# Differenziamento e funzioni effettrici dei linfociti T helper

Prof Giovanni Bernardini 11/11/2026

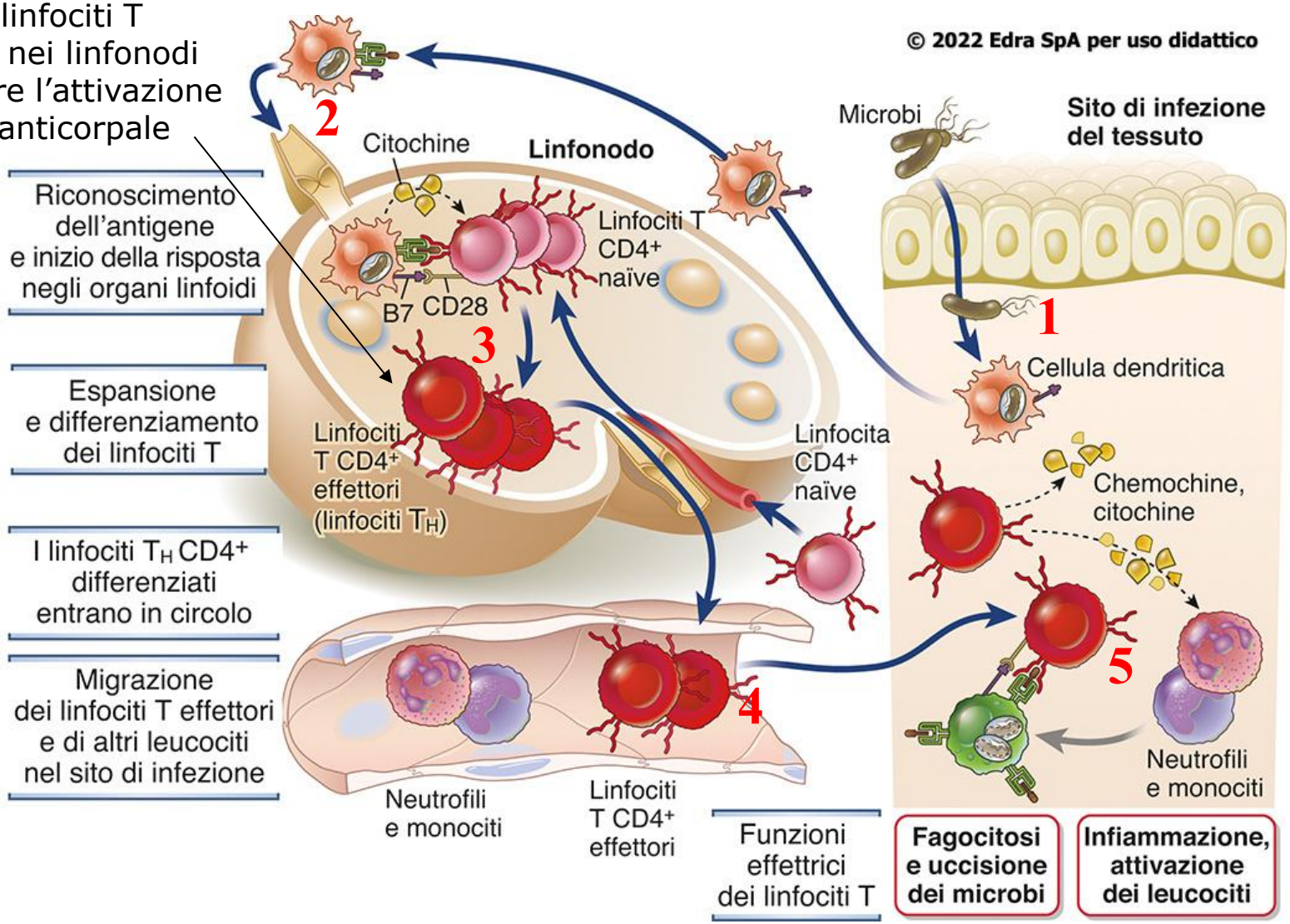
Il materiale contenuto in questo documento e distribuito a uso interno e a puro scopo didattico

# Today's Topics

- What are the functions of helper T lymphocytes?
- How are their functions accomplished?
- How are their functions acquired?

# Induzione e fasi effettrici dell'immunita cellulo-mediata

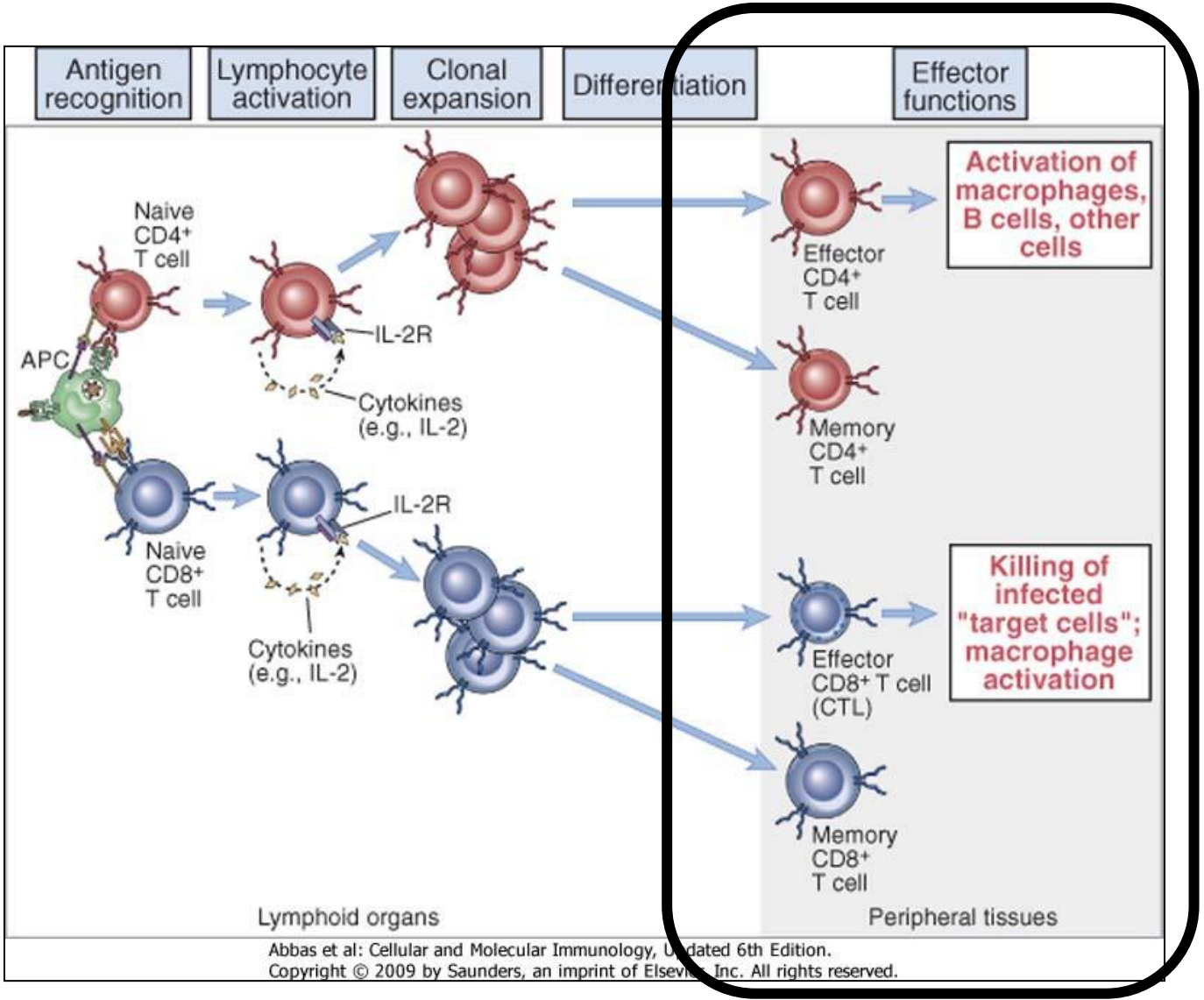
Una parte dei linfociti T helper rimane nei linfonodi per co-adiuvare l'attivazione della risposta anticorpale



What happens following T cell activation?

# T cell differentiation and effector phases of cell-mediated immunity

## Acquisition of effector functions by T lymphocytes




Abbas et al: Cellular and Molecular Immunology, Updated 6th Edition.
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# Domanda

Quando i linfociti T, attivati dall'antigene presentato dalle APC, secernono IL-2 cosa succede ai linfociti T naive non antigene specifici che si trovano nelle vicinanze ?

A) proliferano in risposta alla IL-2
B) spesso vanno in apoptosi
C) esprimono il recettore della IL-2
D) secernono citochine associate al loro fenotipo Th
E) non succede nulla

- What are the functions of helper T lymphocytes?

Migration to effector site (T lymphocytes in general)

Help (regulate the function of) cells that participate to the immune response

- What are the functions of helper T lymphocytes?

**Migration to effector site (T lymphocytes in general)**

Help (regulate the function of) cells that participate to the immune response

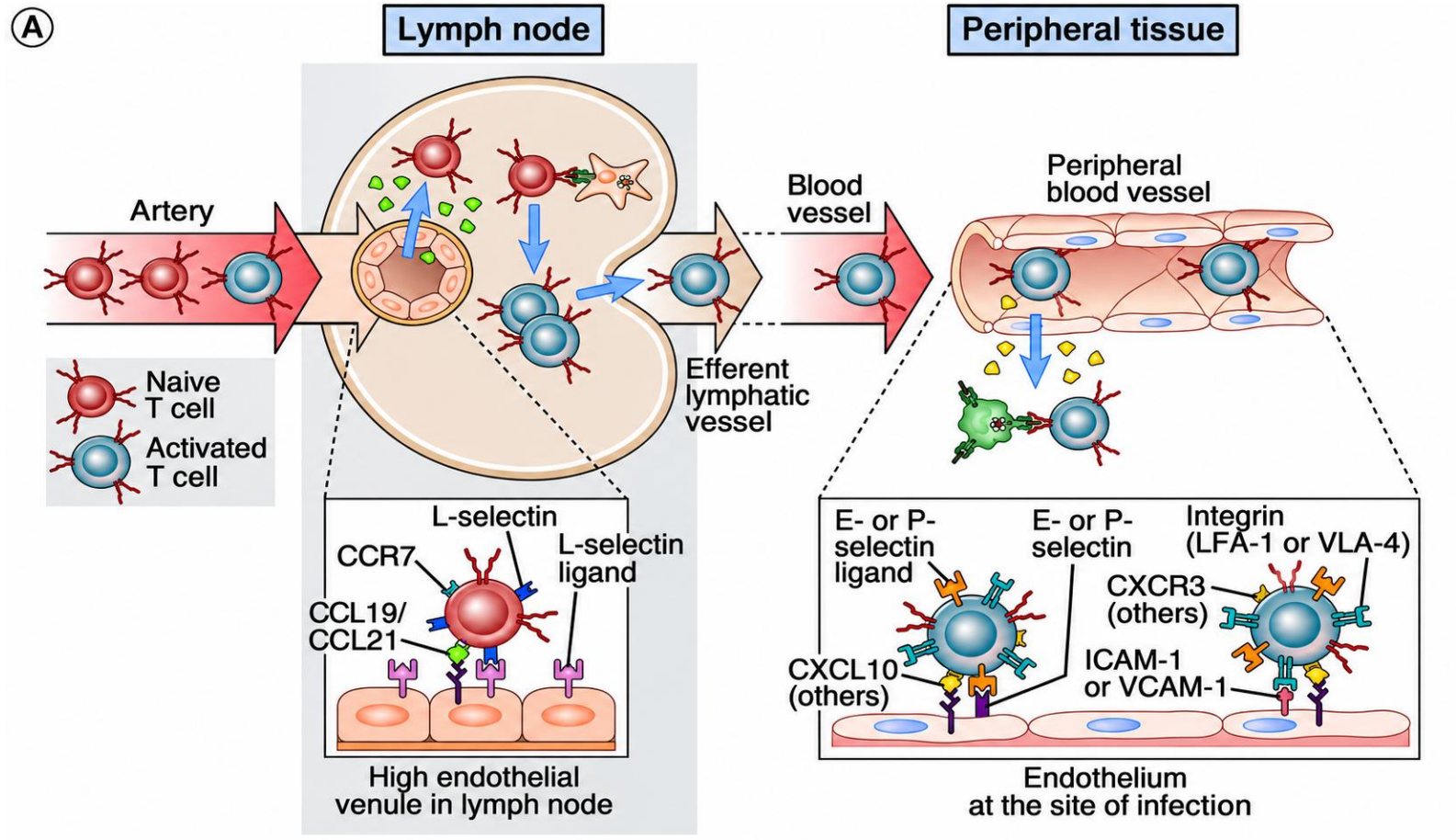
# Homing tessuto specifico

**La stimolazione antigenica “riprogramma” le proprieta’ di traffico di cellule B e T “vergini” inducendo il differenziamento di cellule effettrici e memoria che**

**a- hanno migliori capacita’ di homing per tessuti extralinfoidi rispetto alle vergini**

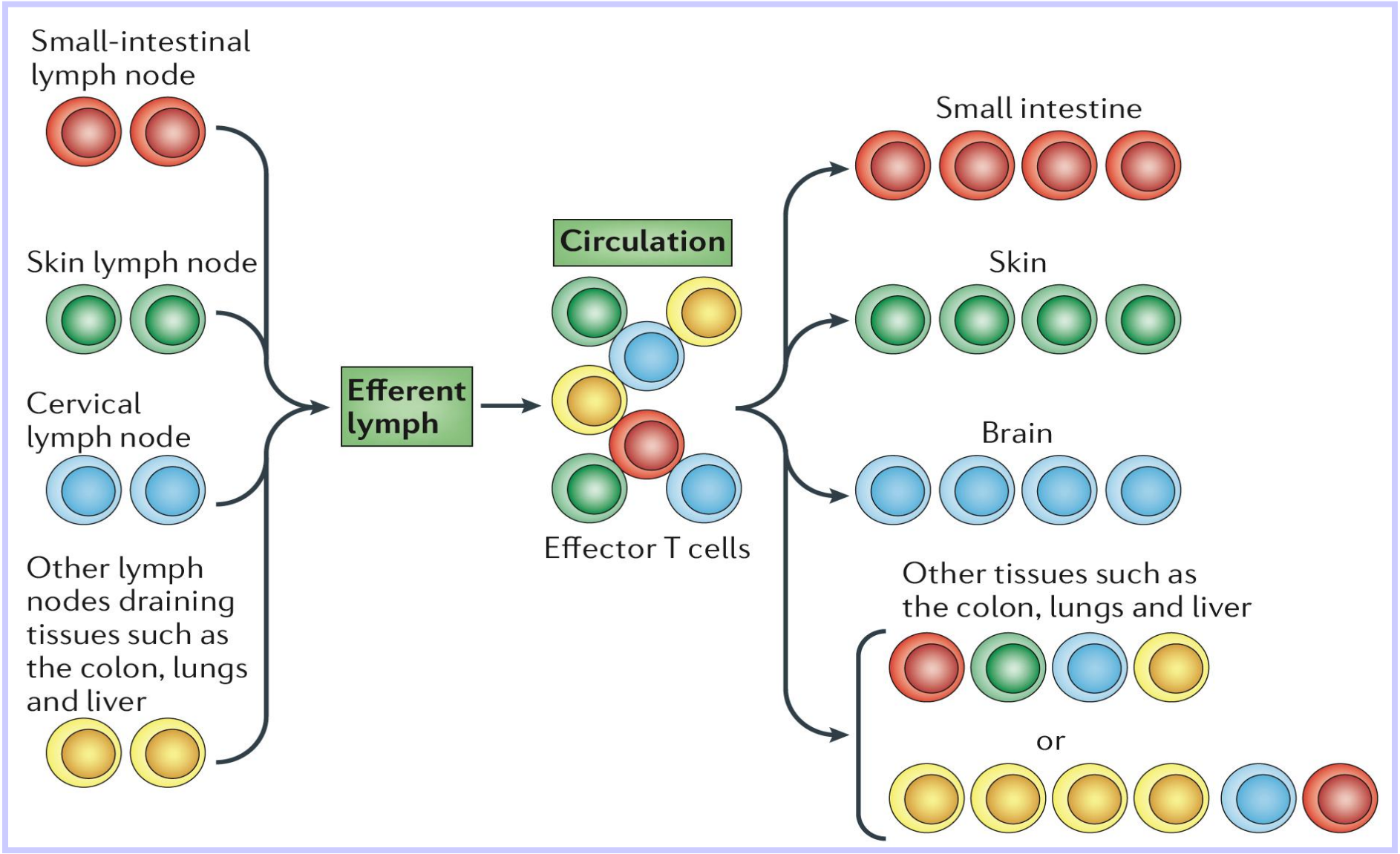
**b- sono in grado di “SELEZIONARE” tessuti e organi specifici dove dirigersi ritornando preferenzialmente nel tessuto che ne ha causato l’attivazione (cioè dove è più probabile trovare l’antigene che li ha attivati).**

# Migrazione di linfociti T vergini e attivati

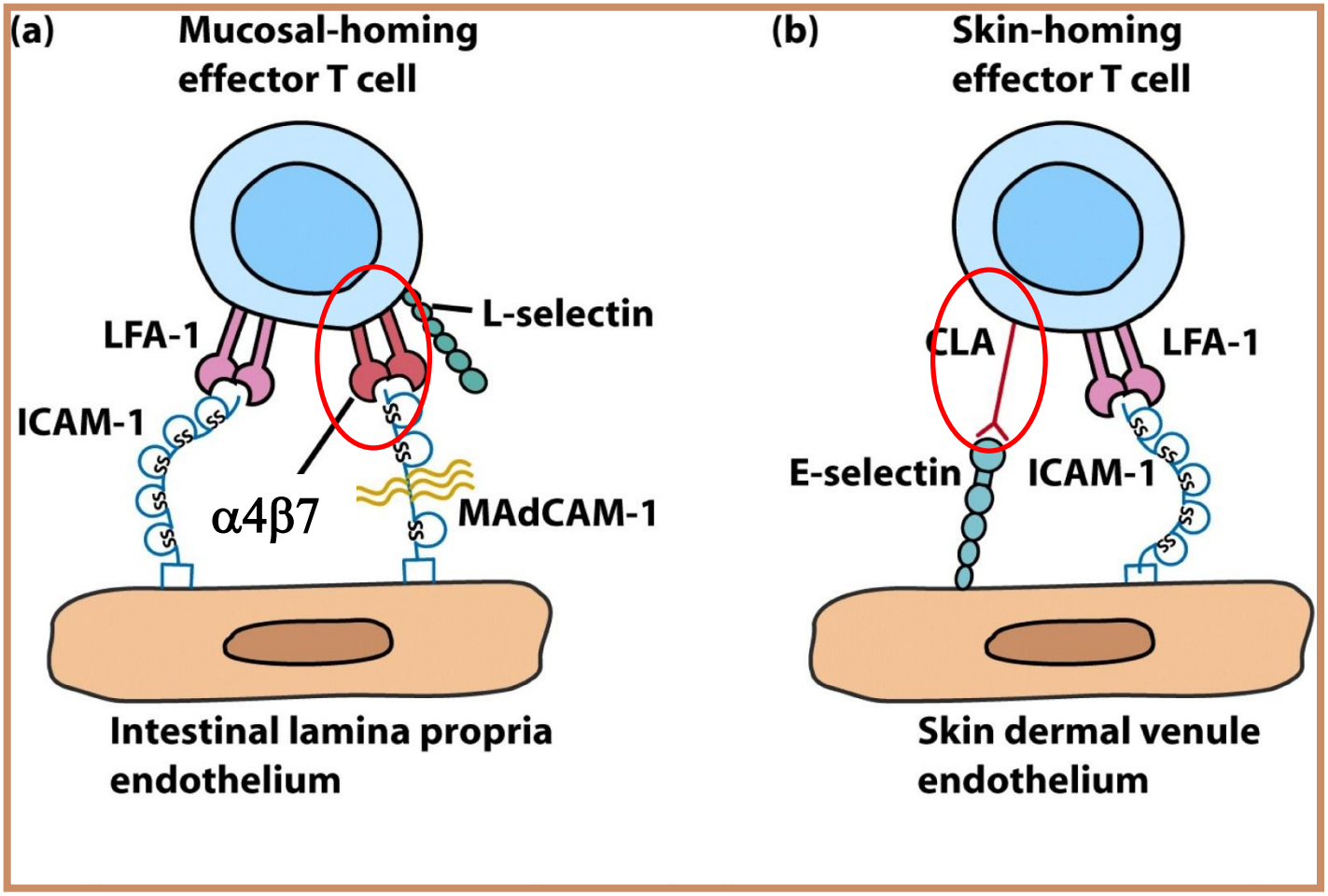


# Generation of effector T cell populations with tissue-specific homing to extra-lymphoid sites

**T cell activation**



# Un differente set di molecole di adesione e di chemochine guida la migrazione tessuto specifica




CLA=cutaneous lymphocyte antigen

- What are the functions of helper T lymphocytes?

