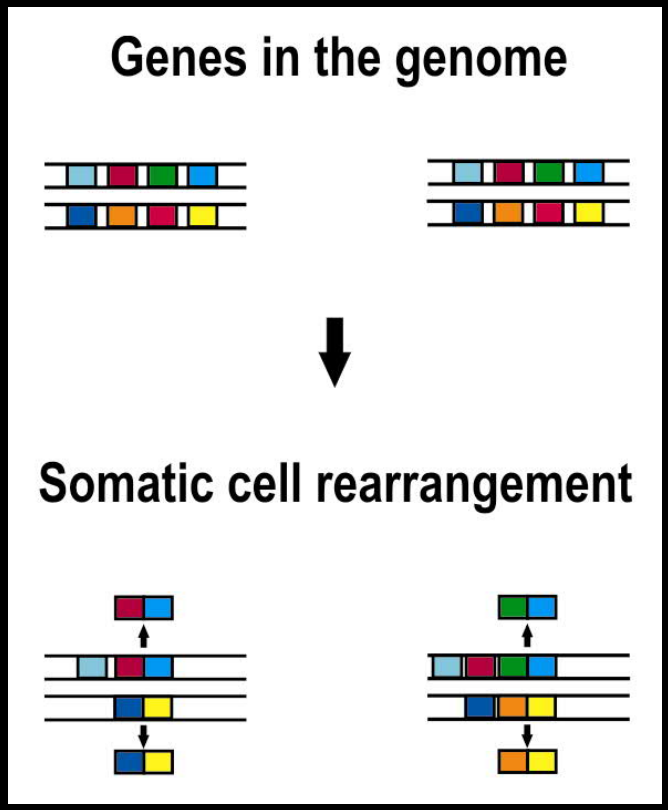
Innate immunity

- we are born with it
- fast
- low diversity
- ~100 receptors
- no memory

Acquired immunity

- acquired
- slow
- high specificity
- ~10^{20} possible antibodies
- memory

Acquired immunity and the diversity of non-self



Acquired Immunity

Advantages	Disadvanatges
Limitless repertoir	Cannot look at „classes“
Plastic	Slow the first time
Memory	
Specificity	

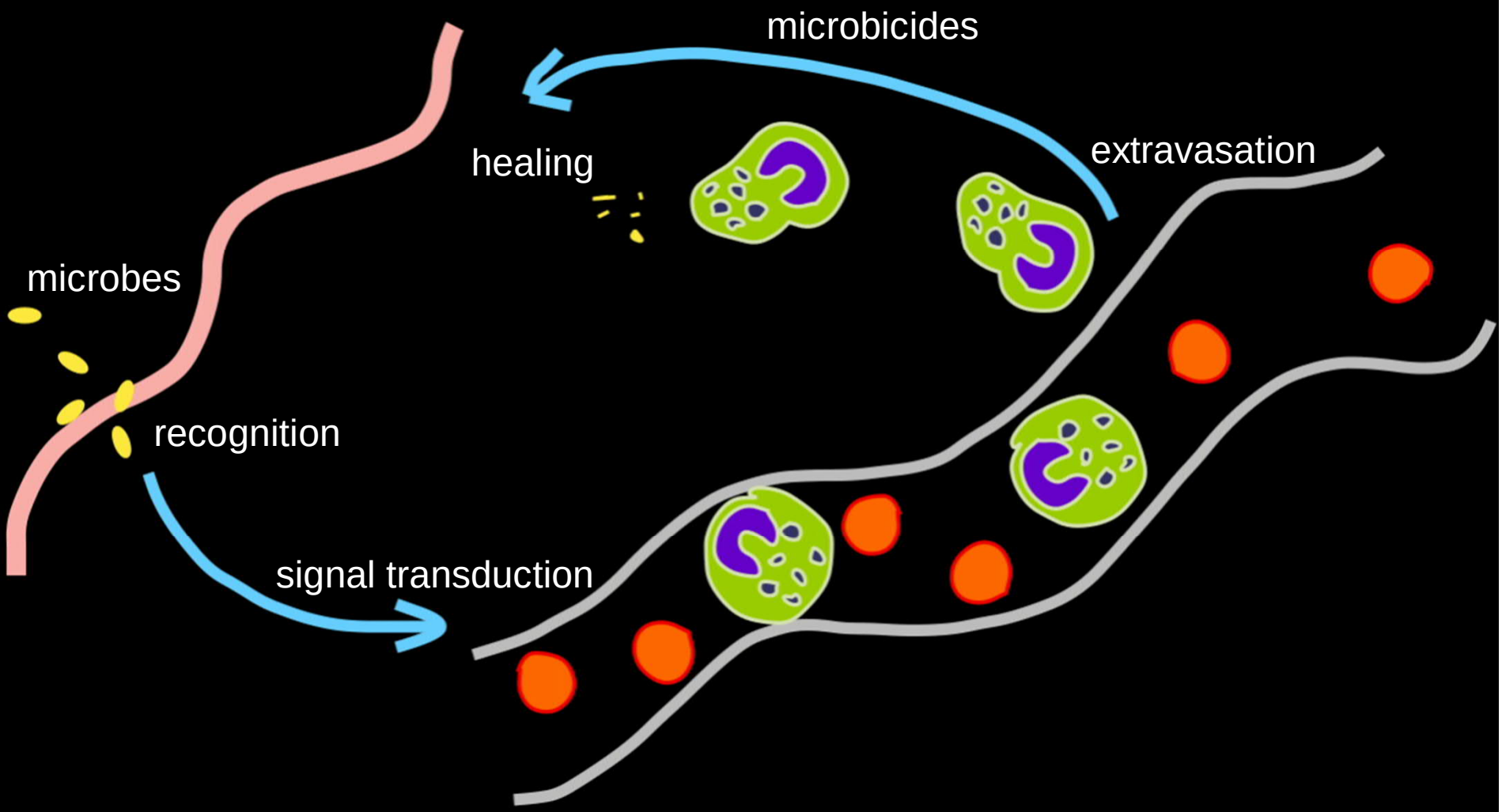
Innate immunity

- we are born with it
- fast
- no memory
- low specificity or rather it looks at “classes”.

Innate immune receptors encoded in the germline

- Allows fast response (no need for recombination)
- Low repertoire
- no memory
- No flexibility

Innate immunity



How to recognize non-self with a few receptors?

