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## Chapter 8

# Anti-infectious Immunity



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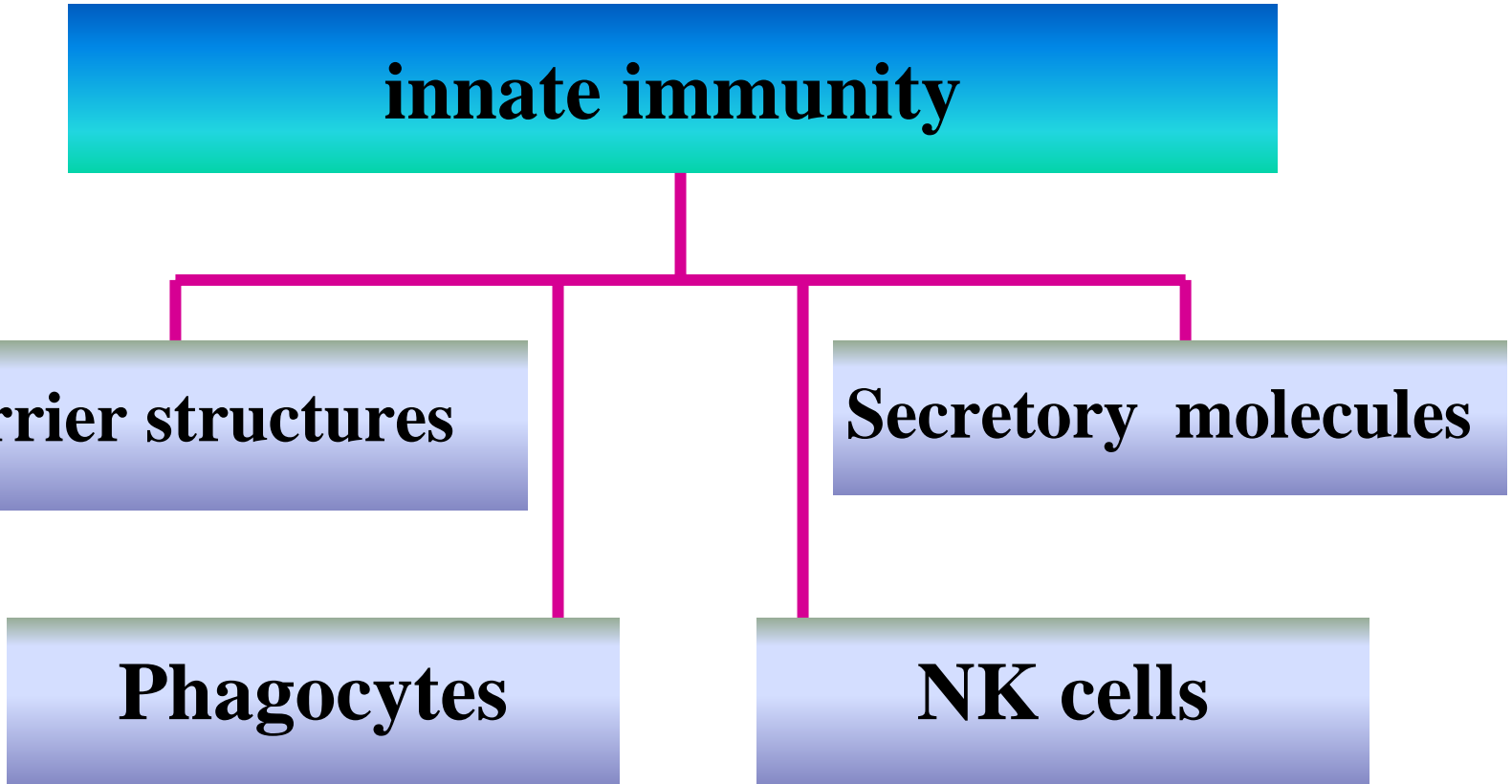
# innate immunity

barrier structures

Secretory molecules

Phagocytes

NK cells





## **Anatomical barriers**

- 1. Skin and mucosa barrier**
- 2.hemo-Spinal Fluid barrier**
- 3. placental barrier**