Migration to effector site (T lymphocyte in general)

**Help (regulate the function of) cells that participate to the immune response**

# Immune specific functions vary on the basis of the nature of the pathogen (two types of adaptive immunity)

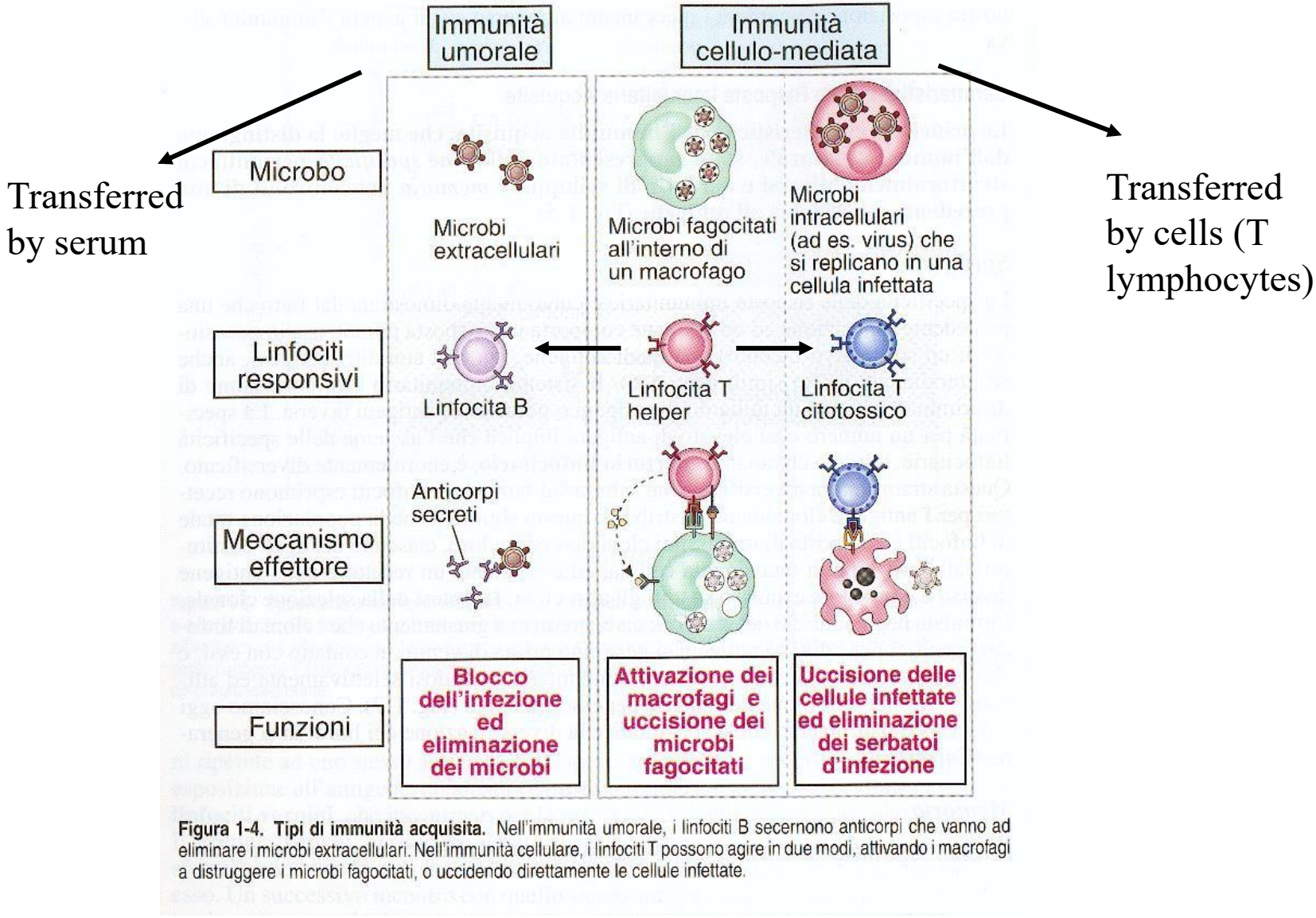
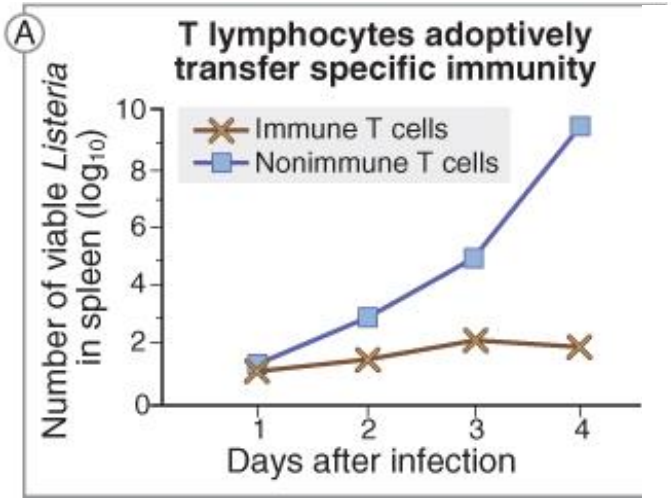
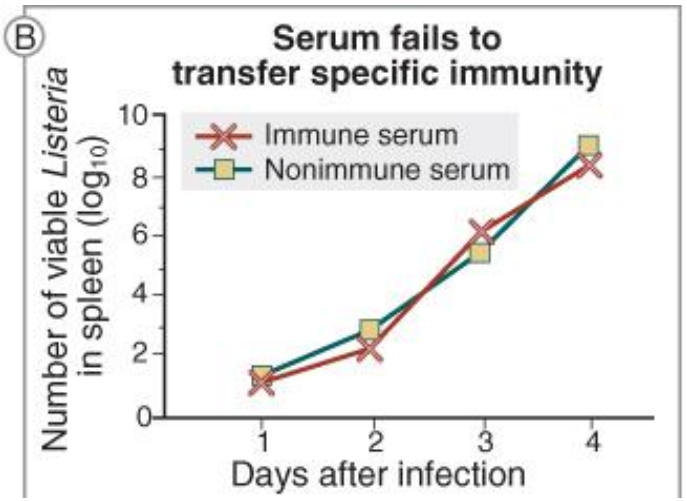
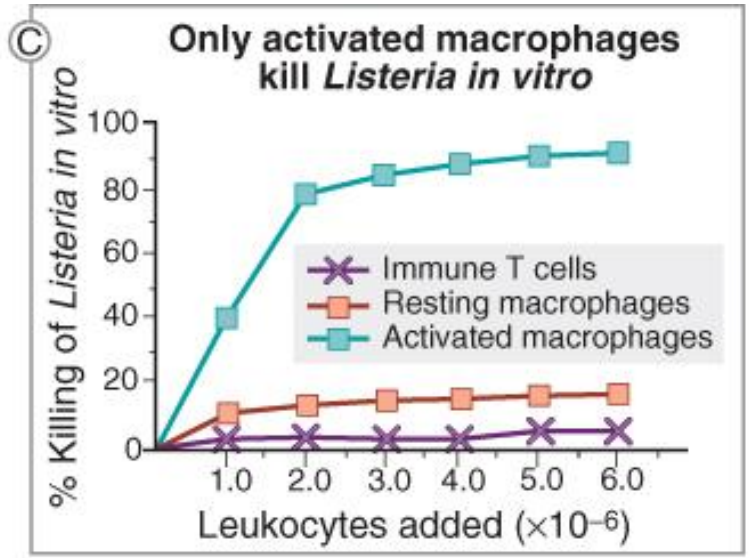



**Figura 1-4. Tipi di immunità acquisita.** Nell'immunità umorale, i linfociti B secernono anticorpi che vanno ad eliminare i microbi extracellulari. Nell'immunità cellulare, i linfociti T possono agire in due modi, attivando i macrofagi a distruggere i microbi fagocitati, o uccidendo direttamente le cellule infettate.

# Helper T lymphocytes are important for the macrophage-mediated response to pathogens



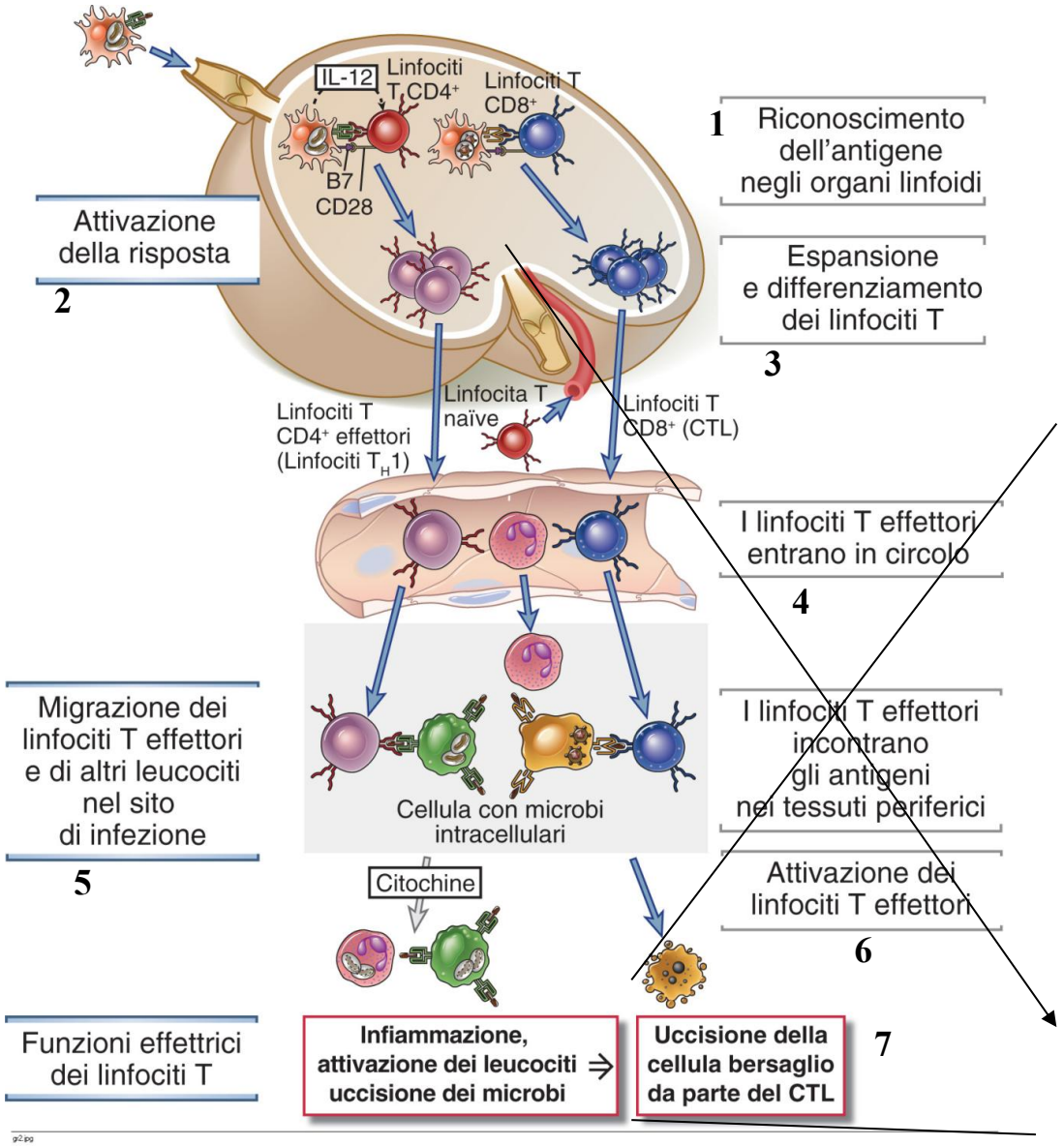




**T cells do not induce direct killing**

Helper T lymphocytes perform their function through membrane molecules and the production of a wide variety of cytokines capable of activating other cells more directly involved in the elimination of microorganisms

# T helper cell function




g2.jpg

Immunologia cellulare e molecolare 7 ed

L'induzione e l'asi effettrici dell'immunità cellulo-mediata. Induzione della risposta: negli organi linfoidi secondari i linfociti T CD4<sup>+</sup> e CD8<sup>+</sup> riconoscono i peptidi derivati dagli antigeni proteici e presentati dalle cellule dendritiche. I linfociti T sono quindi stimolati a proliferare e a differenziarsi in cellule effettrici o della memoria, per poi entrare in circolo. Migrazione dei linfociti T effettori e di altri leucociti verso il focolaio d'infezione: i linfociti T effettori e altri leucociti migrano nei vasi sanguigni verso i tessuti periferici legandosi alle cellule endoteliali che sono state attivate da citochine prodotte a livello dei tessuti infettati. Funzioni effettrici dei linfociti T: i linfociti T effettori riconoscono l'antigene nei tessuti infettati secernendo citochine che reclutano ancora più leucociti e stimolano i fagociti a eradicare l'infezione. Anche i CTL migrano nei tessuti periferici e uccidono le cellule infettate.

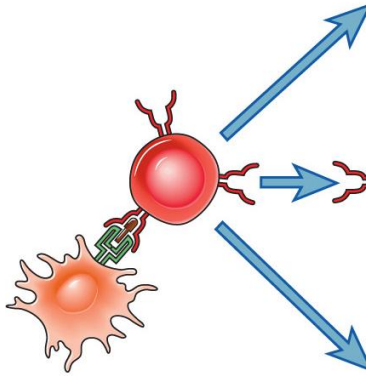
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| Principali reazioni immunitarie | Difesa contro |
|---|---|
| Attivazione dei macrofagi | Patogeni intracellulari |
| Attivazione degli eosinofili e dei mastociti; attivazione alternativa dei macrofagi | Elminti |
| Reclutamento e attivazione dei neutrofili | Batteri extracellulari e funghi |
| Produzione di anticorpi | Patogeni extracellulari |

How is it possible that such a specialized (and appropriate) response to the microbe can depend on a single cell type capable of producing diversified responses depending on the microbe involved? ...