- Molecules in many microbes
- Constant in microbes
  - since innate immunity cannot create new receptors
  - No mutations!
- Different from “self”
  - to prevent autoimmunity

PAMPs

- lipopolysaccharide LPS
- bacterial lipopeptide BLP
- flagelin
- dsRNA
- CpGDNA
- Pepydoglycan
- Teichoic acid

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- lipopolysaccharide LPS
- bacterial lipopeptide BLP
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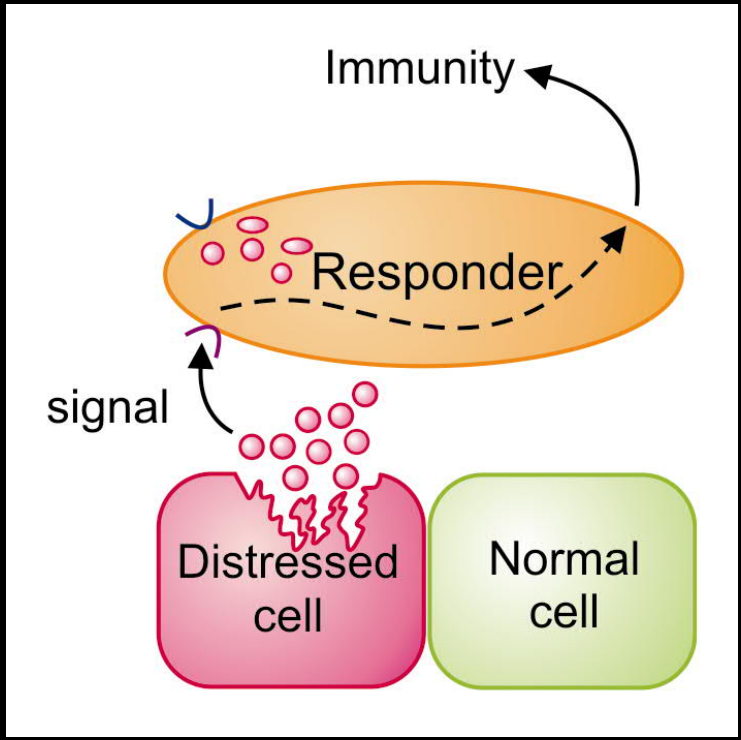
- Teichoic acid
- What else?

Can self be non-self?
The Danger theory



Innate immune receptors

Toll Like Receptors

NOD

Scavangers

GPI anchored (CD14)

Integrin

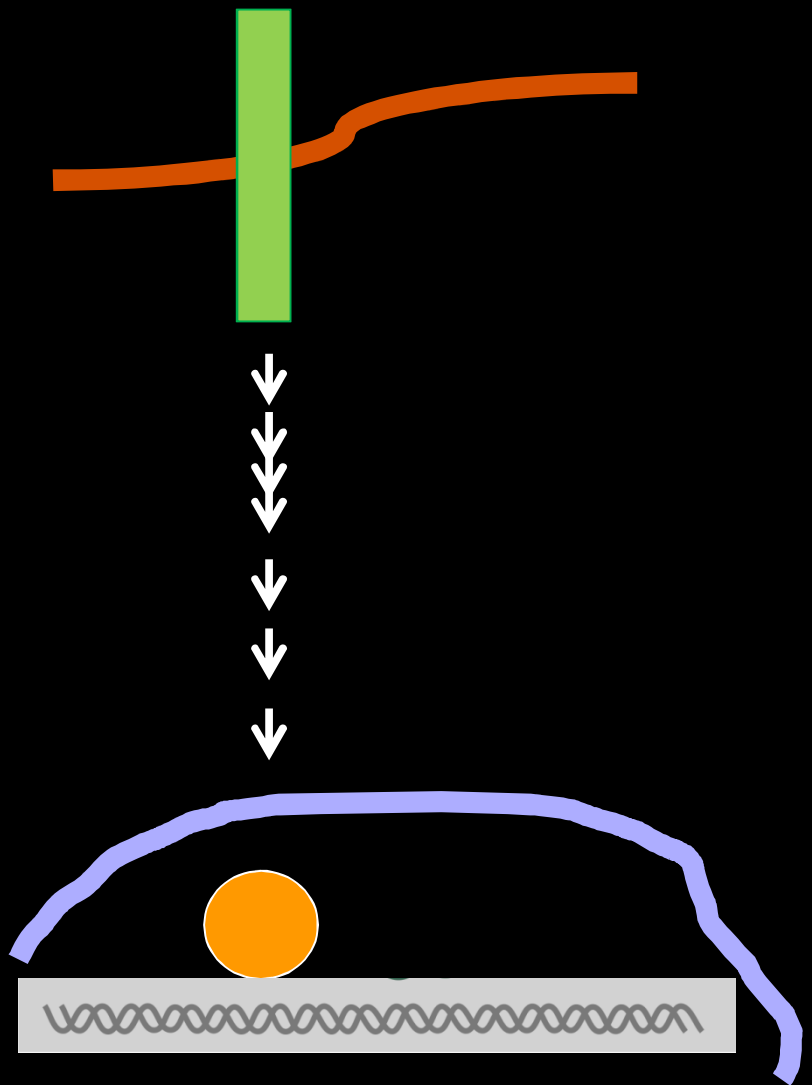
C-type lectin and C-type lectin like.

G-protein-coupled receptors.