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## Phagocytic cells

Small phagocytic cell --- neutrophils

larger phagocytic cell --- MPS  
mononuclear phagocyte system



# 1. The steps of phagocytosis :

**chemotaxis**



**recognition and binding**



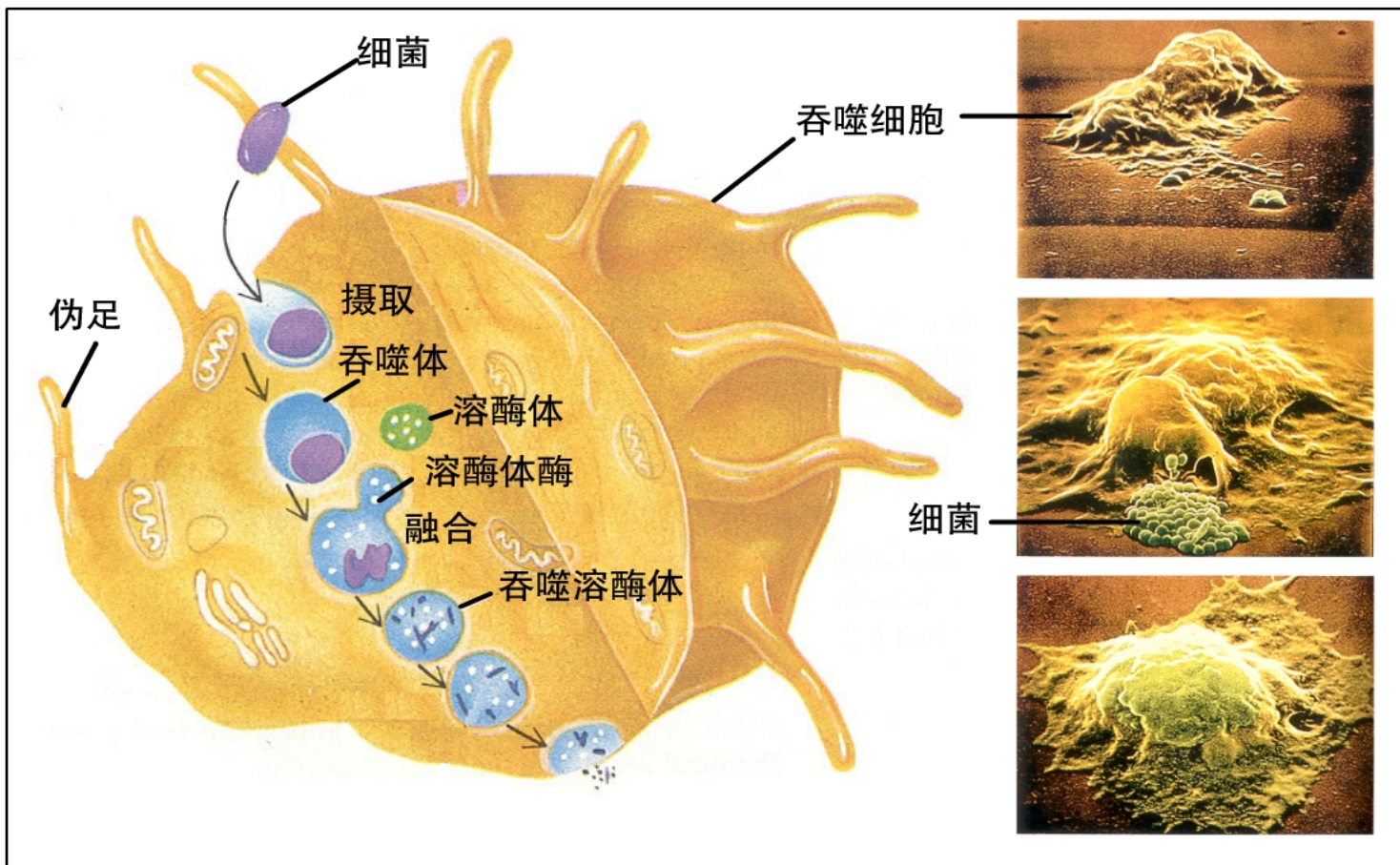
**ingestion** (phagosome)