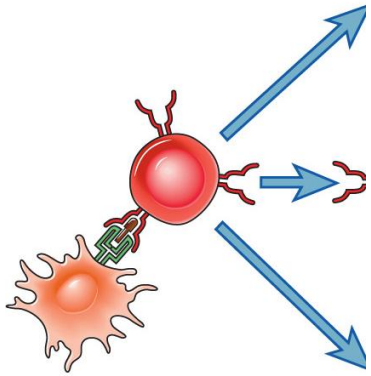
the CD4+ T lymphocyte

# Diverse sottopopolazioni di linfociti Th combattono patogeni diversi



| Linfociti T effettori | Citochine caratteristiche | Principali cellule bersaglio | Principali reazioni immunitarie | Difesa contro |
|---|---|---|---|---|
| $T_H1$ | IFN-γ | Macrofagi | Attivazione dei macrofagi | Patogeni intracellulari |
| $T_H2$ | IL-4<br>IL-5<br>IL-13 | Eosinofili | Attivazione degli eosinofili e dei mastociti; attivazione alternativa dei macrofagi | Elminti |
| $T_H17$ | IL-17<br>IL-22 | Neutrofili | Reclutamento e attivazione dei neutrofili | Batteri extracellulari e funghi |
| $T_{FH}$ | IL-21 (e IFN-γ o IL-4) | Linfociti B | Produzione di anticorpi | Patogeni extracellulari |

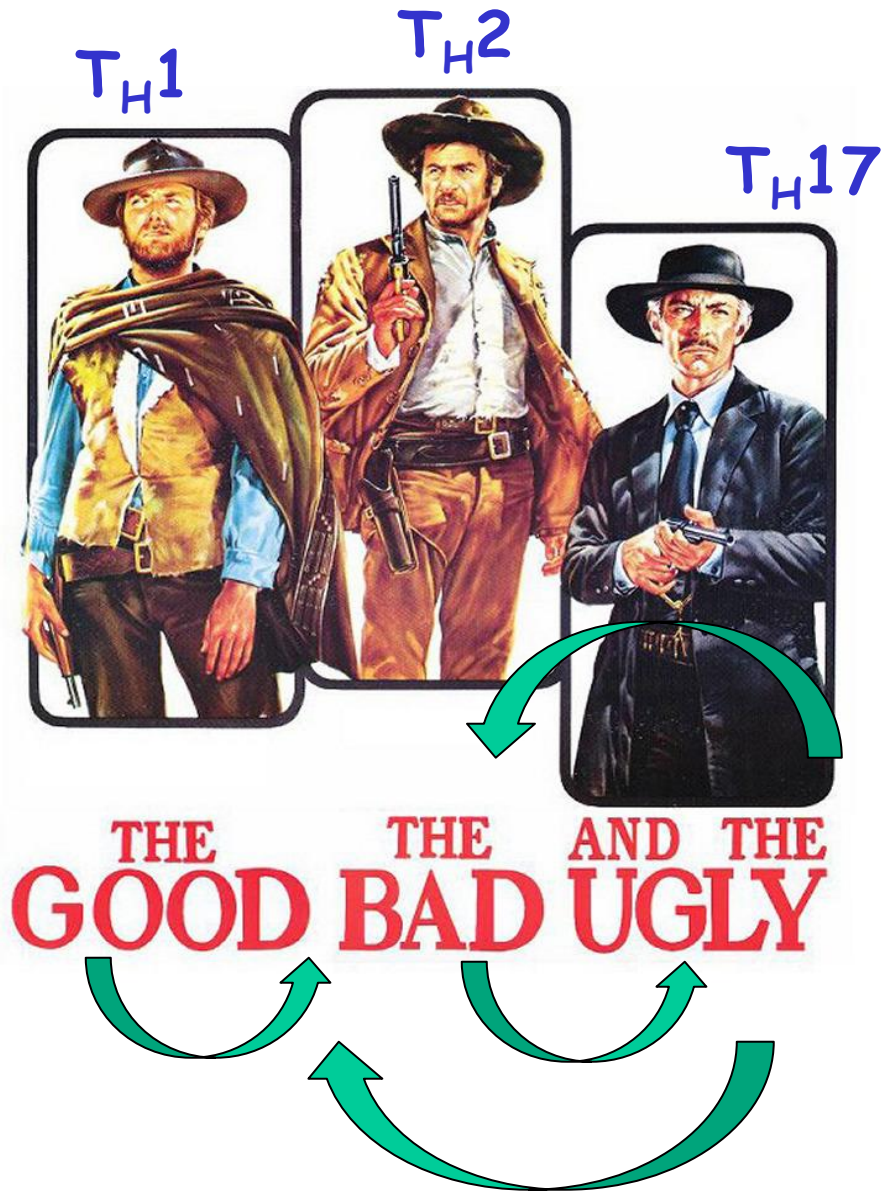
# Diverse sottopopolazioni di linfociti Th combattono patogeni diversi ma possono svolgere un ruolo patogenetico in diverse malattie immunitarie



| Linfociti T effettori | Citochine caratteristiche | Principali cellule bersaglio | Principali reazioni immunitarie | Difesa contro | Ruolo in patologia |
|---|---|---|---|---|---|
| $T_H1$ | IFN-γ | Macrofagi | Attivazione dei macrofagi | Patogeni intracellulari | Autoimmunità; infiammazione cronica |
| $T_H2$ | IL-4<br>IL-5<br>IL-13 | Eosinofili | Attivazione degli eosinofili e dei mastociti; attivazione alternativa dei macrofagi | Elminti | Allergia |
| $T_H17$ | IL-17<br>IL-22 | Neutrofili | Reclutamento e attivazione dei neutrofili | Batteri extracellulari e funghi | Autoimmunità; infiammazione |
| $T_{FH}$ | IL-21<br>(e IFN-γ o IL-4) | Linfociti B | Produzione di anticorpi | Patogeni extracellulari | Autoimmunità (autoanticorpi |

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# Effector helper T cells are divided into three main subpopulations on the basis of the produced cytokines




negative feedback

# Helper T cells coordinate two types of responses

$T_H1$

Cell-mediated response

$T_{H....}$ (es Tfh).

Humoral response

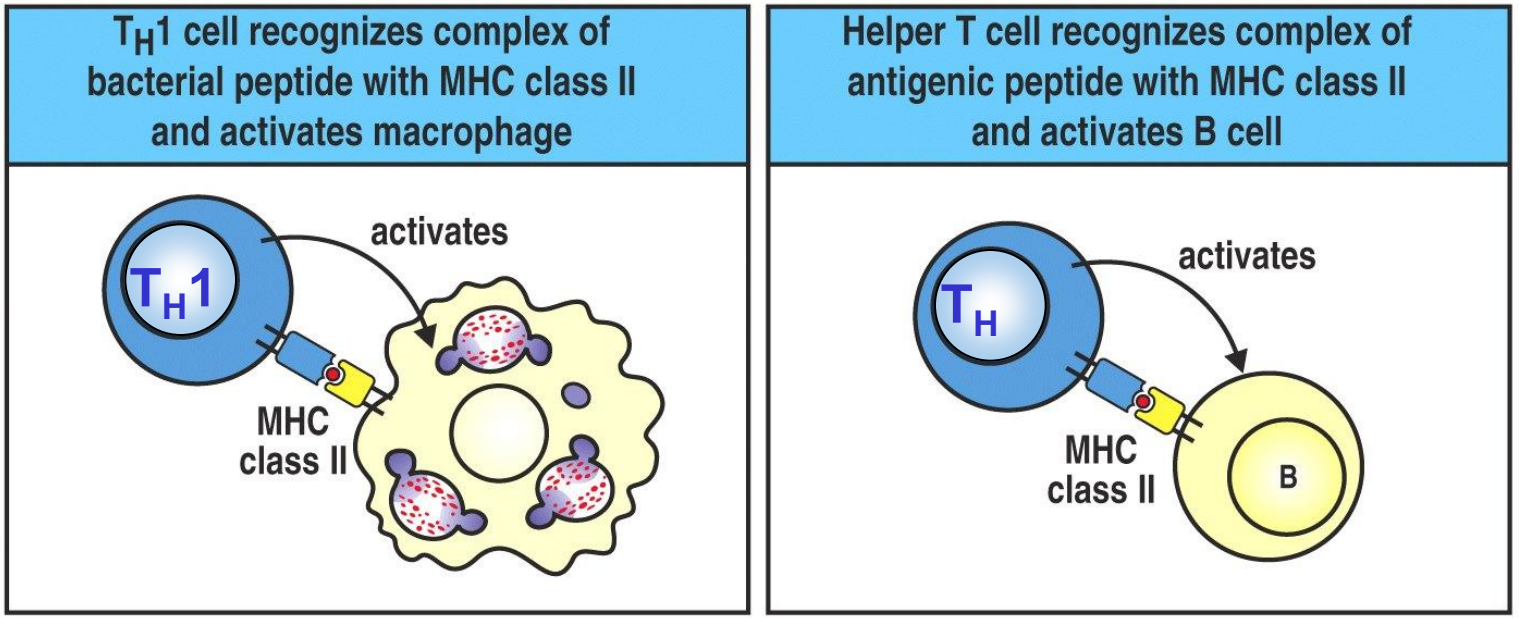
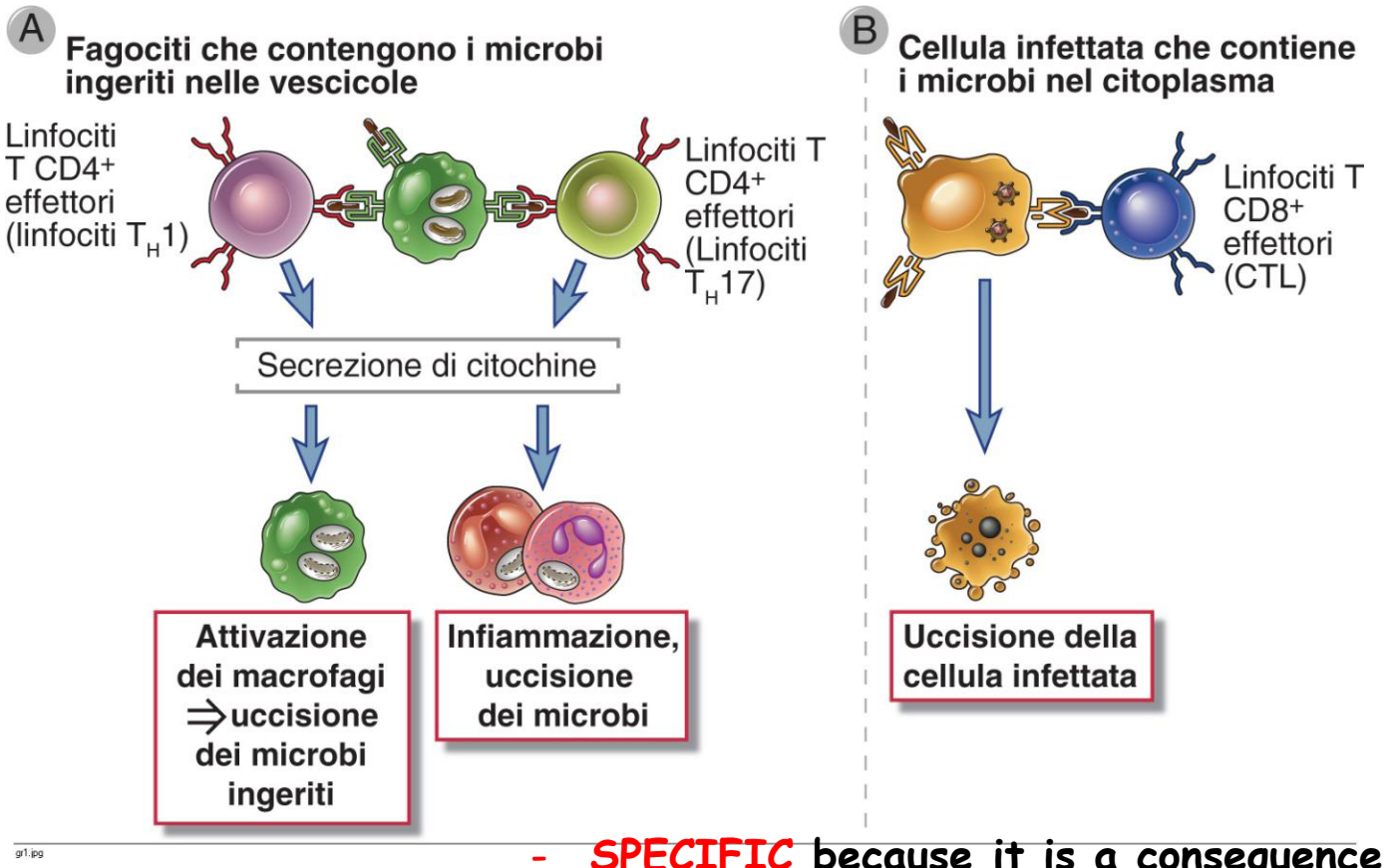



Figure 1-31 Immunobiology, 6/e. (© Garland Science 2005)

# Cell-mediated responses activated by T lymphocytes to eliminate cell-associated microbes



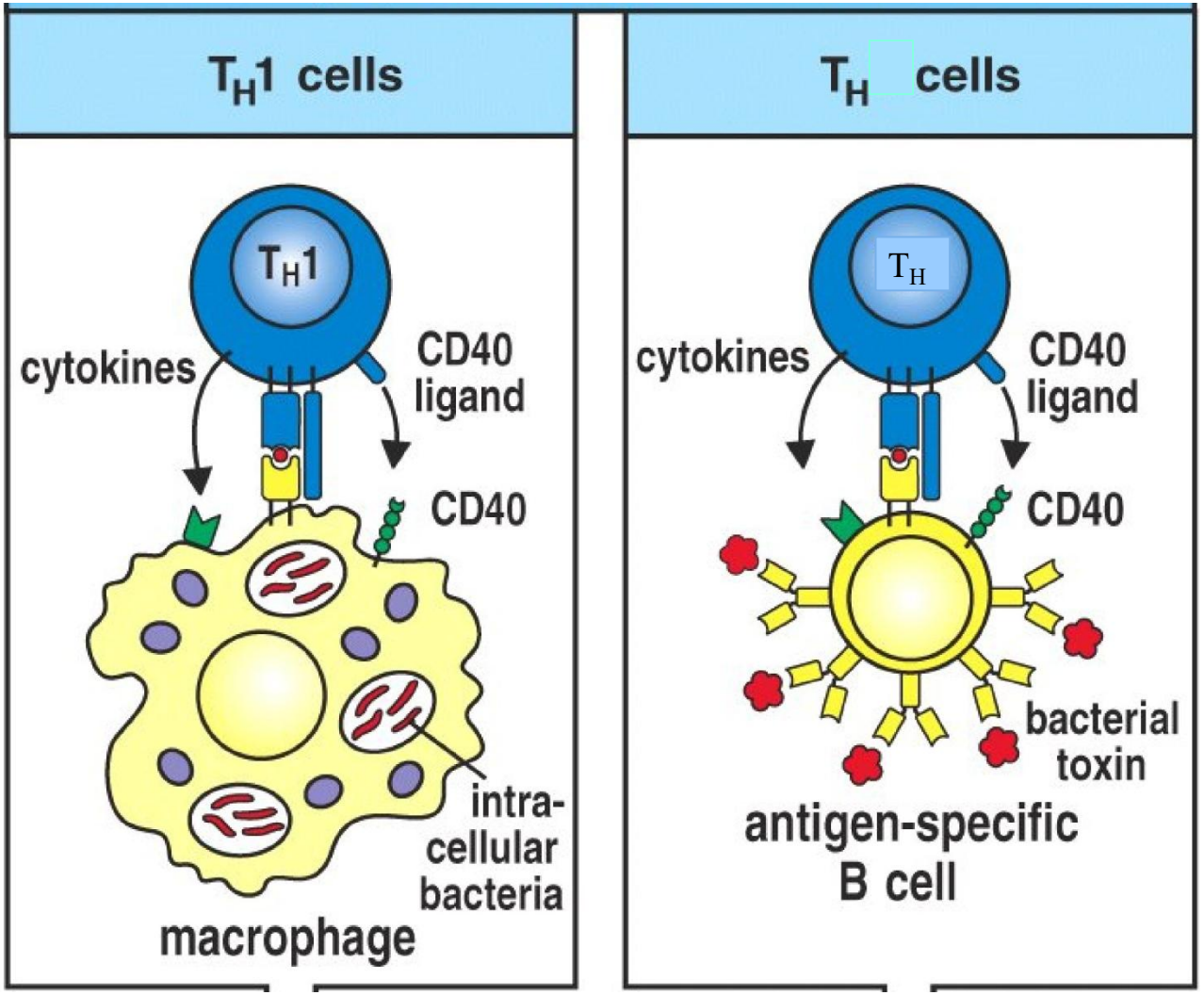

Effector helper T lymphocytes promote the **activation of specific leukocyte populations** involved in the elimination of the microorganism which is made:

- **SPECIFIC because it is a consequence of SPECIFIC RECOGNITION and promote an appropriate response**

- **POWERFUL/EFFECTIVE because it is induced by activation by appropriate CYTOKINES and membrane molecules**

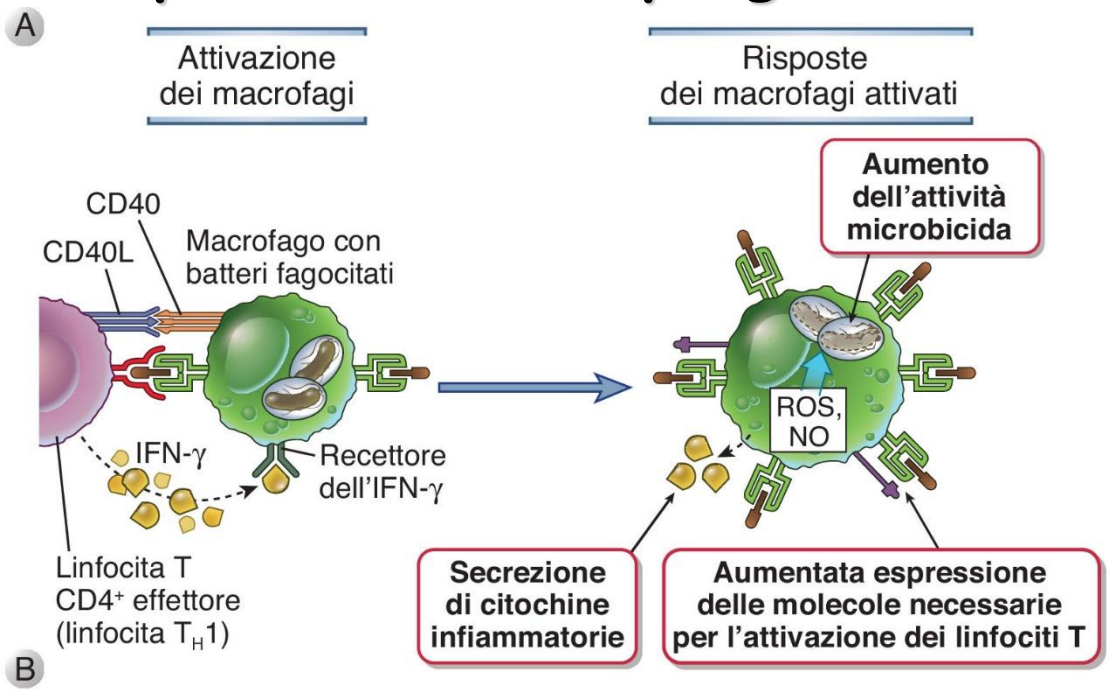
# Helper T cells modulate the functional responses of macrophages and B lymphocytes through membrane-molecule interactions and cytokine secretion

Le APC esprimono il CD40 mentre il ligando CD40L è espresso dai linfociti T effettori attivati dall'antigene



# Molecules expressed by type 1 helper T cells activate a series of responses in macrophages

**Macrophages are the main cellular target of IFNγ**




| Risposta dei macrofagi | Ruolo nell'immunità cellulo-mediata |
|---|---|
| Produzione di ossido nitrico, produzione di enzimi lisosomiali, specie reattive dell'ossigeno | Uccisione dei microbi nei fagolisosomi (funzione effettrice dei macrofagi) |
| Secrezione delle citochine (TNF, IL-1, IL-12) e delle chemochine | TNF, IL-1, chemochine: reclutamento dei leucociti (infiammazione)<br>IL-12: differenziazione dei linfociti $T_H1$, produzione dell'IFN-γ |
| Aumentata espressione delle molecole costimolatorie B7, delle molecole MHC | Aumentata attivazione dei linfociti T (amplificazione della risposta T) |

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**The main functions of helper T lymphocytes are mediated by the production of cytokines**

**Cytokines are a heterogeneous class of secreted proteins produced by various cell types, which act as intercellular signals**

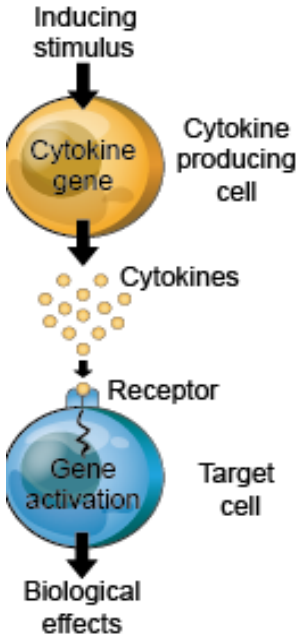
The word comes from the union of the word **cyto** (from greek "κύτος" or kitos:cavity, cell) + **kines** (from greek κίνησις or kinesis or movement)

# Modalità d azione delle citochine

- **La secrezione di citochine e' un evento di breve durata e autolimitato** (concentrazioni basse…pico<>nanomolari)

Vengono sintetizzate rapidamente e in maniera transiente.