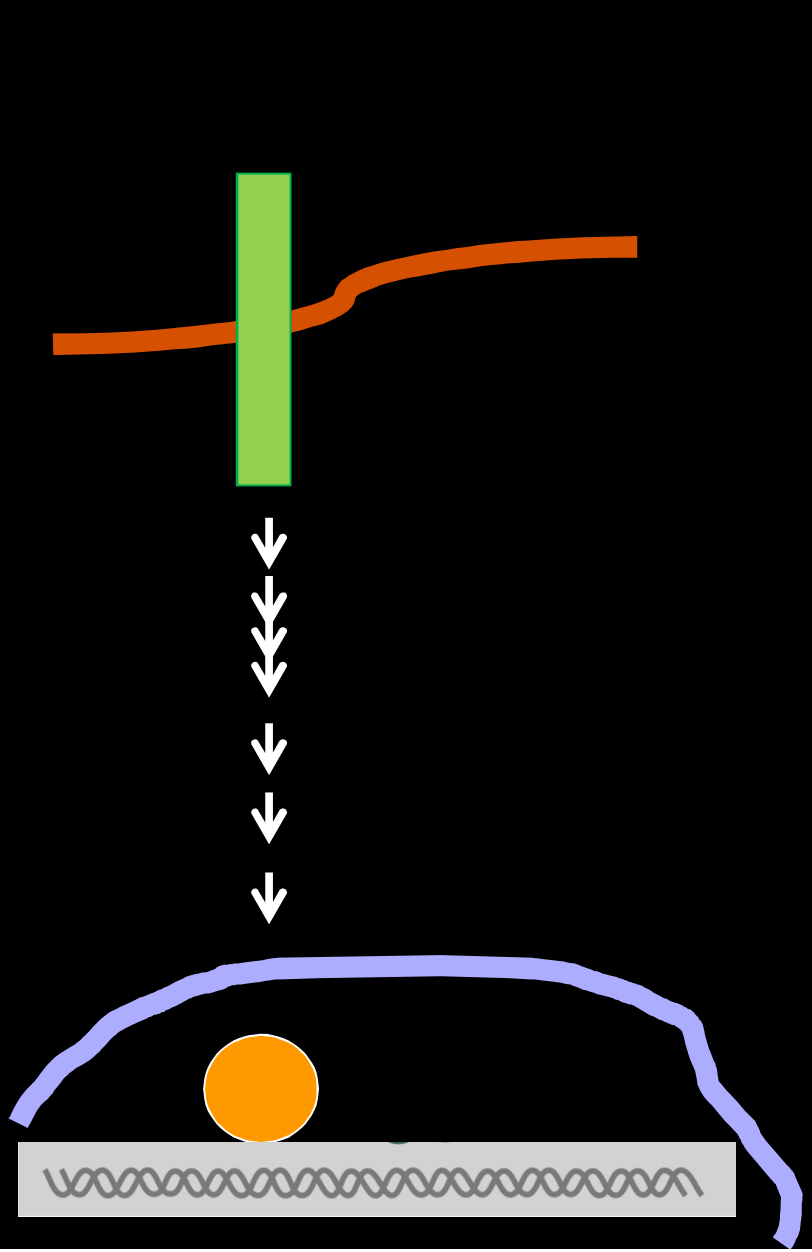
RIG-I

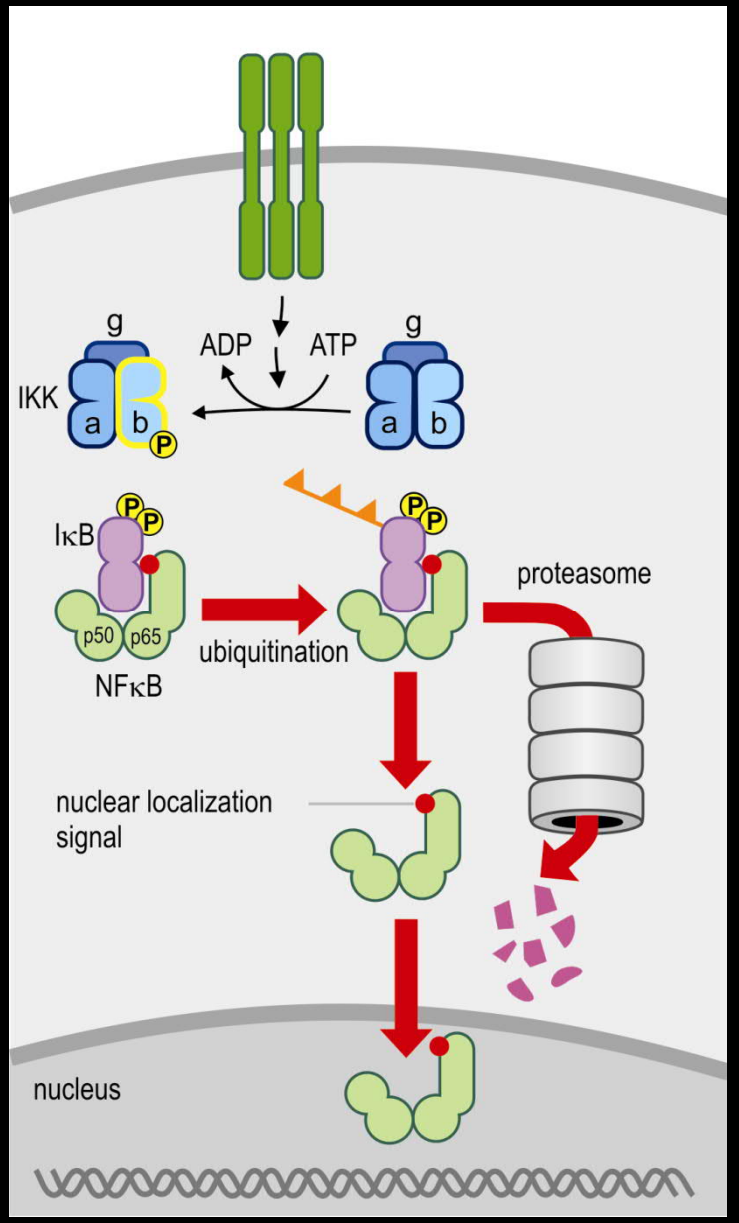
Cytosolic DNA sensors

Innate Immune Receptors

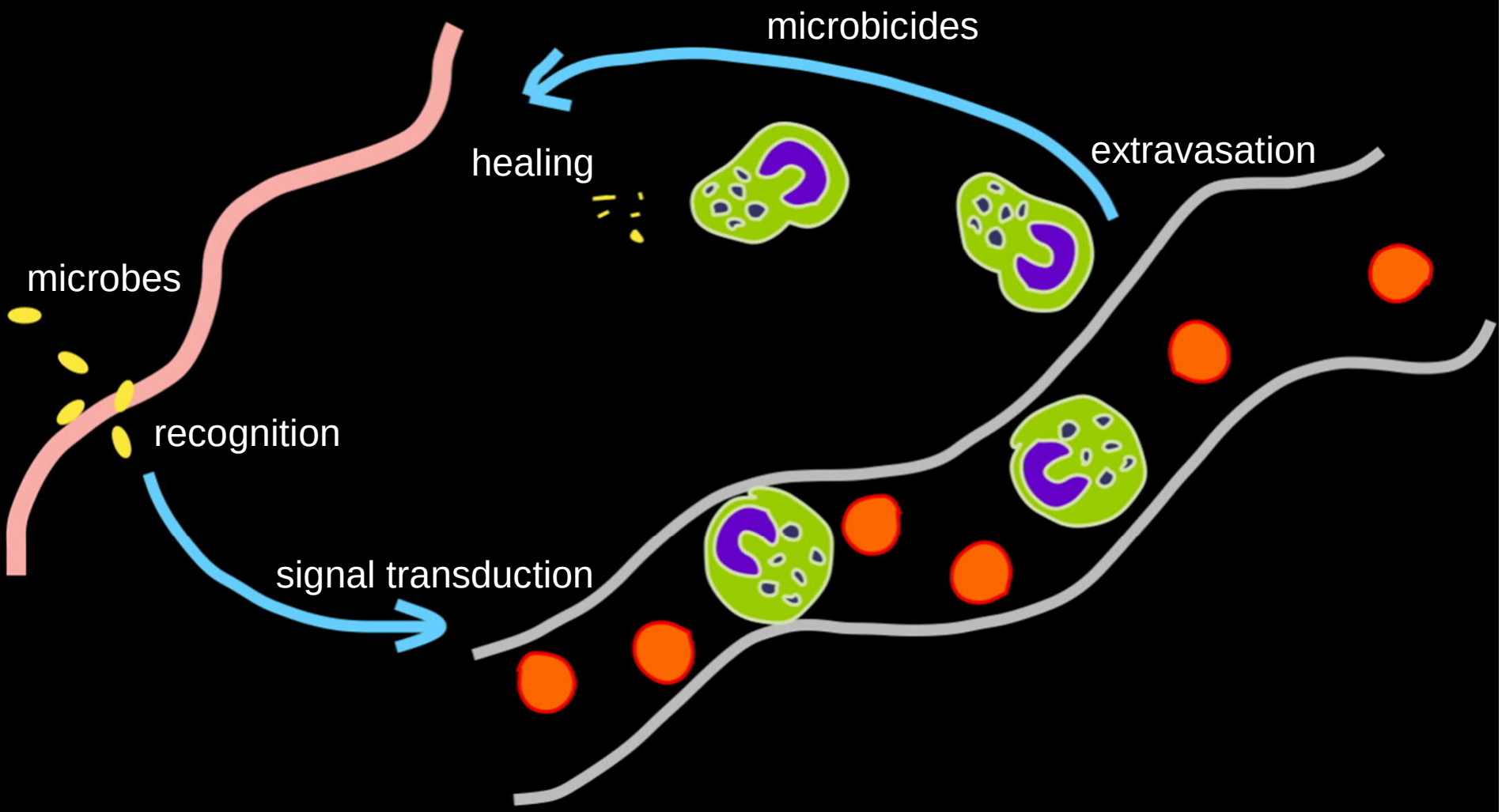


NF-κB activation