**digestion** (phagolysosome)



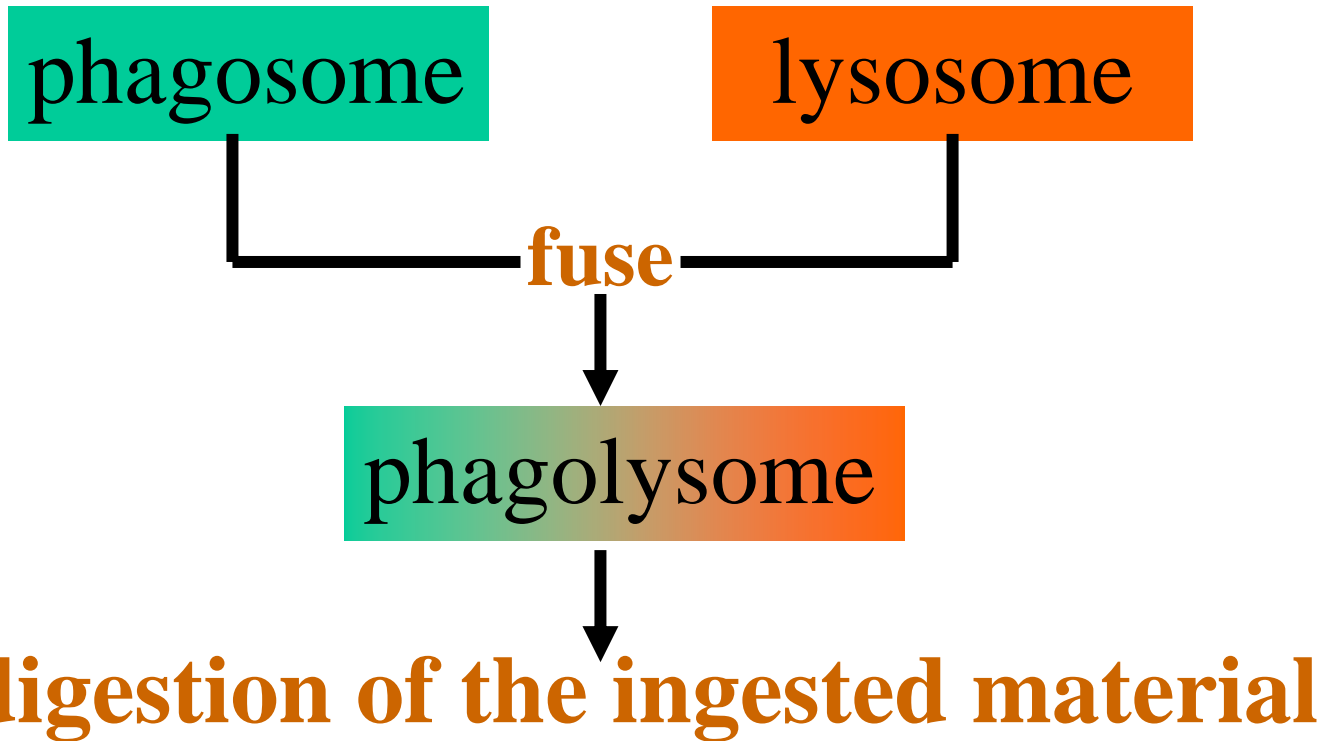




吞噬细胞的吞噬杀伤过程示意图



## 2. Microbicidal mechanism :





## *Oxygen-dependent mechanism (respiratory burst)*

ROI:  $\text{O}_2^-$ ,  $\text{H}_2\text{O}_2$ ,  $\text{OH}^-$

RNI:  $\text{NO}$ ,



## *Oxygen-independent mechanism*

enzyme: *lysozyme; elastase; hydrolase*





## 3. Results of Phagocytosis

### *complete phagocytose :*

The lysosomes fuse with the phagosomes containing the ingested microbes and the microbes are destroyed.