La produzione può essere controllata da eventi post-traduzionali.




**Interagiscono con recettori ad alta affinita' espressi sulle cellule bersaglio che ne mediano l'azione.**

L'espressione di questi recettori, e quindi la responsivita' alle citochine e' solitamente regolata da segnali esterni alla cellula.

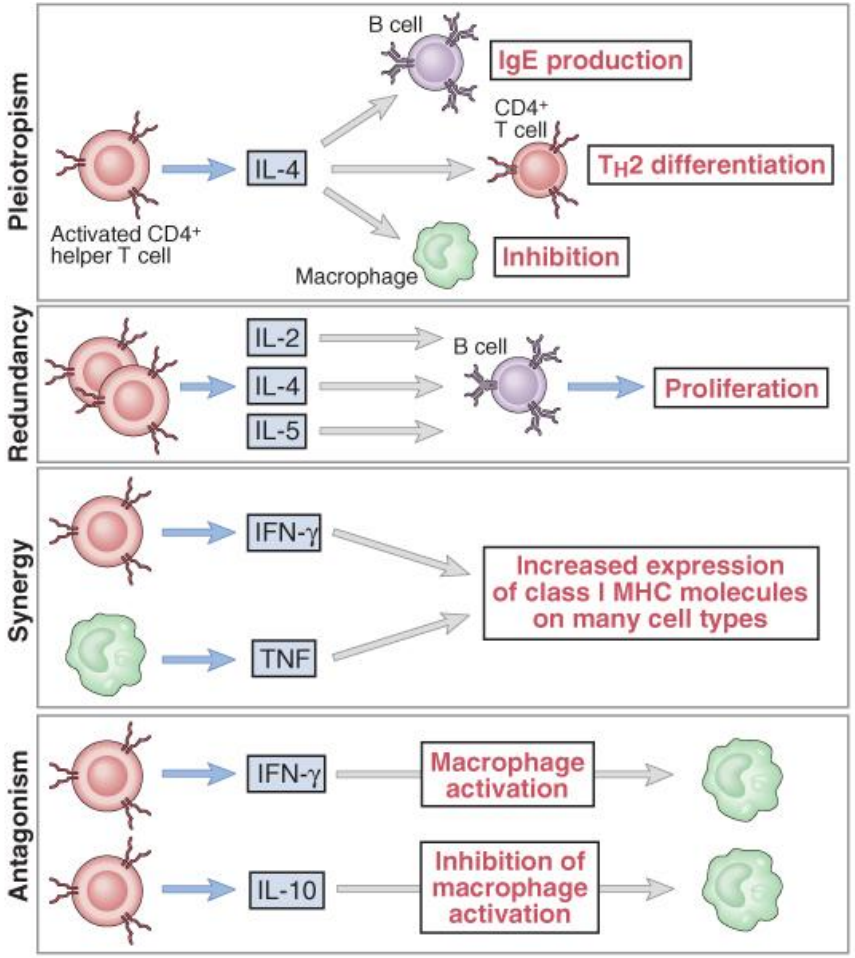
# Proprieta' delle citochine

**L' azione delle citochine puo' essere svolta in maniera:**

1. ***Pleiotropica***
2. ***Ridondante***

**Possono influenzare la sintesi e azione di altre citochine:**

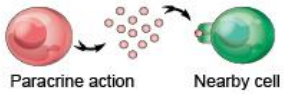
1. **in maniera *Sinergica***
2. **in maniera *Antagonistica***
3. **Stimolando la *produzione a "cascata"* di altre citochine**

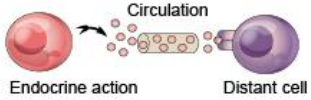



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**La loro azione può essere locale e raramente sistemica:**
***autocrina, paracrina*** **e a volte** ***endocrina*****.**



# Cytokines are produced during inflammatory responses

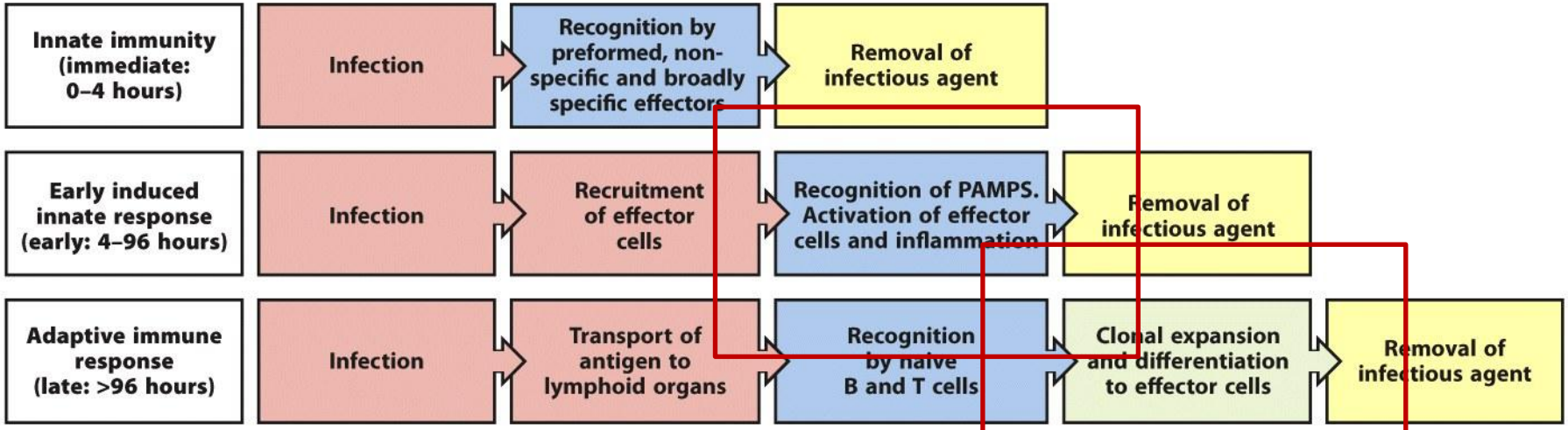
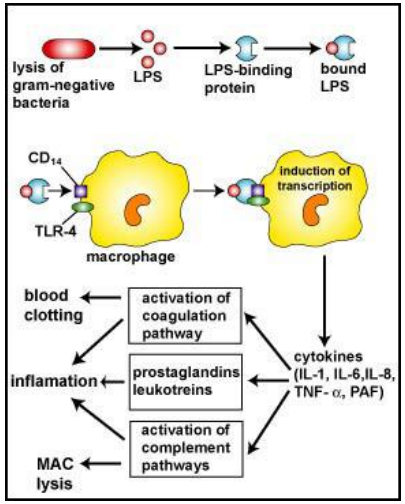
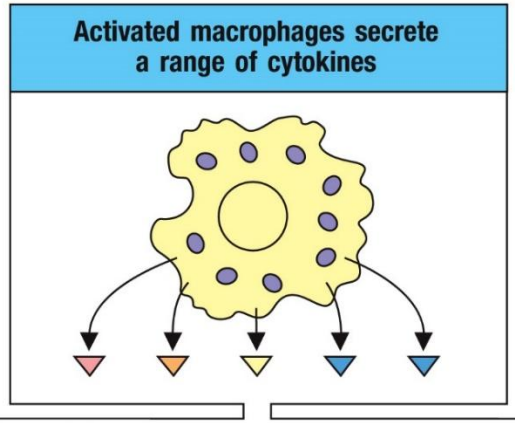


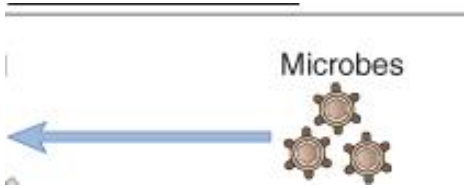

Figure 2.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

PAMPS: Patogen-associated molecular Pattern

# How do the cytokines of innate immunity work?



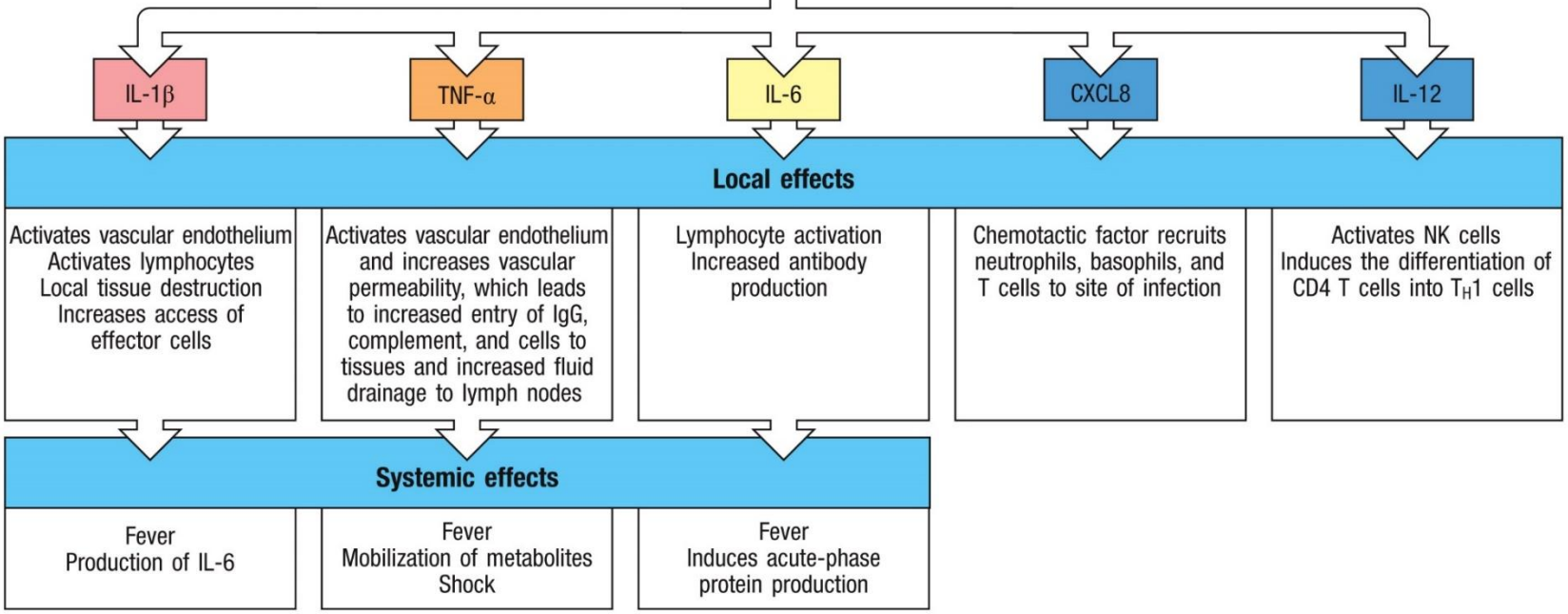
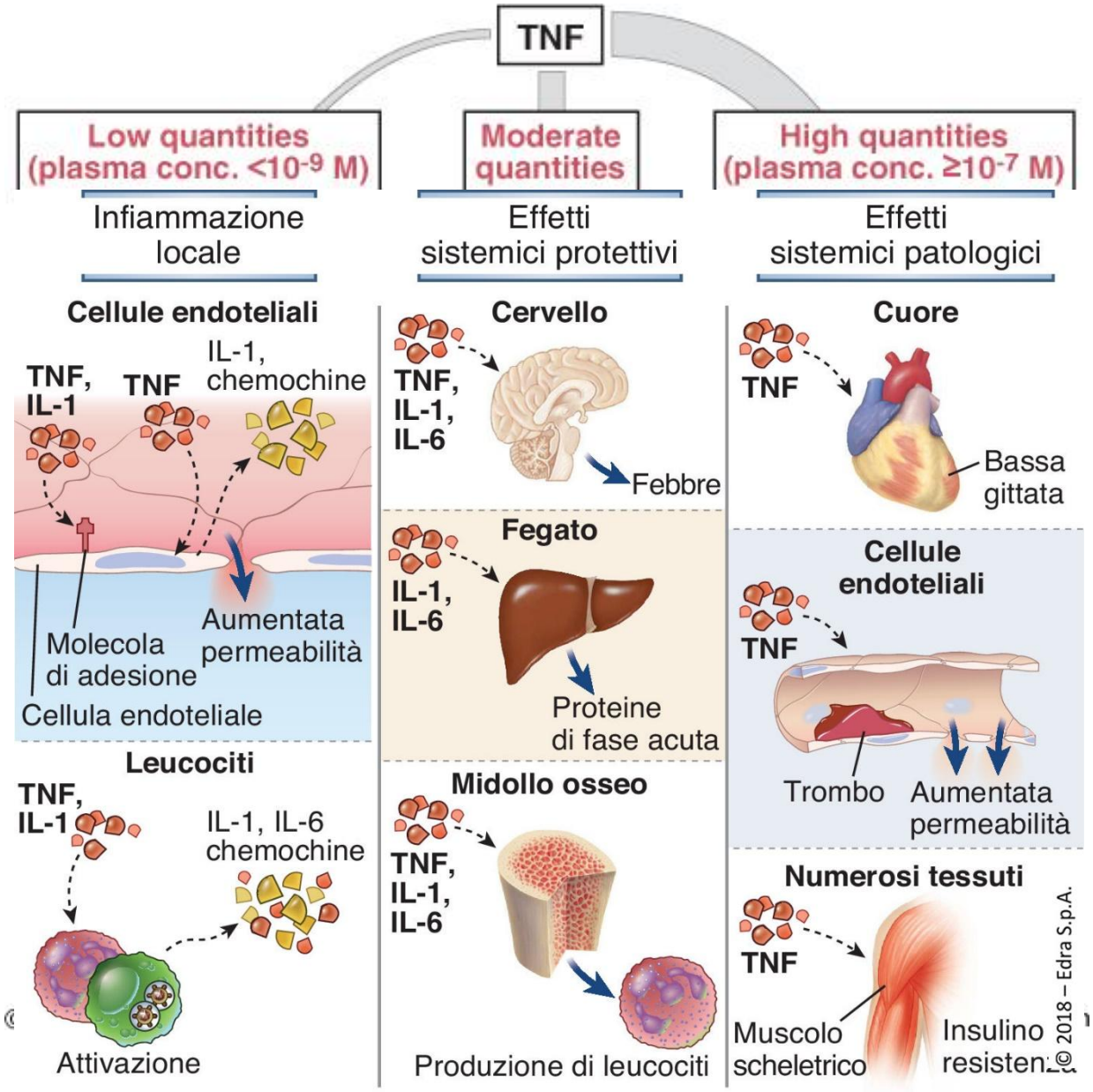
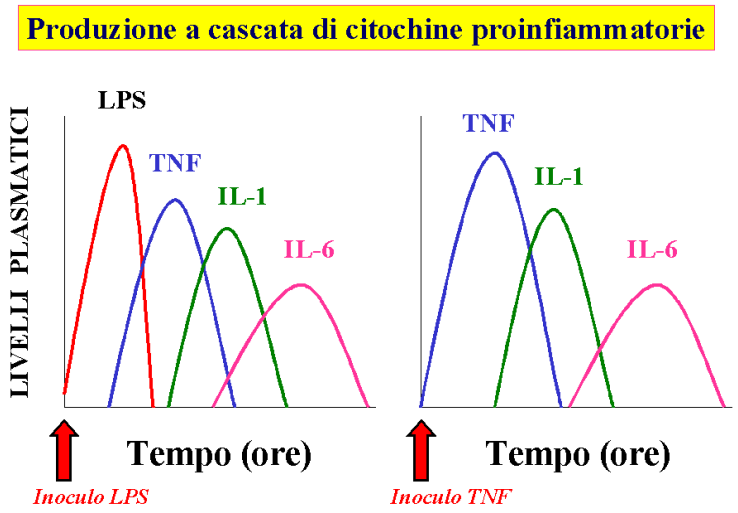




Figure 3.27 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)


TNF
Low quantities (plasma conc. <10-9 M)
Moderate quantities
High quantities (plasma conc. ≥10-7 M)
Infiammazione locale
Effetti sistemici protettivi
Effetti sistemici patologici
Cellule endoteliali
TNF, IL-1
TNF
IL-1, chemochine
Molecola di adesione
Aumentata permeabilità
Cellula endoteliale
Leucociti
TNF, IL-1
IL-1, IL-6 chemochine
Attivazione
Cervello
TNF, IL-1, IL-6
Febbre
Fegato
IL-1, IL-6
Proteine di fase acuta
Midollo osseo
TNF, IL-1, IL-6
Produzione di leucociti
Cuore
TNF
Bassa gittata
Cellule endoteliali
TNF
Trombo
Aumentata permeabilità
Numerosi tessuti
TNF
Muscolo scheletrico
Insulino resisten
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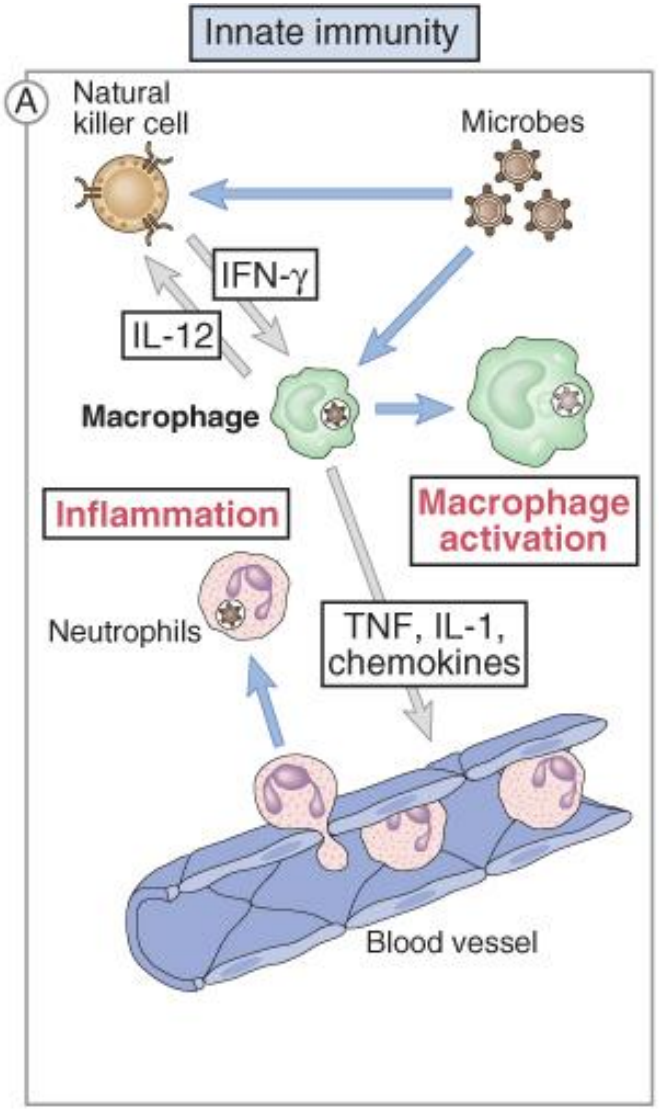
# DIFFERENZE TRA EFFETTI DI IL-1 e di TNF