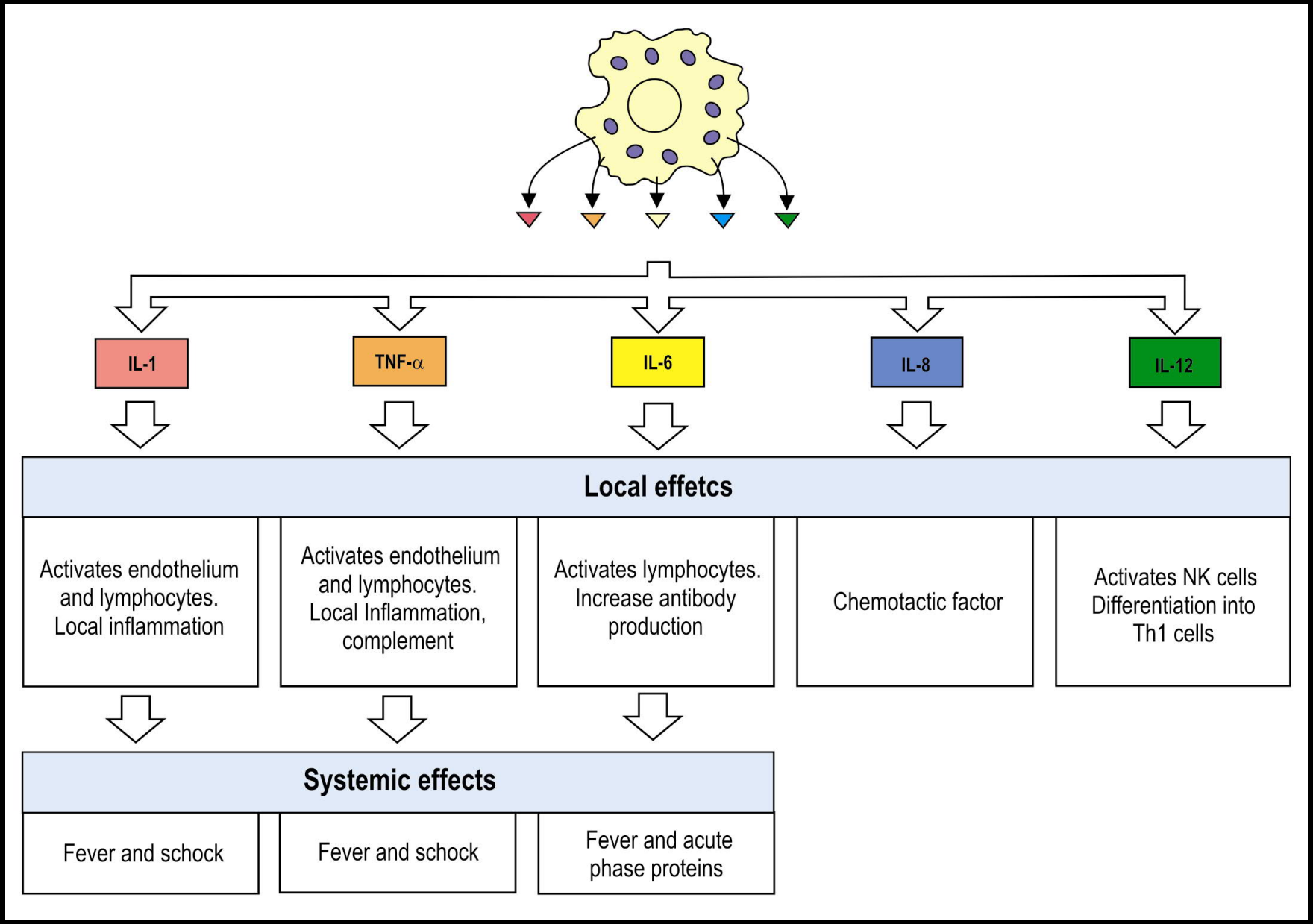
Innate immunity



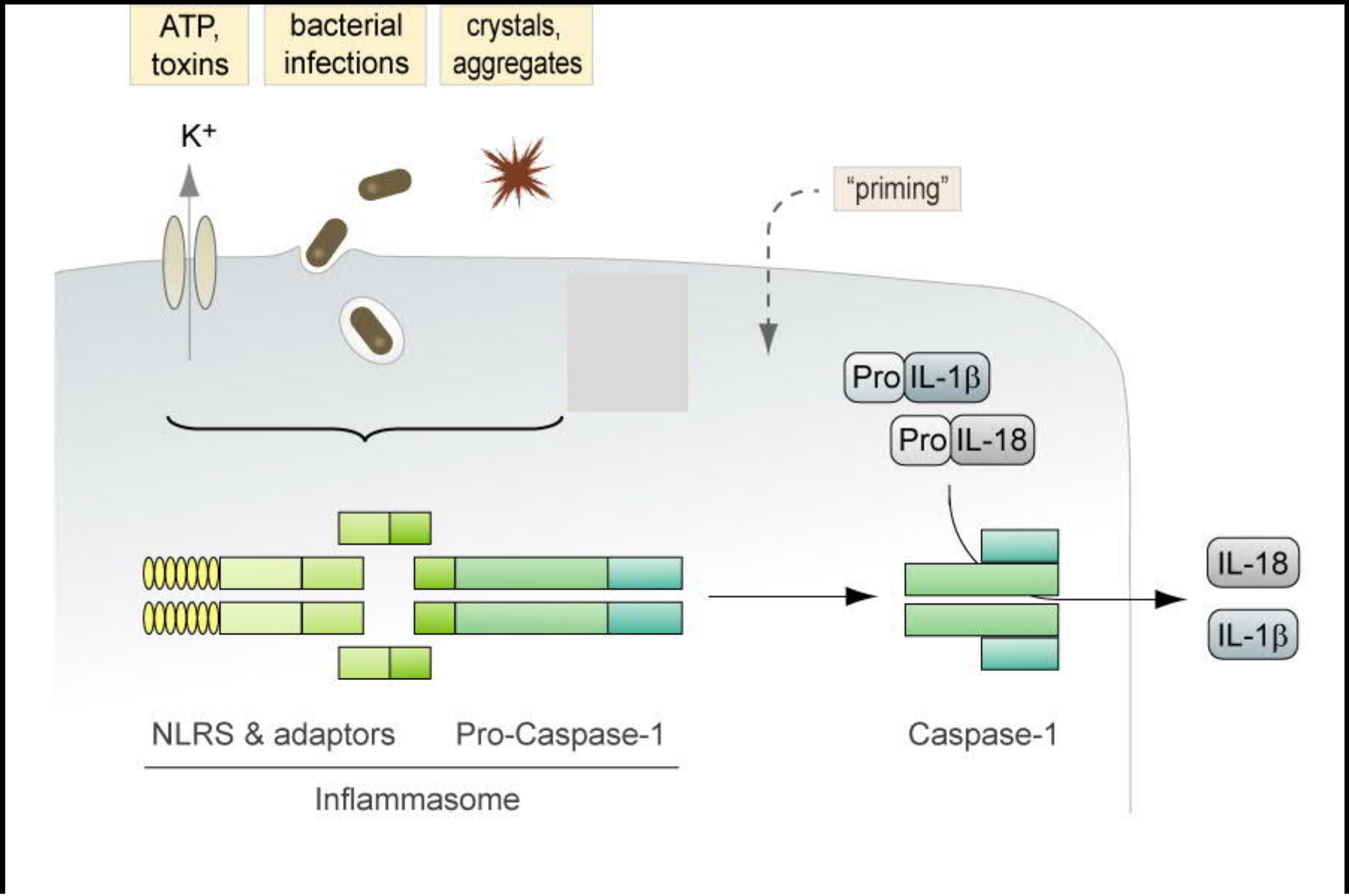
Genes turned on by NF-κB

- Cytokines
- Chemokines
- Antiapoptosis