### *un-complete phagocytose:*

Some bacteria(**intracellular bacteria**), such as Mycobacterium species , are more resistant to phagocytic destruction once engulfed.

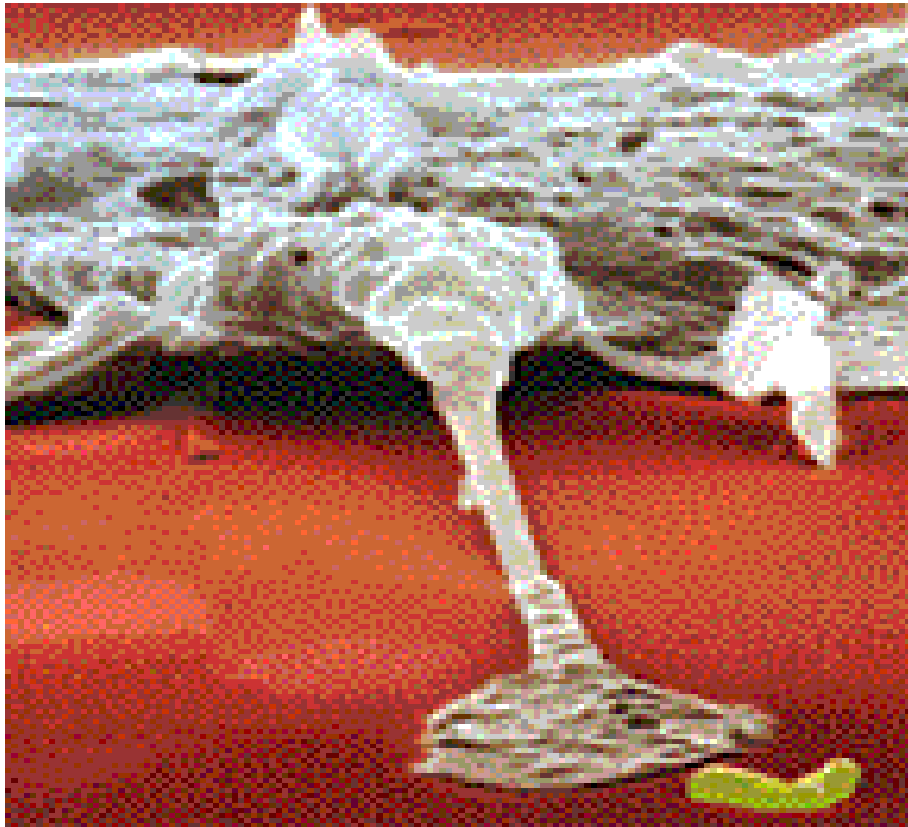
*tissue damage :* hydrolase → inflammation