1.l'IL-1 non provoca effetti sistemici patologici (sebbene sia secreta in risposta all'LPS)
2.non è letale
3.Il TNF può provocare apoptosi mentre IL1 non uccide le cellule tumorali
4.Il TNF ma non IL1 aumenta l'espressione di molecole MHC I
5.IL1 stimola la replicazione delle cellule staminali midollari
6. IL1 è più potente come stimolo per le cellule T



# Citochine dell'immunità innata

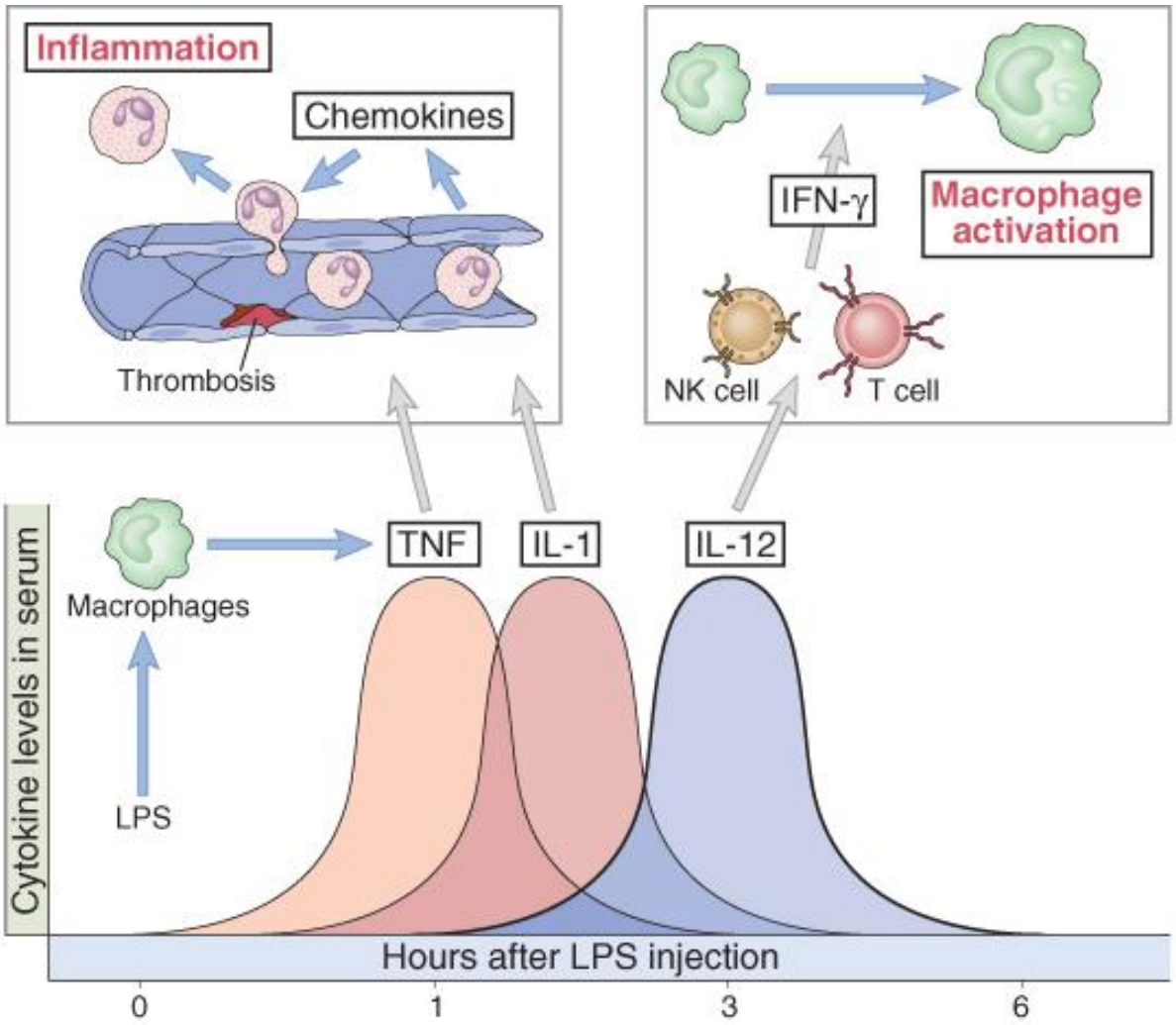
Citochine prodotte da macrofagi o cellule Natural Killer promuovono una rapida risposta infiammatoria che porta a eliminazione del microbo




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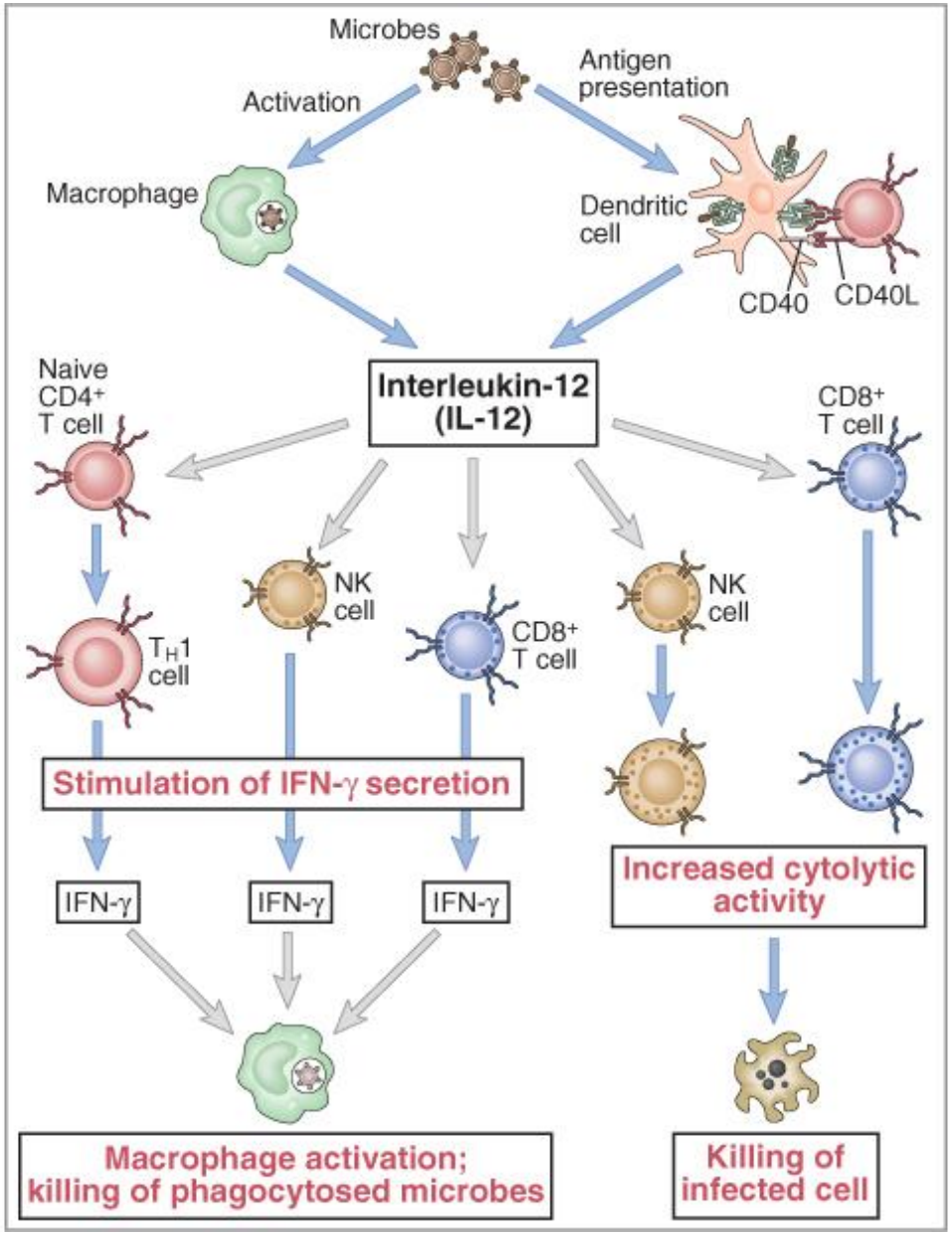
Coffe time

# Citochine prodotte durante l'infiammazione, l'interleuchina-12




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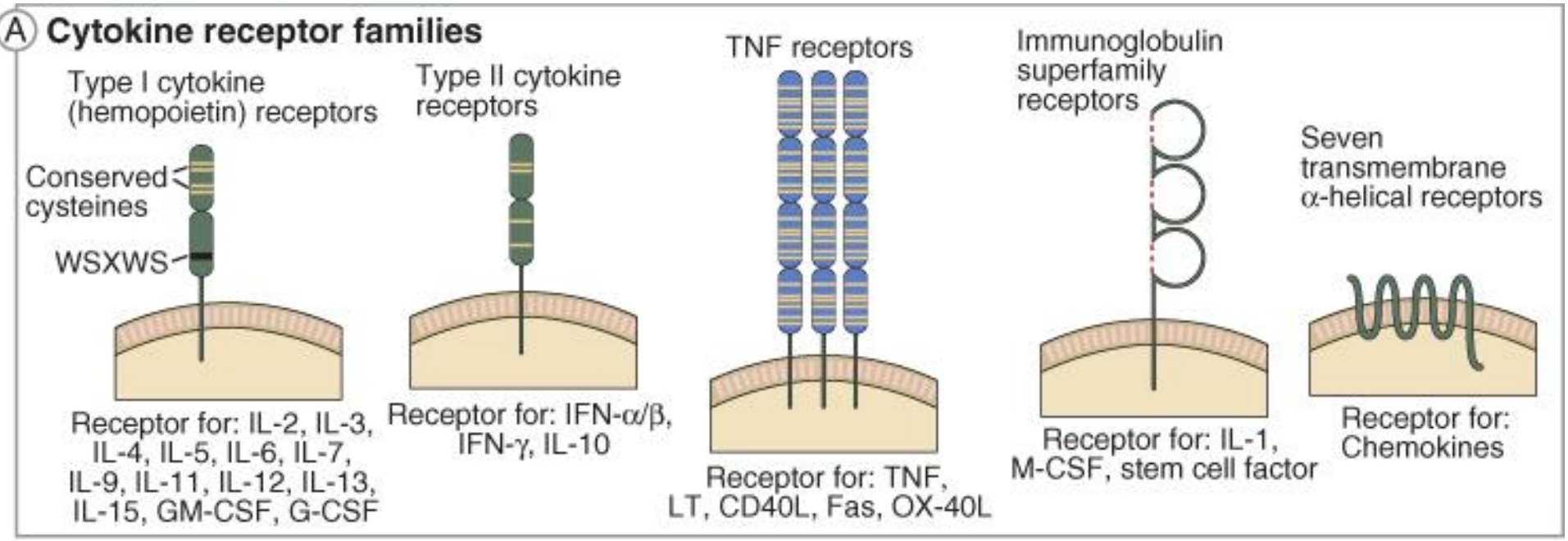
# INTERLEUCHINA-12, UNA CITOCHINA FONDAMENTALE NELLA COMUNICAZIONE TRA IMMUNITA' INNATA E ADATTATIVA



Le citochine interagiscono con 5 gruppi principali di

FAMIGLIE DI RECETTORI PER CITOCHINE

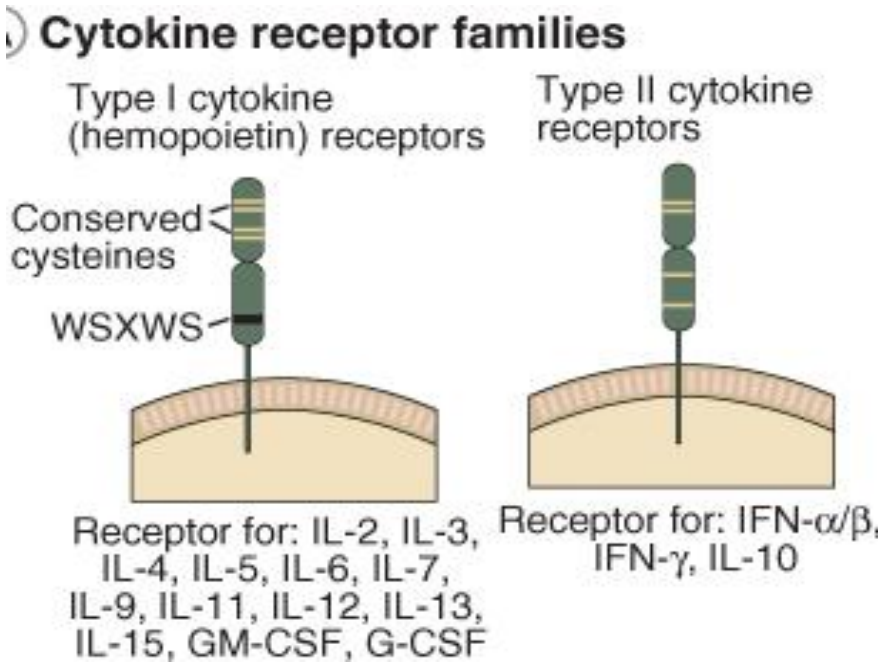
# FAMIGLIE DI RECETTORI PER CITOCHINE




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I recettori per citochine sono costituiti da una o più catene transmembrana con una porzione extracellulare che riconosce il ligando ed una intracellulare che trasduce il segnale.
Sono raggruppati in famiglie sulla base di omologie strutturali dei domini coinvolti nel riconoscimento e dell'utilizzo comune di meccanismi di trasduzione del segnale

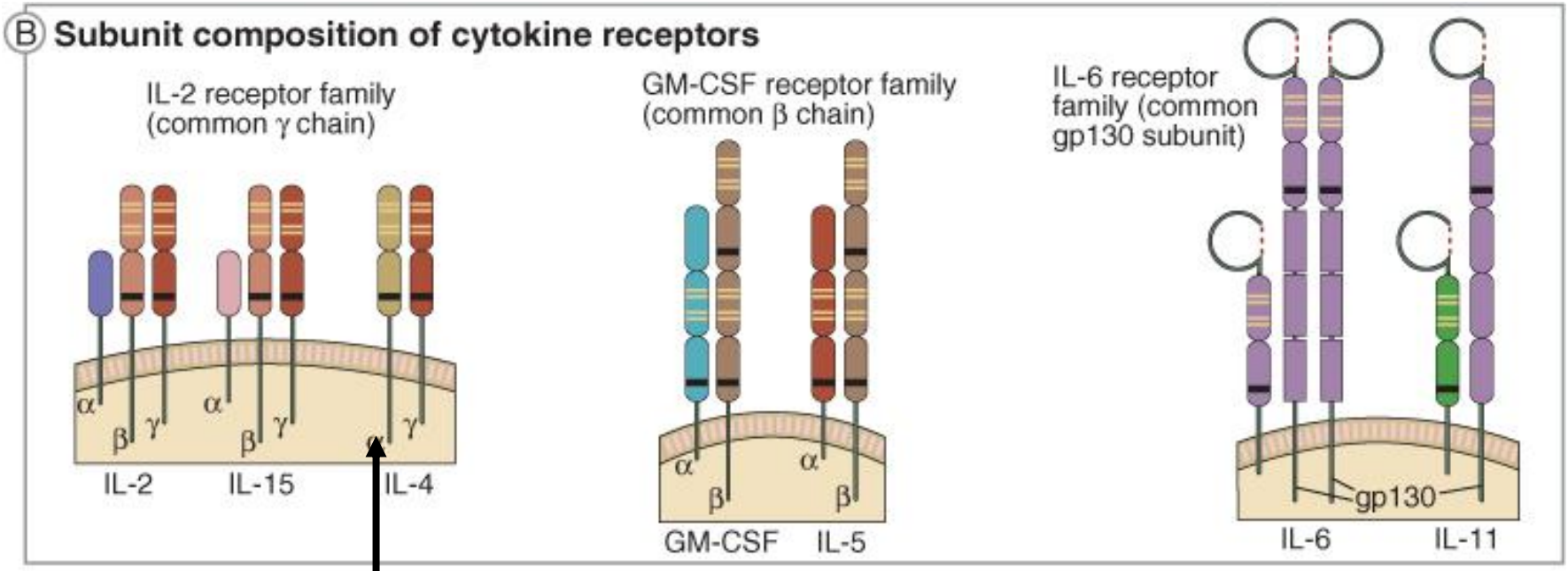
# RECETTORI PER CITOCHINE di tipo I e II




**Recettori di tipo I** : contengono una sequenza triptofano-serina-X-triptofano-serina (WSXWS) nella porzione prossimale alla membrana e una o più copie di un dominio contenente coppie di residui di cisteina.
**Recettori di tipo II**: non hanno la sequenza WSXWS conservata

Per queste due famiglie recettoriali una catena trasduce il segnale e l'altra regola l'interazione con il ligando.