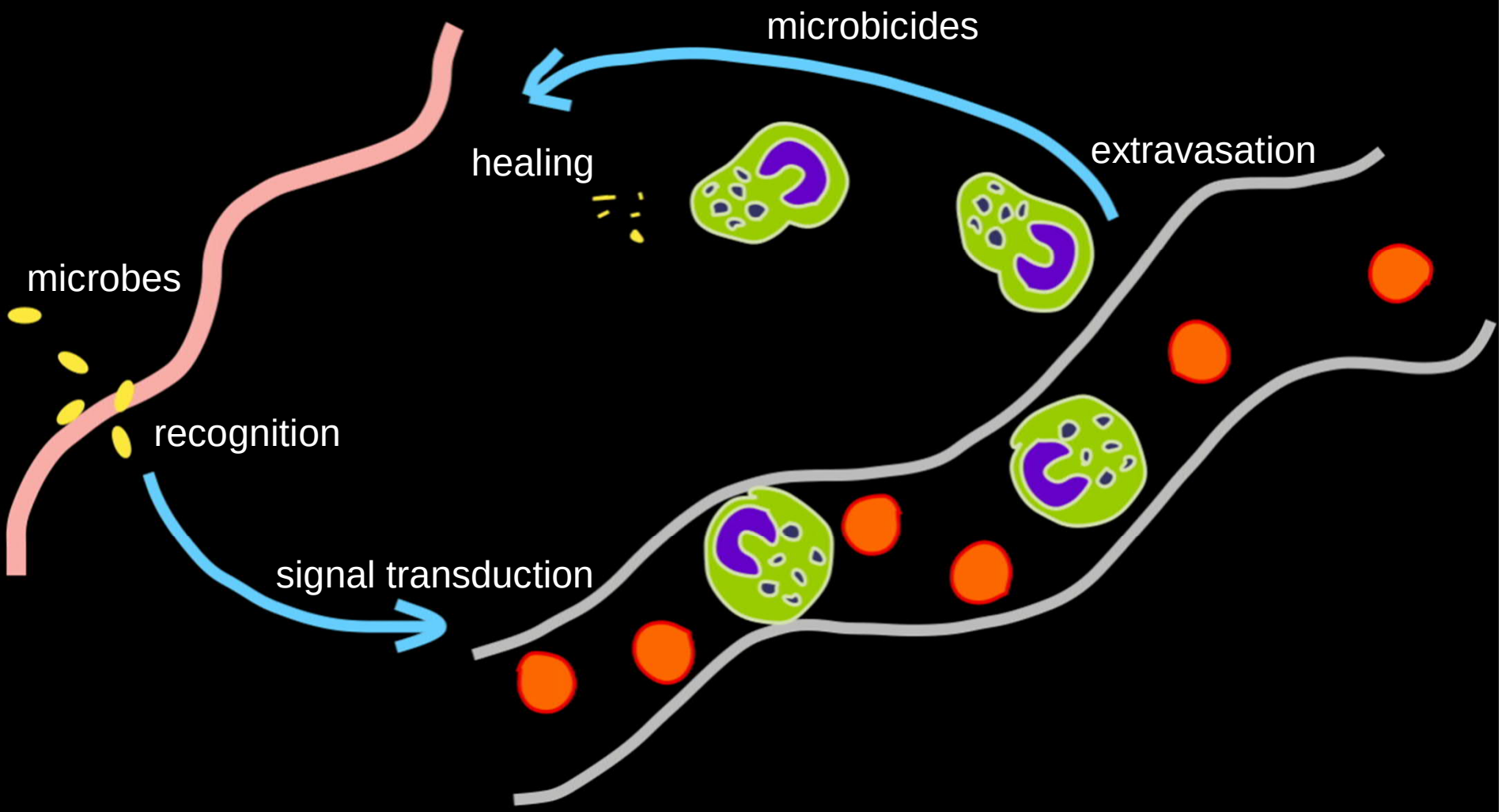
Cytokines and Chemokines



Inflammasome



Innate immunity

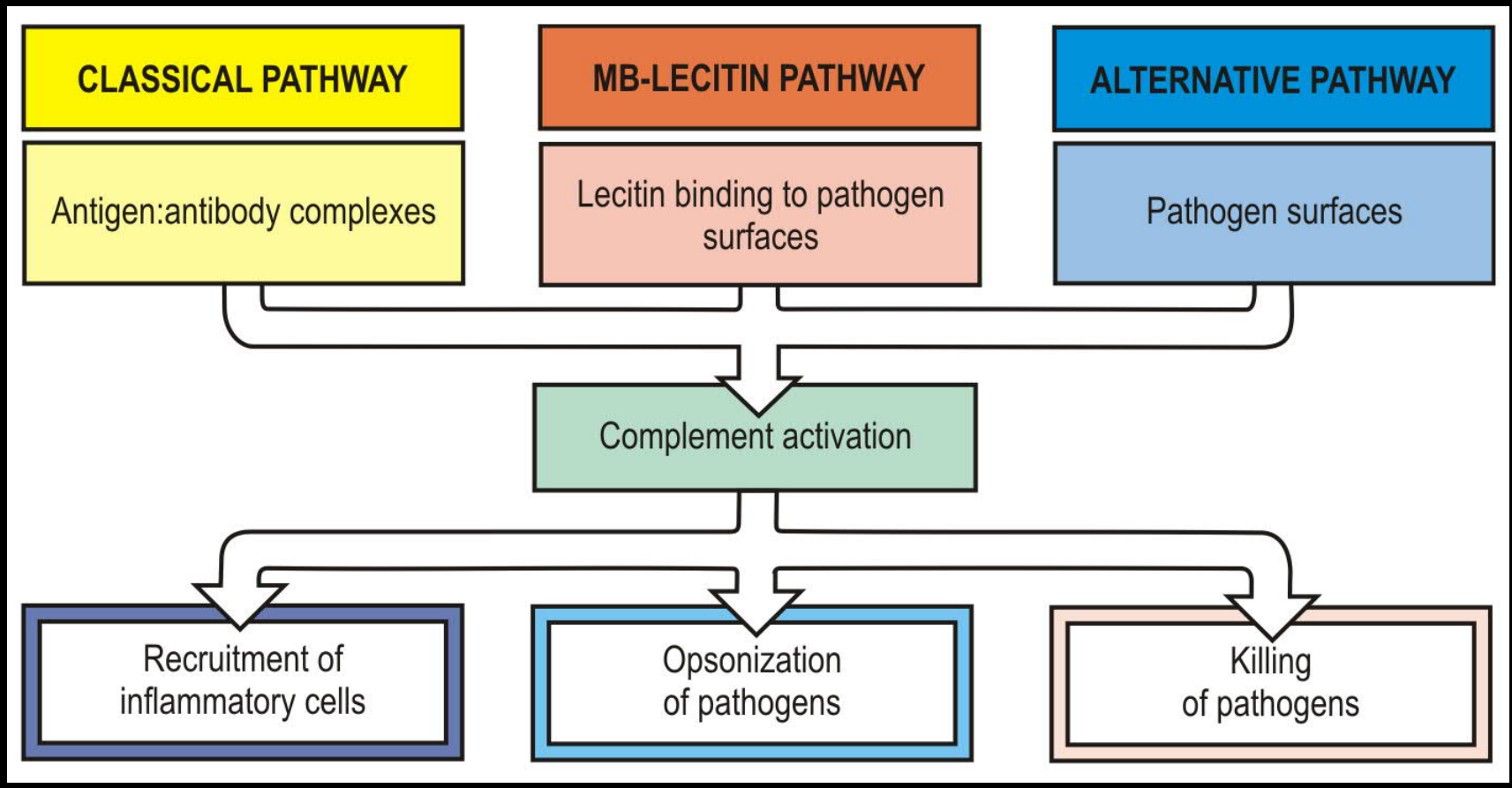


Innate immunity - components

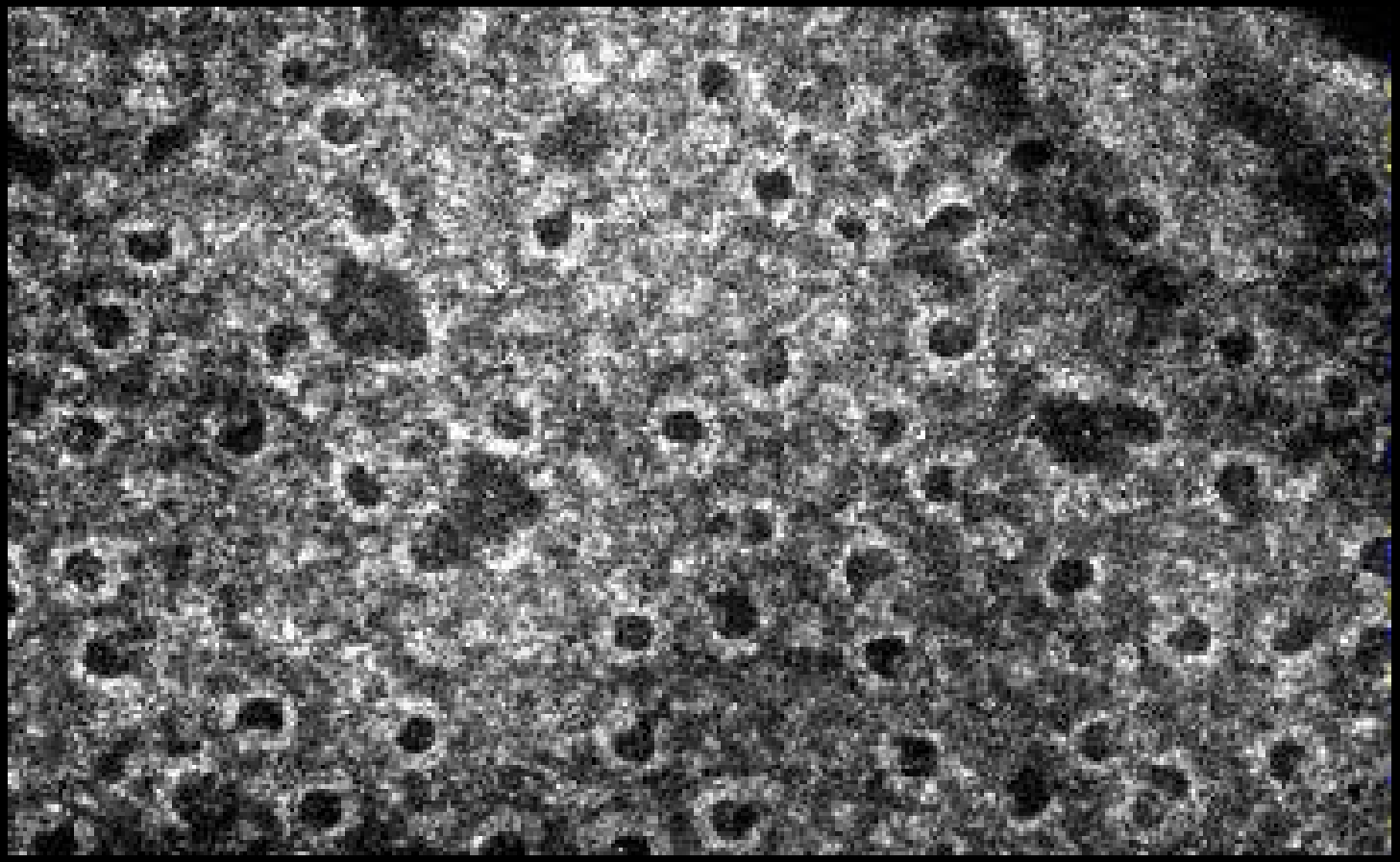
- cellular
  - phagocytes: granulocytes and macrophages
  - secretory cells: basophiles, mast cells, eosinophiles
  - natural killer cells
  - Innate lymphocytes
- humoral
  - complement