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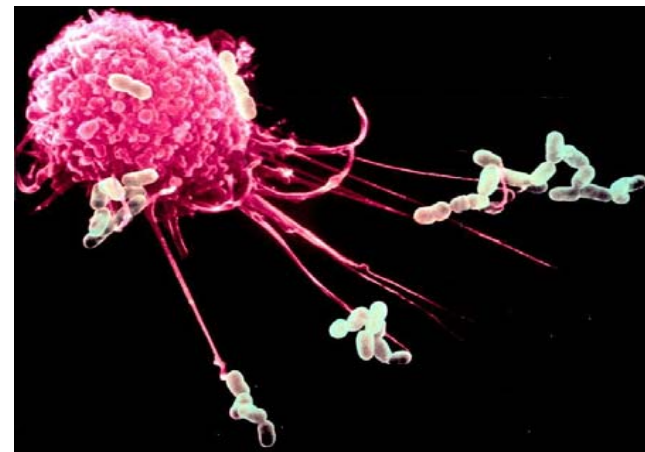
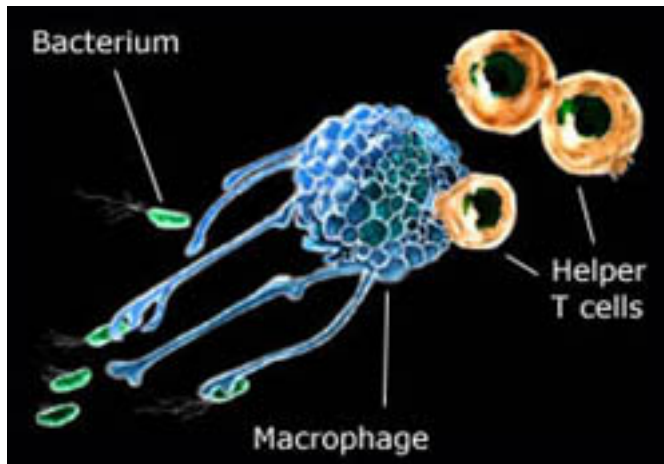
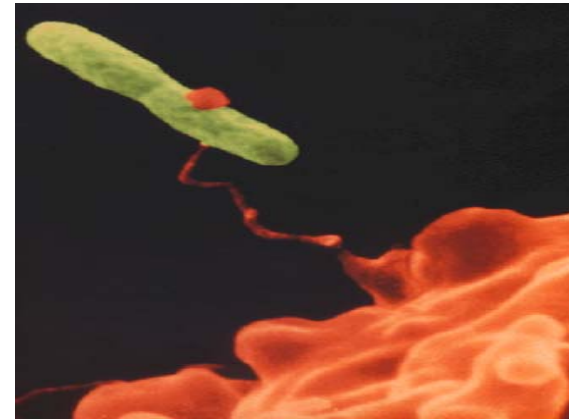
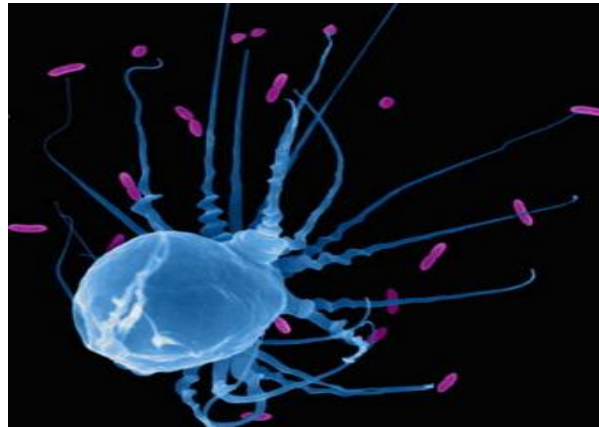