## Recettori di tipo I

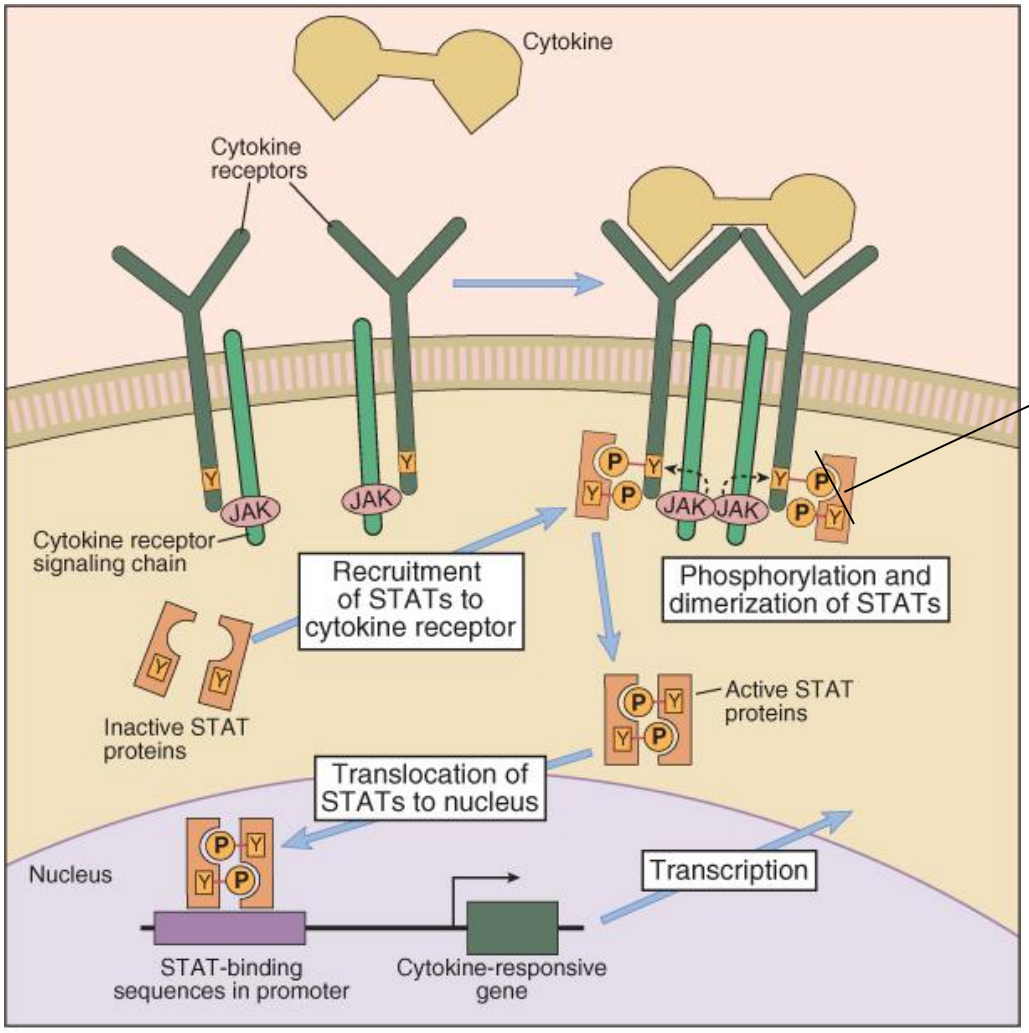



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Diverse citochine possono legare diversi recettori con una catena che trasduce il segnale in comune (per esempio la catena gamma comune)

**Conseguenza in caso di alterazioni geniche:**
Topi privi di IL2Rγc (c vuol dire comune) evidenziano gravi immunodeficienze perché non rispondono a una serie di citochine.

# Vie di trasduzione del segnale dei recettori per citochine di tipo I e II




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SOCS (SUPPRESSOR OF CYTOKINE SIGNALING) Famiglia di inibitori del JAK-STAT pathway

JAK: Janus kinase

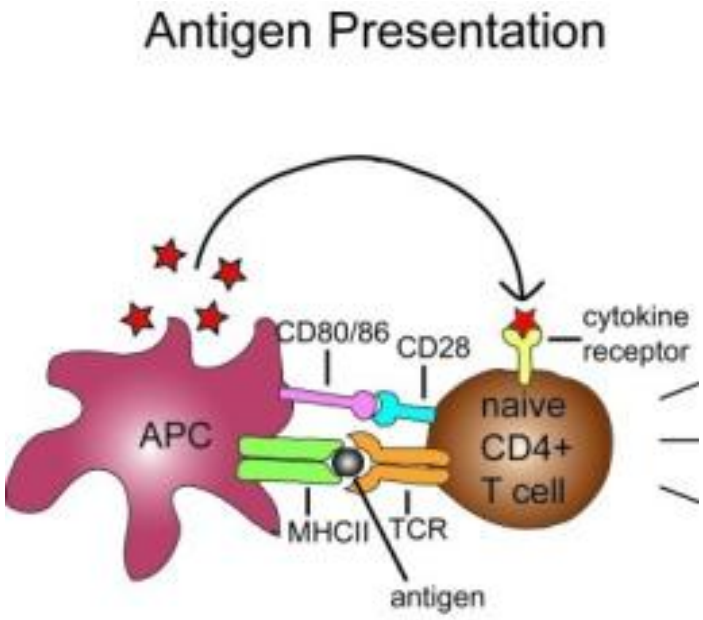
STAT: Signal transducers and activators of transcription

# Vie di trasduzione del segnale dei recettori per citochine di tipo I e II

| JAK/STAT | Involved cytokines* | Phenotype of knockout mice |
|---|---|---|
| STAT1 | IFN-α/β, IFN-γ | Defect in innate immunity; no reponse to IFNs |
| STAT2 | IFN-α/β | Defective immunity to viruses |
| STAT3 | IL-6, IL-10 | Embryonic lethal |
| STAT4 | IL-12 | Defect in $T_H1$ development, IFN-γ production |
| STAT5a | Prolactin | Lactation defect |
| STAT5b | Growth hormone | Dwarfism |
| STAT5a and STAT5b | IL-2, IL-7, IL-9 (in addition to above) | Lactation defect, dwarfism, and defective T cell proliferation in response to IL-2 |
| STAT6 | IL-4 | Defect in $T_H2$ development, IL-4–dependent Ig isotypes |
| JAK1 | IFN-α/β, IFN-γ, cytokines using $\gamma_c$ and gp130 (e.g., IL-2, IL-4, IL-6) | Perinatal lethal; defective innate immunity, possible defect in neuronal viability |
| JAK2 | Epo, IL-3, IFN-γ | Embryonic lethal, hematopoietic failure |
| JAK3 | Cytokines using $\gamma_c$ chain (IL-7, IL-2, IL-4) | Defect in T cell maturation |
| Tyk2 | IFN-α/β, IFN-γ, IL-12, IL-10, others | Defective IL-12 response of NK cells, defective immunity to viruses |

*Selected examples of involved cytokines are shown.

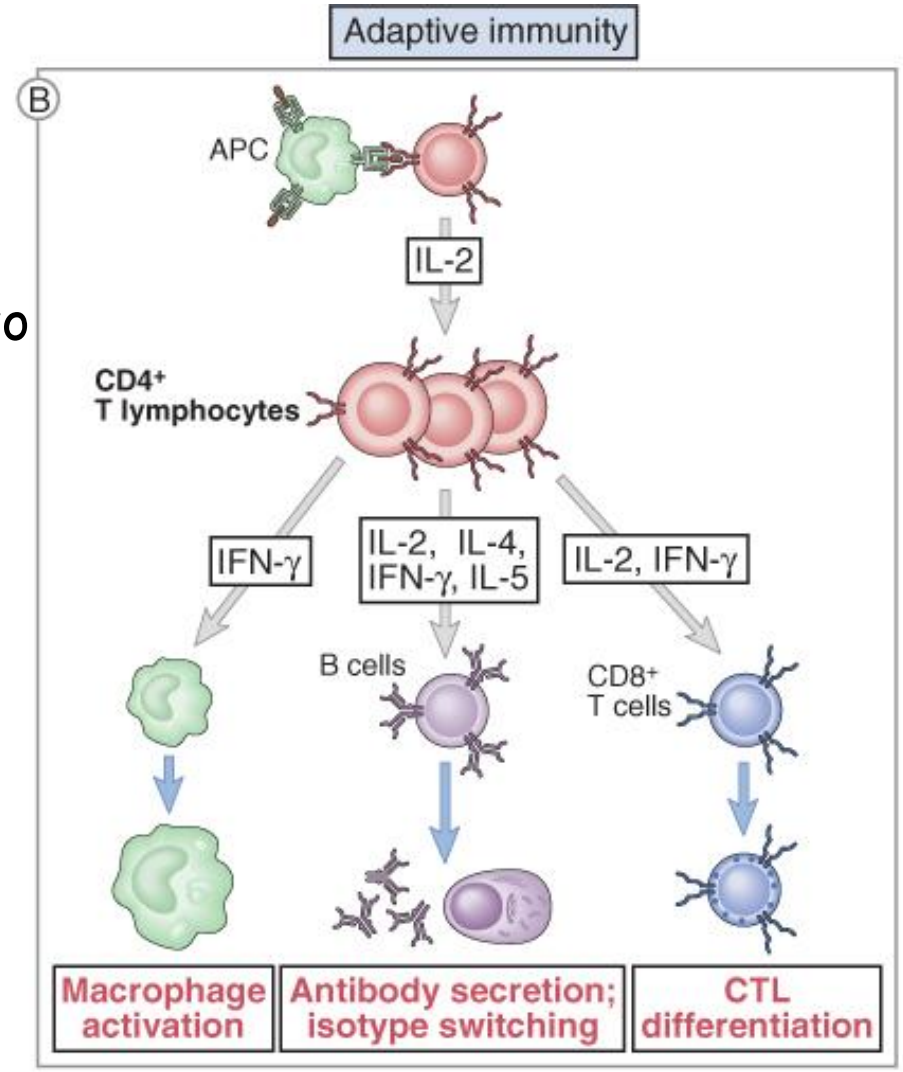
# Cytokines in adaptive immunity




The function of cytokines is

1-To stimulate the growth and differentiation of adaptive lymphocytes in the early stages (in peripheral lymphoid tissue)
2-To activate the different cells, i.e. macrophages, responsible for the elimination of the antigen during the effector phase of the immune response (in the infected tissue)

Durante la risposta adattativa:
1-Le citochine stimolano la proliferazione e differenziamento di linfociti antigene-specifici
2-attivano cellule effettrici (es. macrofagi)



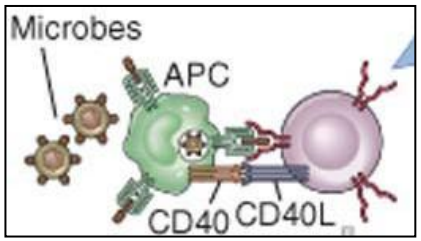

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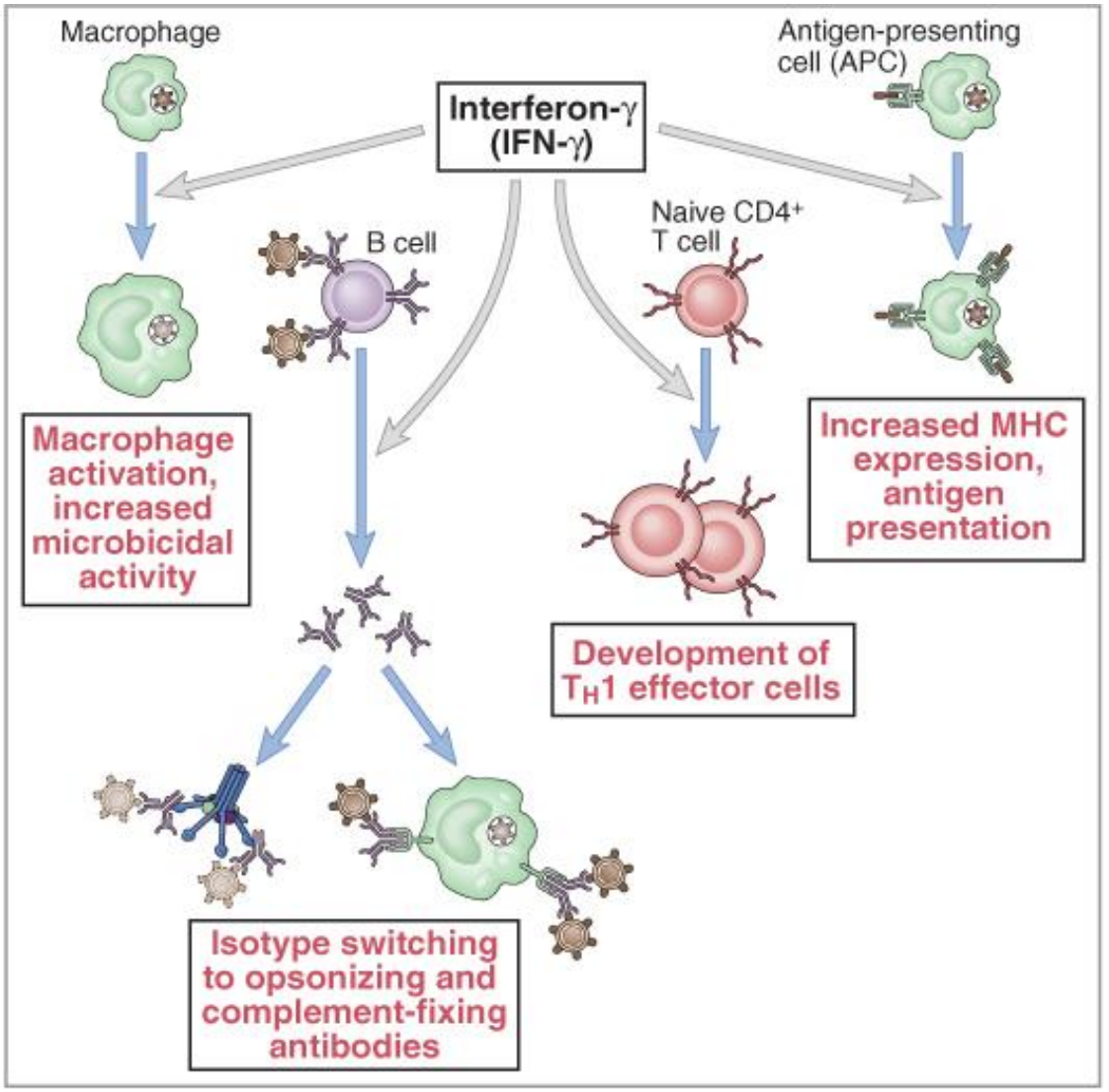
Le citochine attivano le cellule dell'immunità innata effettrici, cioè le cellule che direttamente eliminano i microbi

- What are the functions of helper T lymphocytes?
- How are their functions accomplished?
- How are their functions acquired?

# Le citochine secrete dai $T_H1$ coordinano la risposta cellulo-mediata verso micro-organismi intracellulari

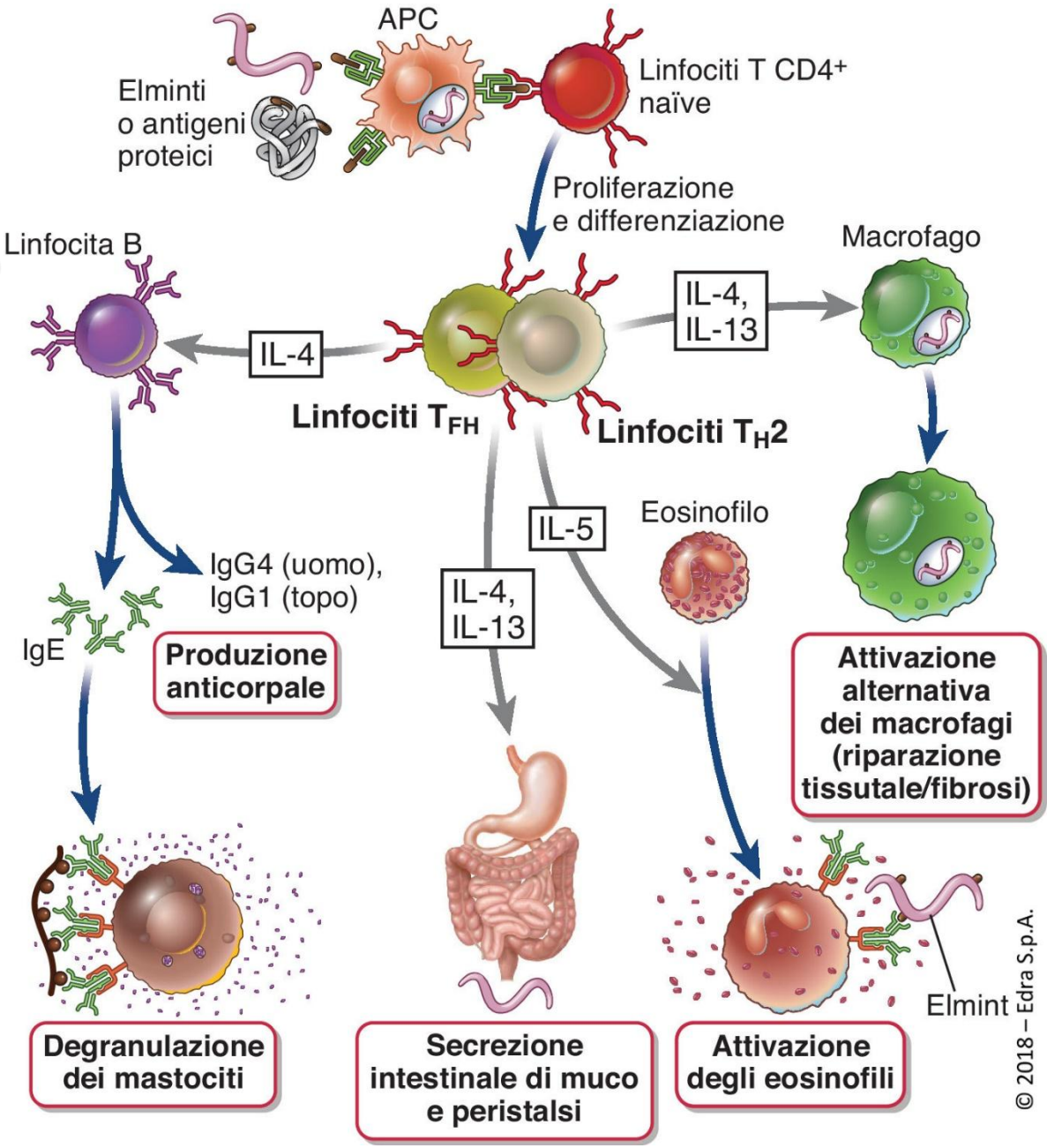
*L'interferone gamma è la principale citochina responsabile dell'attivazione dei macrofagi*