Humoral innate immunity

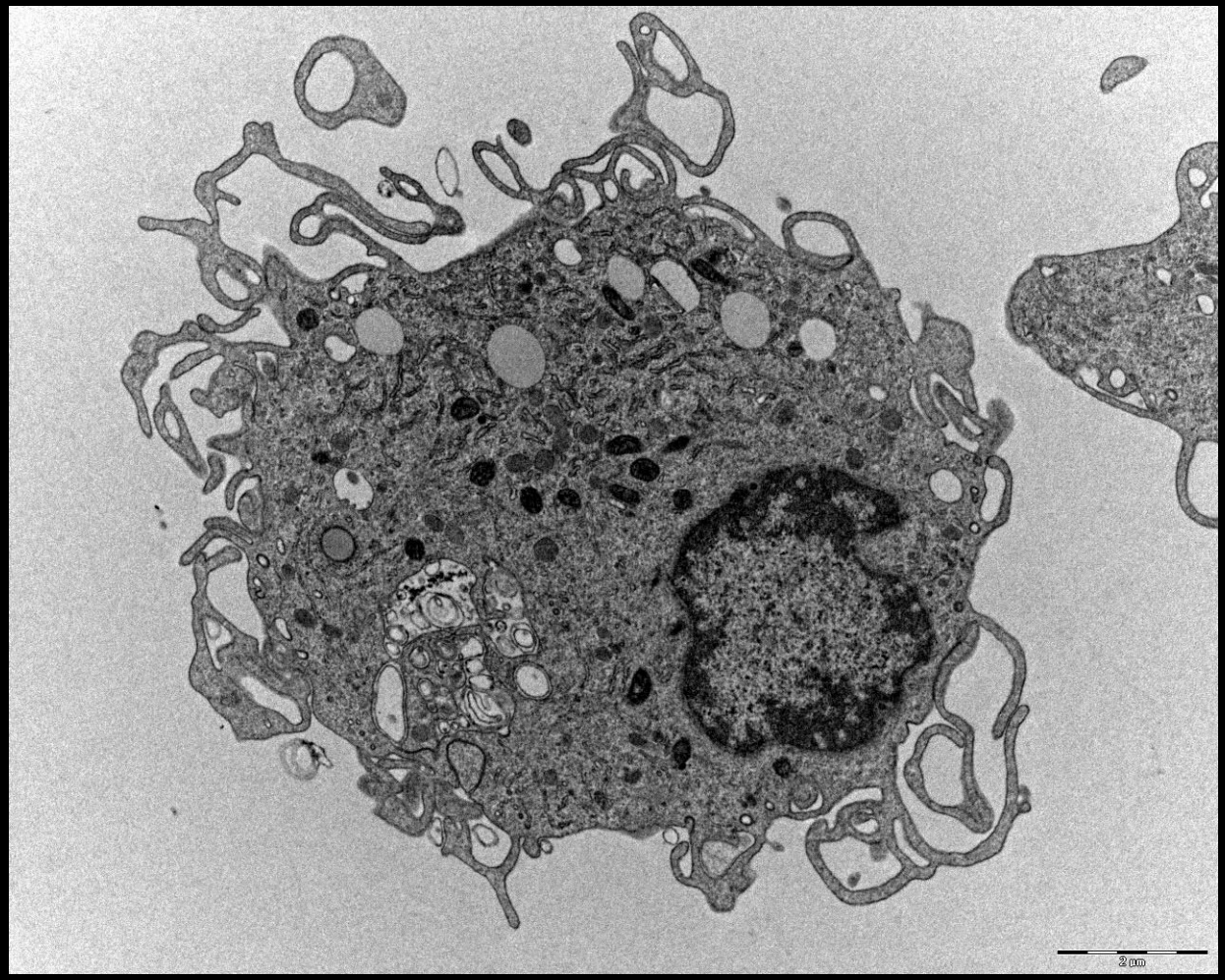
- Complement. What is it good for.