# Phagocytosis





# Phagocytosis





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# Natural Killer Cell

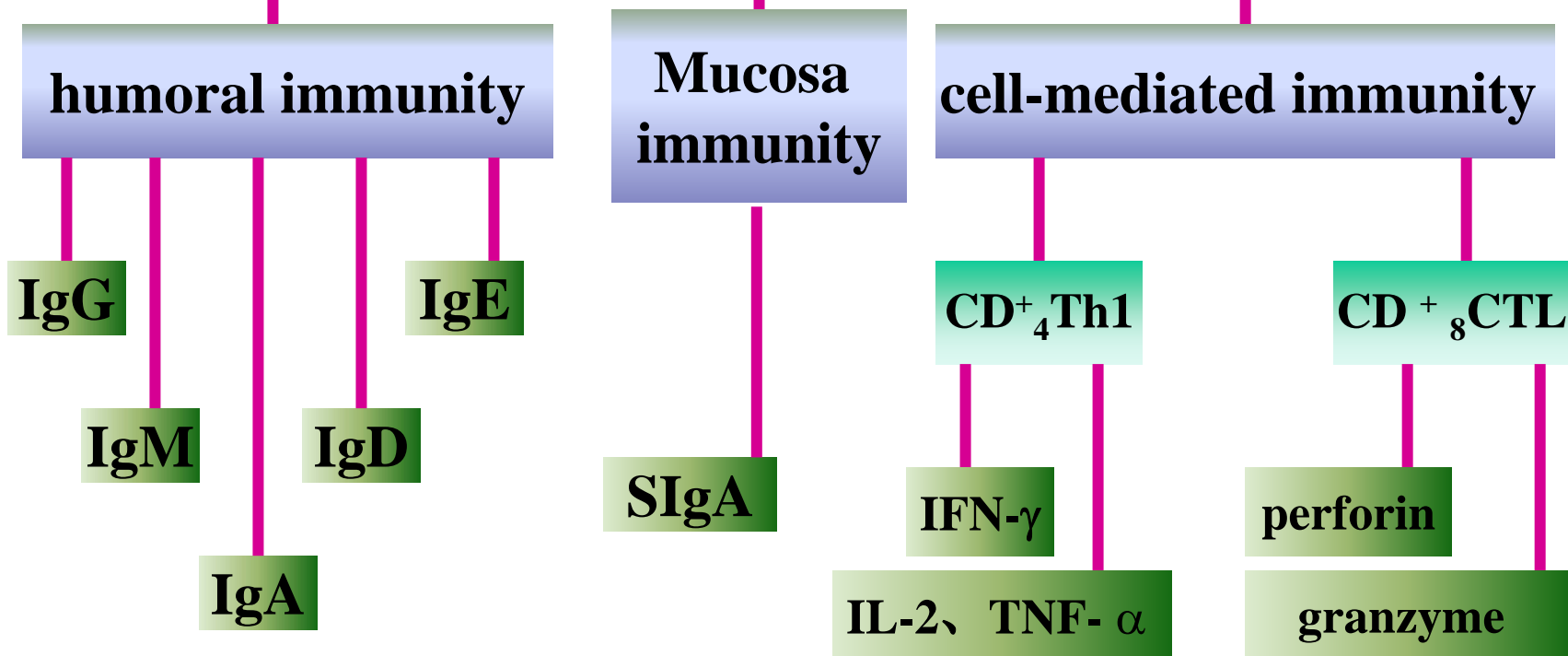
## Secretory molecules

1. complement
2. lysozyme
3. defensin
4. interferon





# Acquired immunity





# Immunity against bacterial infections





# I. Anti- extracellular bacteria

## ▲ extracellular bacteria

--- most of pathogenic bacteria.



## I. Anti- extracellular bacteria

**1. Phagocytic cells:** neutrophils and macrophages

**2. Antibody and complement:**

----- **important factor**

The main function of antibodies :

(1) neutralize bacterial toxins (IgG),

(2) opsonize bacteria(IgG),

(3) activate complement( IgG, IgM)

(4) interferes with attachment to mucosal surfaces (sIgA).

**3. Cell mediated immune response:** CD4 T cell





## II. Anti- intracellular bacteria

1. Phagocytic cells:

2. Cell mediated immune response:

--- **important factor:** the main function of cell mediated immunity (CD4,CD8 T cell) are to protect against intracellular bacteria.

3. **Mucosa immunity:** sIgA is important in local (mucosal) immunity.



## ▲ facultative intracellular bacteria

*Mycobacterium tuberculosis*;

*Mycobacterium leprae*;

*Salmonella typhi* ;

*Brucella*;

*Legionella pneumophila*;

*Listeria monocytogenes*;

## ▲ obligate intracellular bacteria

*rickettsia*, *chlamydia*



## Section II

# Immunity against viral infections





## Innate immunity



### ◆ Inherent Barriers

Skin, Mucus, Ciliated epithelium , Low pH

### ◆ NK cell

### ◆ Interferon (IFN)







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## Interferon ( IFN )

### *Concept:*

A class of protein (glycoprotein ) produced by cells in response to viral infection or other interferon inducers that protected other cells of same species from attack by a wide range of viruses.