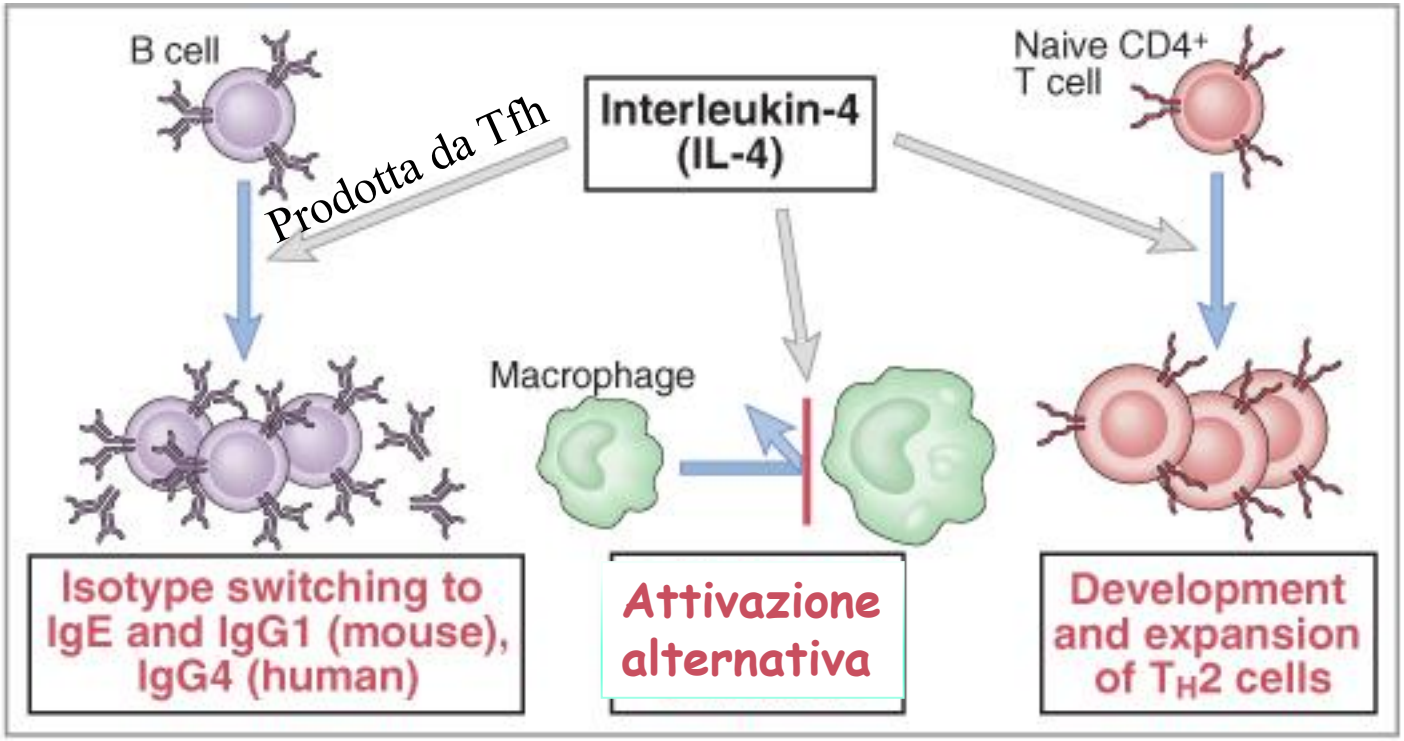

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**Le citochine secrete dai $T_H2$ stimolano le reazioni immunitarie di difesa verso le infezioni elmintiche e promuovono il riparo dei tessuti**




**AUMENTO DI PRODUZIONE DI FATTORI CHE RICHIAMANO EOSINOFILI**

# Azioni principali dell'IL-4




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# Classically and alternatively activated macrophages

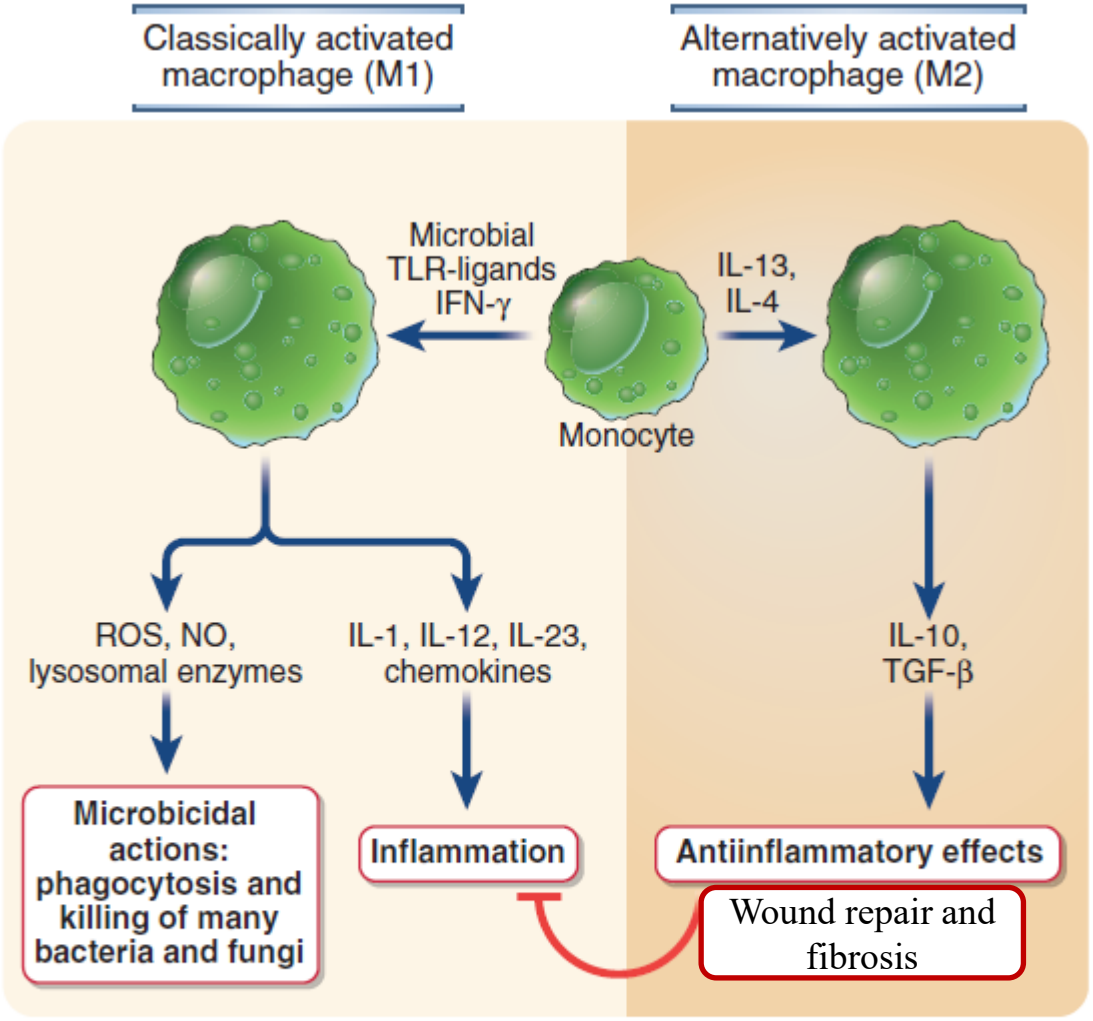



**FIGURE 10.10 Classical and alternative macrophage activation.** Different stimuli activate tissue macrophages to develop into functionally distinct populations. Classically activated macrophages are induced by microbial products and cytokines, particularly IFN-γ, and are microbicidal and involved in potentially harmful inflammation. Alternatively activated macrophages are induced by IL-4 and IL-13 produced by Th2 cells and other leukocytes and function to control inflammation and to promote tissue repair and fibrosis. Some investigators divide the M2 macrophage population into subpopulations, some of which are mainly antiinflammatory and others are responsible for tissue repair.

# Le citochine secrete dai $T_H$ coordinano la risposta umorale

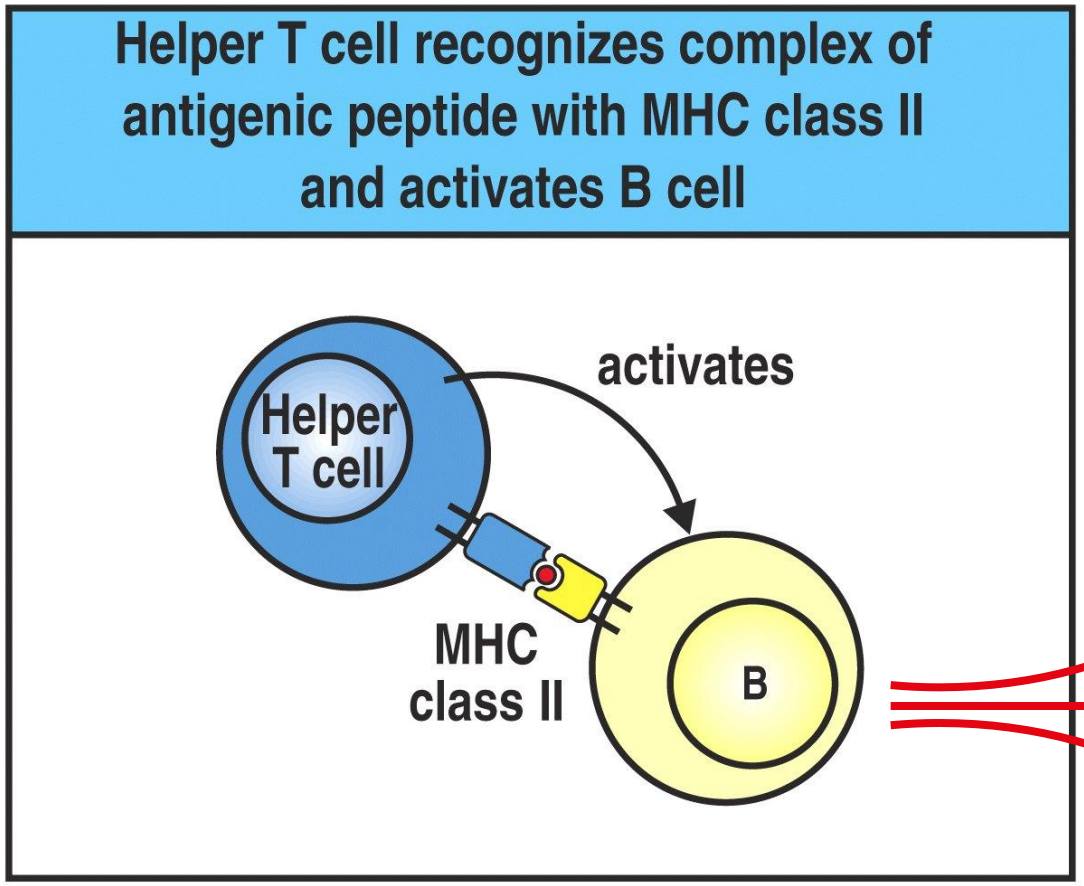



Figure 1-31 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

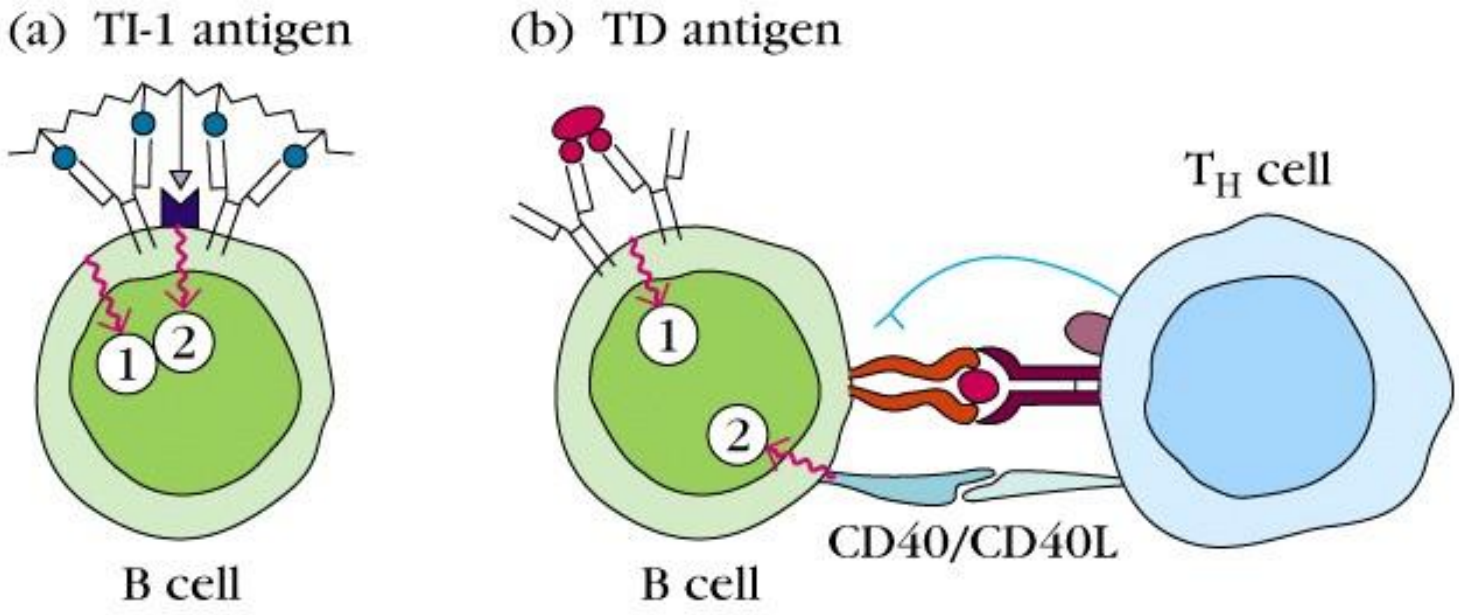
proliferation

differentiation

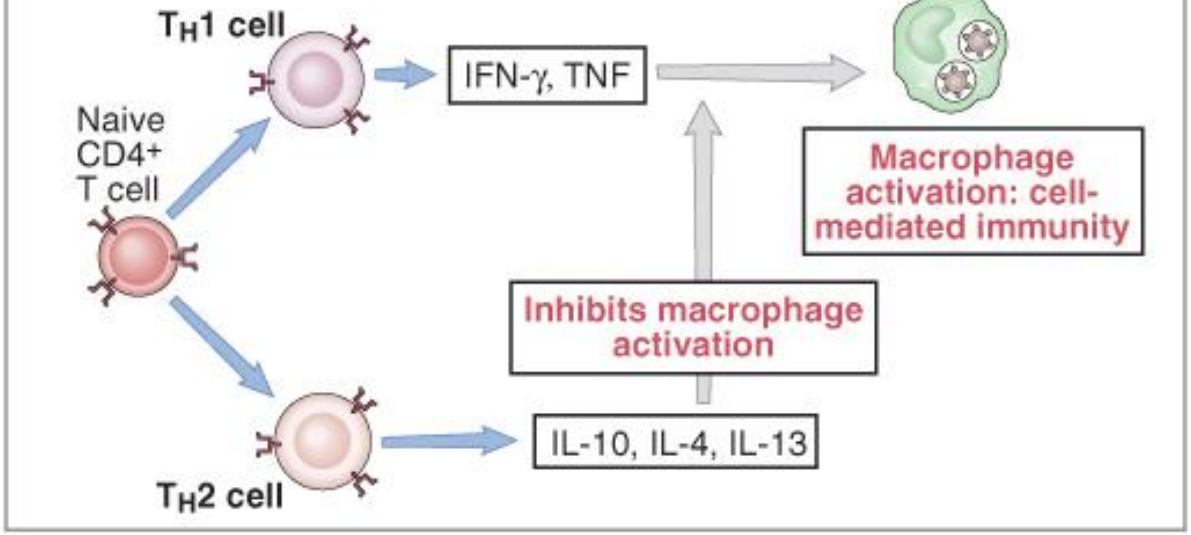
antibody secretion

# Funzioni dei linfociti TH

## Attivazione dei linfociti B



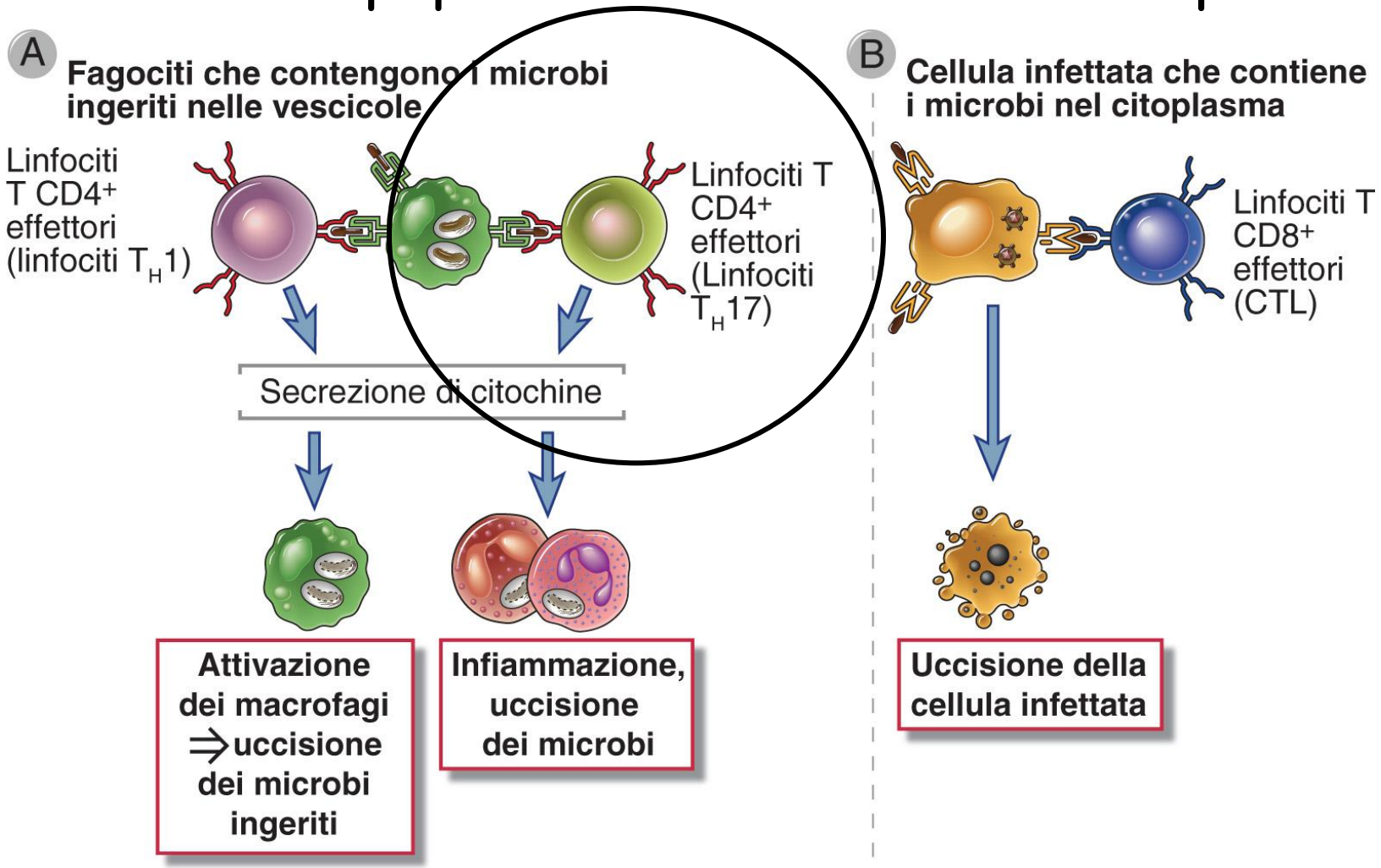
# The balance between $T_H1$ and $T_H2$ cell activation determines the outcome of intracellular infections




| Infection | Response | Outcome |
|---|---|---|
| *Leishmania major* | Most mouse strains: $T_H1 \Rightarrow$<br>BALB/c mice: $T_H2 \Rightarrow$ | Recovery<br>Disseminated infection |
| *Mycobacterium leprae* | Some patients: $T_H1 \Rightarrow$<br>Some patients: Defective $T_H1$ or dominant $T_H2 \Rightarrow$ | Tuberculoid leprosy<br>Lepromatous leprosy (high bacterial count) |