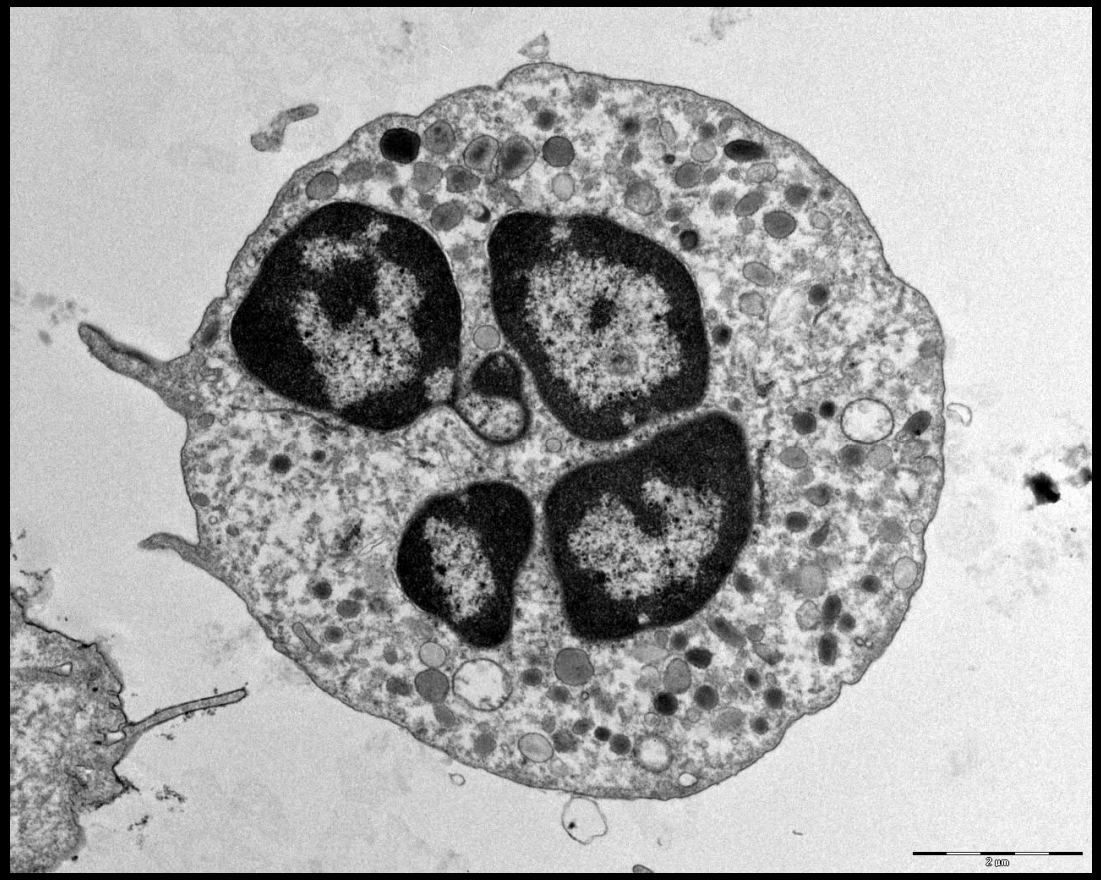
Membrane Attack Complex



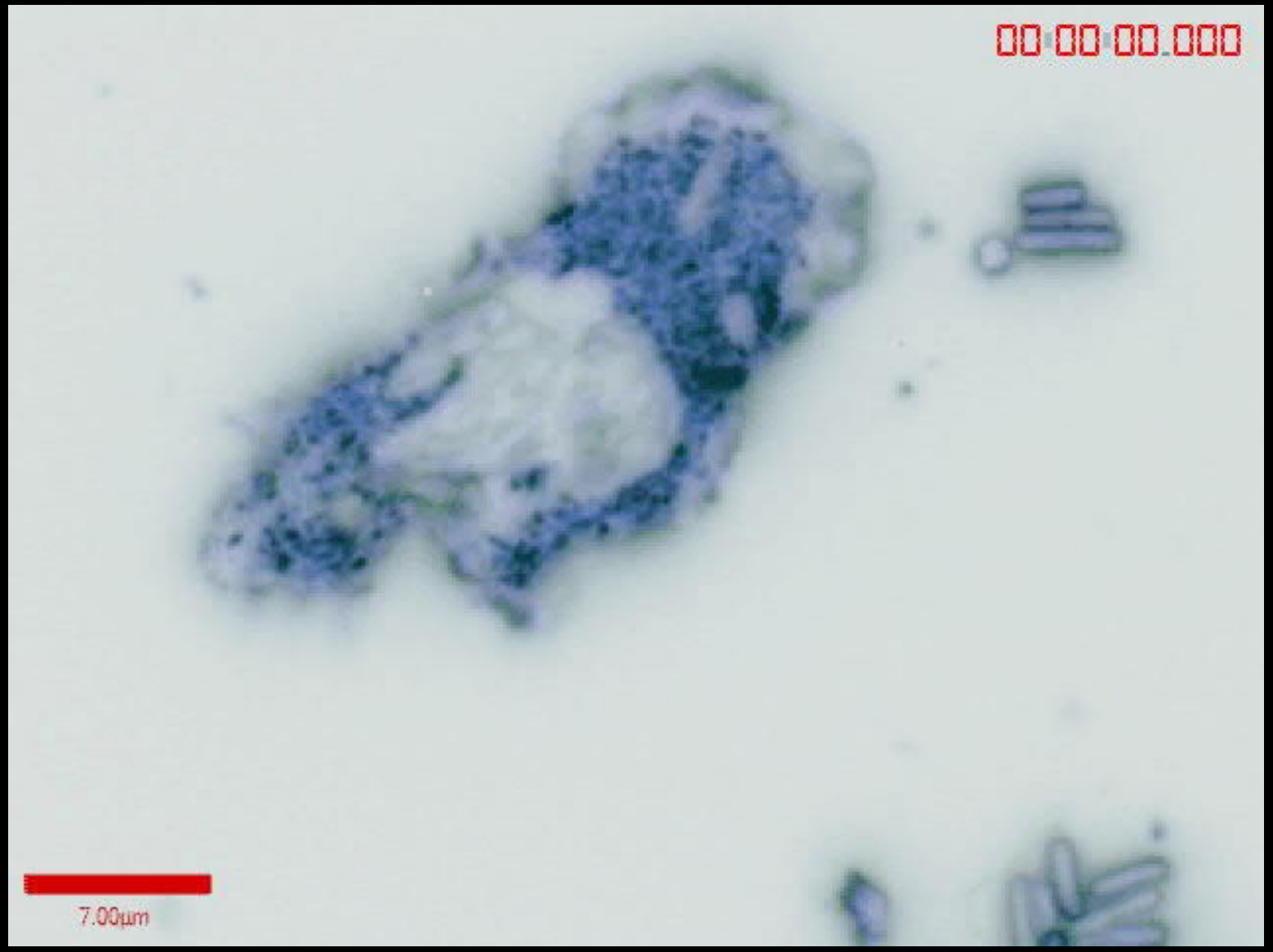
Cellular Innate Immune effectors: macrophage



Cellular Innate Immune effectors: Neutrophil



Phagocytosis: the movie



What happens in the phagolysosome

- Low pH.
- Production of Oxygen Radical Species.
- Enzymes
- Antimicrobial peptides.

Radical Oxygen in Neutrophils

Phox SOD MPO

$$O_2 \rightarrow O_2^- \rightarrow H_2O_2 \rightarrow \begin{matrix} HOBr \\ HOI \\ HOCl \end{matrix}$$

Antimicrobial peptides and proteins

- All Cationic
- Granule associated
- Low cytotoxic activity to mammalian cells
- „are they for real?“

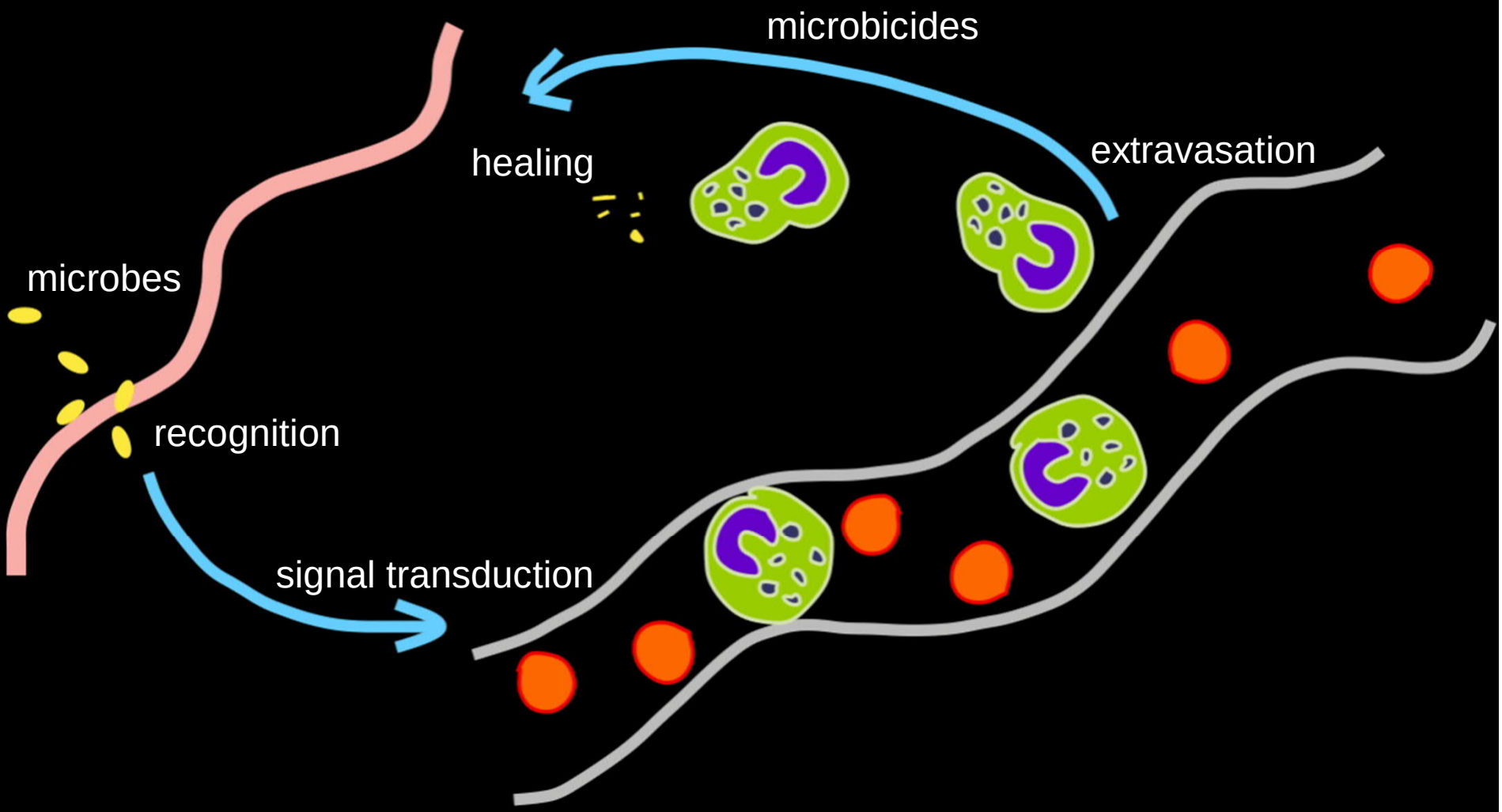
Iron

- Lactoferrin sequesters Fe, necessary for most bugs.
- Many pathogens have their own siderophores.

Enzymes

- Lysozyme
- Phosphilipases (PLA_2) →
- Proteases:
  - Protease 3.
  - Cathepsin G.
  - Neutrophil Elastase.

Innate immunity



Side effects of Inflammation:

Tissue destruction
Autoimmunity

What‘s next?

Systems: real infections

New diseases of direct (or indirect) microbia pathogenesis.

New hosts (model species, specific patients)

Ecology of diseases (systems epidemiology)