## *Production of IFN:*

### ■ interferon inducers:

PolyI:C

viruses

bacterial endotoxins, etc

### ■ production of IFN:

IFN inducer acts on cell receptors --- IFN gene activation---transcribe IFN mRNA---IFN synthesis  
--- IFN released



## *classification of IFNs:*

Hu IFN;

	<b>IFN-<math>\alpha</math></b>	<b>IFN-<math>\beta</math></b>	<b>IFN-<math>\gamma</math></b>
Gene	<b>chromosome 9</b>	<b>chromosome 9</b>	<b>chromosome 12</b>
cell	<b>blood mononuclear cell</b>	<b>fibroblasts</b>	<b>Ag-activated T cell</b>
anti-viral Activity	<b>+++</b>	<b>+++</b>	<b>++</b>
Modify- immune responses	<b>++</b>	<b>++</b>	<b>+++</b>



*antiviral activity:*

cannot act directly on virus, but through  
induction of **antiviral proteins (AVP)**.





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## Mechanisms:

IFN combines with specific receptor on cell surface → AVP gene activated → AVP mRNA transcribed → AVP synthesis.

**AVP** consists of two new cell-encoded enzymes:

**2,5-A synthetase; protein kinase R (PKR);**

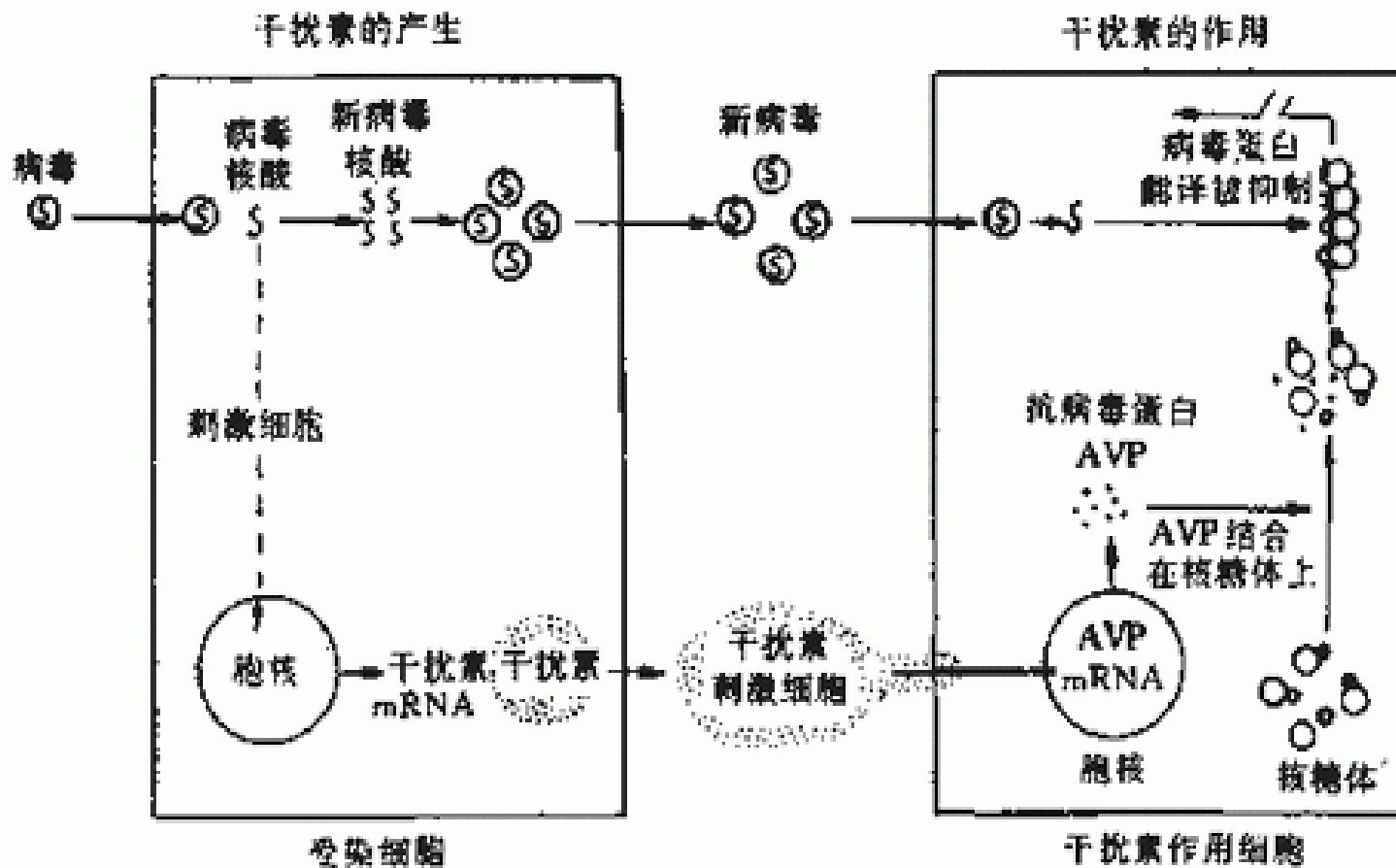


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**2,5-- oligoA synthetase** --- activation of Rnase L  
--- degrad viral mRNAs---inhibit viral protein  
synthesis

**protein kinase** ----phosphorylate eIF-2  
( inactivating eIF-2 ) --- inhibit viral protein  
synthesis.



IFN 抗病毒作用示意图



## *Antiviral characteristics of IFN:*

- 1) **have no direct effect on extracellular virus:**  
( through induction of AVP).
- 2) **broad-spectrum antiviral activity:** IFN inhibit the intercellular replication of a wide variety of both DNA and RNA viruses .
- 3) **host species specific:** IFN inhibit viral replication only in the species in which it was produced.
- 4) **Act in the early phase of viral infection:** IFN are produced within a few hours of the viral infection.







## Other activities of IFN:

### Anti-tumor :

---inhibit the growth of certain cancer cells

### Modify immune responses:

--- activation of NK cell

--- activation of macrophage

---Increased expression of MHC molecules



## NK cell

NK cell: Lyse virus- infected cell directly, play an important role in early viral infection before activation of acquired immunity.





## Acquired immunity



### Humoral immunity

Neutrilizing antibody

### Cell mediated immunity

$CD^+_8$  CTL

$CD^+_4$  Th1

NK cell



**1) Neutrizing antibodies :** antibodies that interfere with the adherence (adsorption and penetration) of viruses to cell surface are called **neutrizing antibodies.**

neutrization of the infectivity of the virus by neutrizing antibody binding to the **surface proteins of the virus.**

**IgG IgM IgA**



- Antibody- coated virus is destroyed:
  - --- by phagocyte
  - --- by complement
  - --- by ADCC
- **Neutrilizing antibodies** act on free viruses , but can't influence intracellular viruses directly.





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## 2). Non-neutralizing antibody

-- antibodies formed against internal components of the virus , they do not neutralize the infectivity of the virus.

Such as:

Complement fixation antibodies:



## 2. Cell mediated immunity:

- act on intracellular viruses .
- the destruction of an infected cell before progeny particles are released --- **an effective way of terminating a viral infection.**



### CD8 CTL:

--- react with membrane-bound viral antigens and lyse the infected cells.



--- release some cytokines (IFN- $\gamma$ , TNF ).

**CD4 Th 1 cell :** --- release cytokines.