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# In alcuni tipi di risposta cellulo-mediata è richiesta un'altra popolazione di linfociti T helper



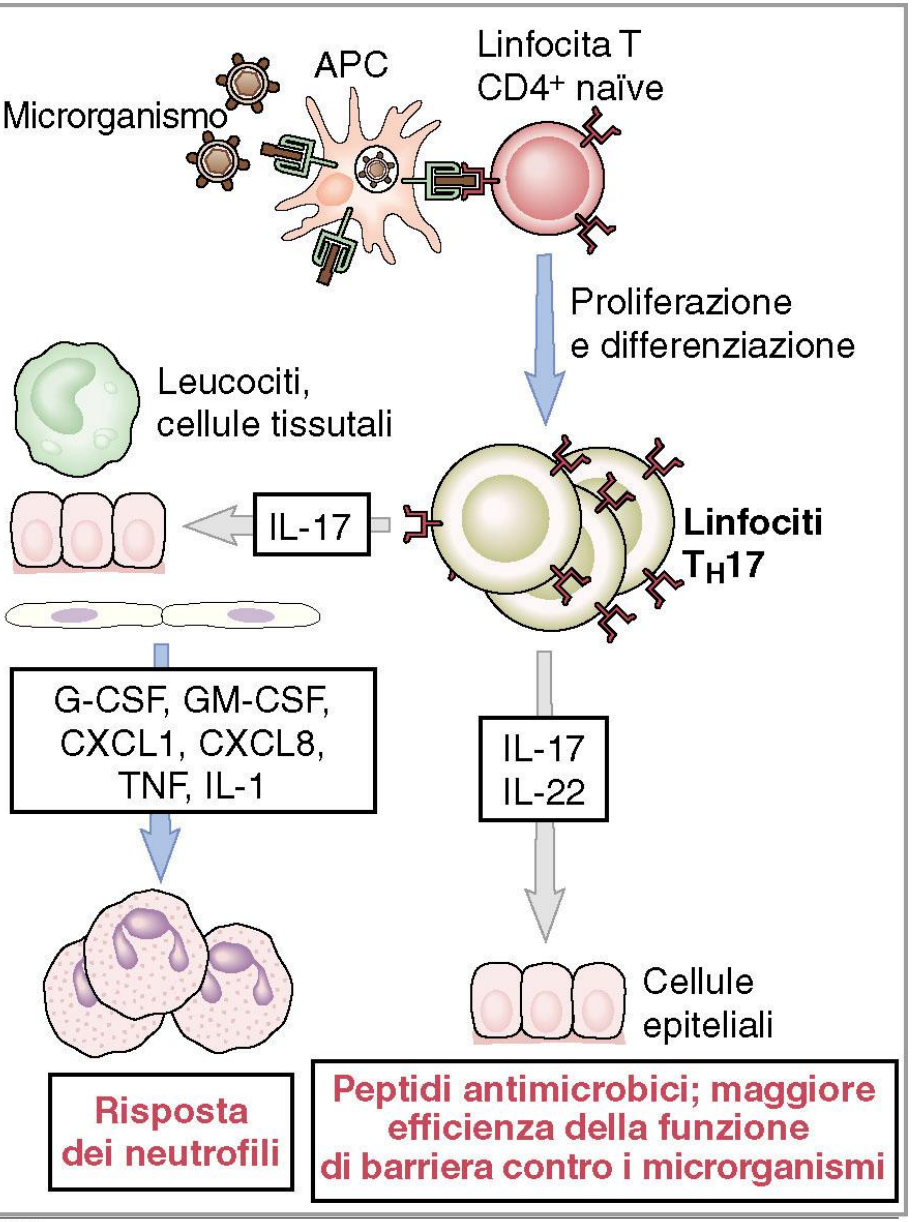

gr1.jpg

Immunologia cellulare e molecolare 7 ed

Risposte immunitarie dei linfociti T. A. I linfociti T CD4<sup>+</sup> riconoscono gli antigeni dei microrganismi extracellulari o fagocitati e producono citochine che stimolano l'attività microbicida e proinfiammatoria dei fagociti. Anche i linfociti CD8<sup>+</sup> possono contribuire a questi processi secernendo citochine. B. I CTL CD8<sup>+</sup> riconoscono gli antigeni peptidici di origine microbica associati a molecole MHC di classe I. Queste cellule sono importanti per combattere i microbi che risiedono nel citoplasma delle cellule infettate provocandone la morte.

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# I linfociti Th17



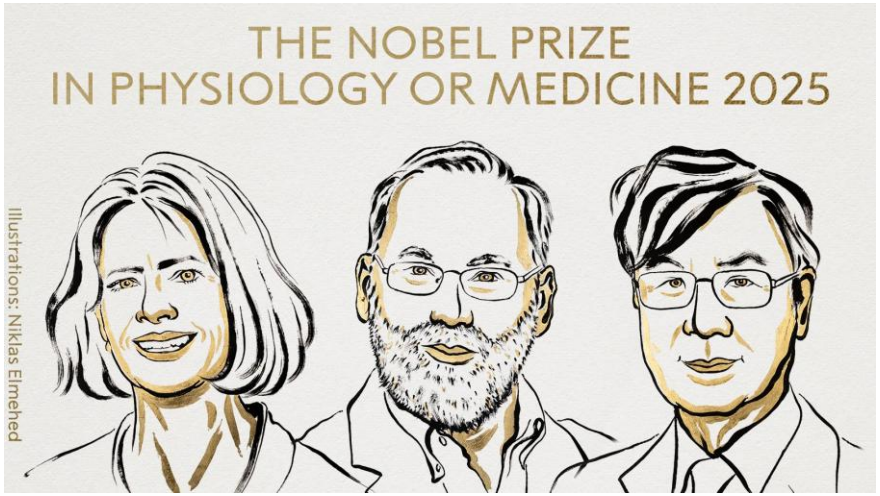

gr16.jpg

Le basi dell'immunologia - 3 Ed. aggiornata

- **Sono posizionati in maniera da attaccare funghi e batteri che invadono le barriere epiteliali secernendo fattori che attirano e attivano neutrofili**

- **Proteggono le superfici esterne e interne (cute e intestino) contro batteri extracellulari e funghi**

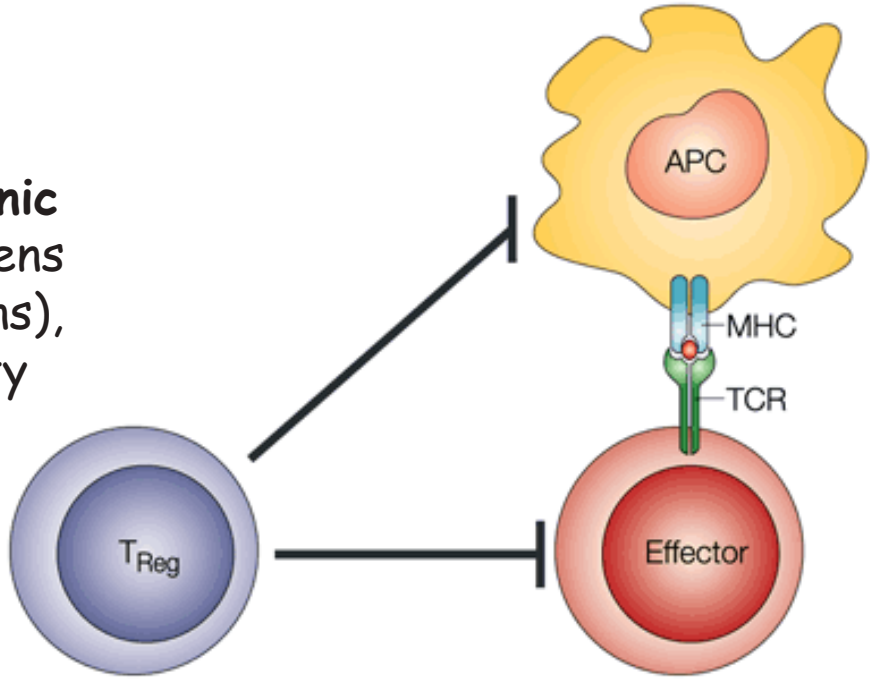
# I linfociti T regolatori controllano la risposta immunitaria in vivo




Mary E. Brunkow, Fred Ramsdell e Shimon Sakaguchi

# Tolerance to self antigens, also called self-tolerance, is a fundamental property of the normal immune system

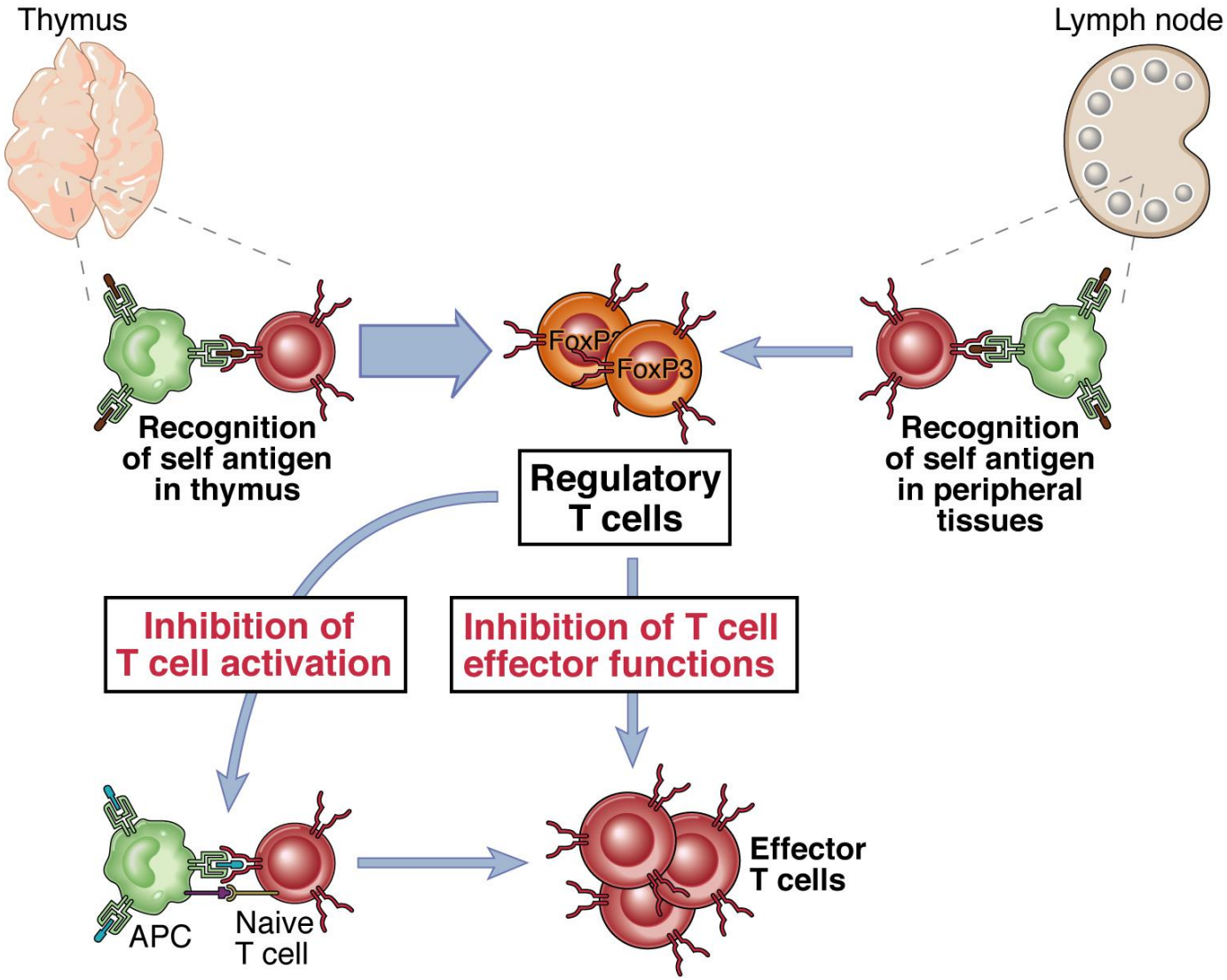
Antigens that induce tolerance are called tolerogens, **or tolerogenic** as opposite to immunogens (or immunogenic antigens), which generate immunity




**Benefits:**
- T-cell homeostasis
- prevents autoimmune disease
- tolerance after transplantation
- prevents GVHD
- prevents allergy
- prevents hypersensitivity

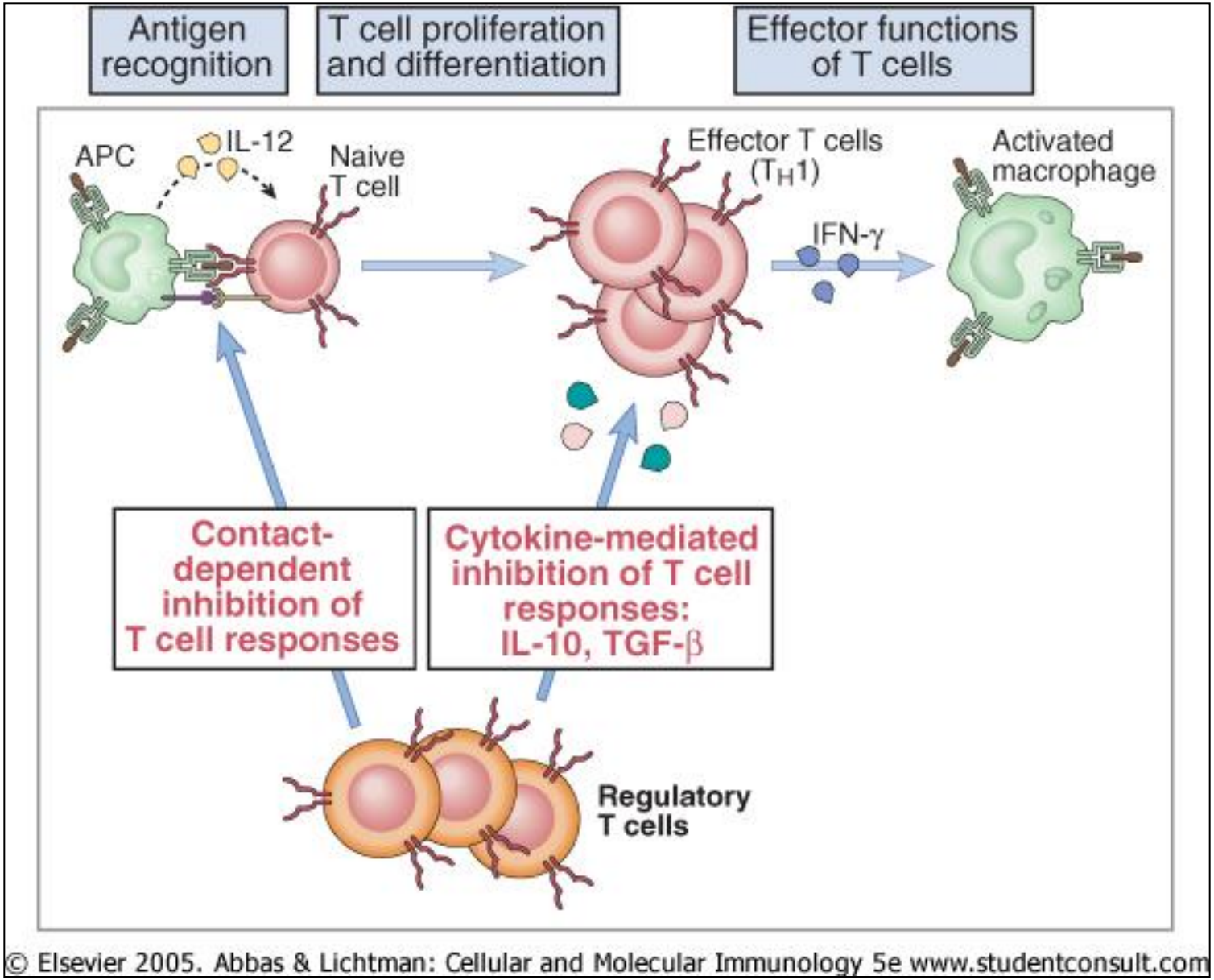
**Detrimental effects:**
- down-regulation of tumour immunity
- down-regulation of immunity to infection

# Treg cells suppress effector T cell responses



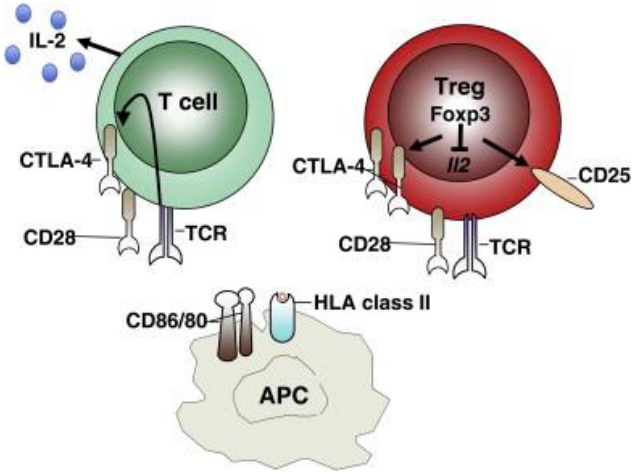

From Abbas, Lichtman and Pillai. Cellular and Molecular Immunology 6th ed, 2007

# Regulatory cells inhibit the activation and differentiation of naive T cells

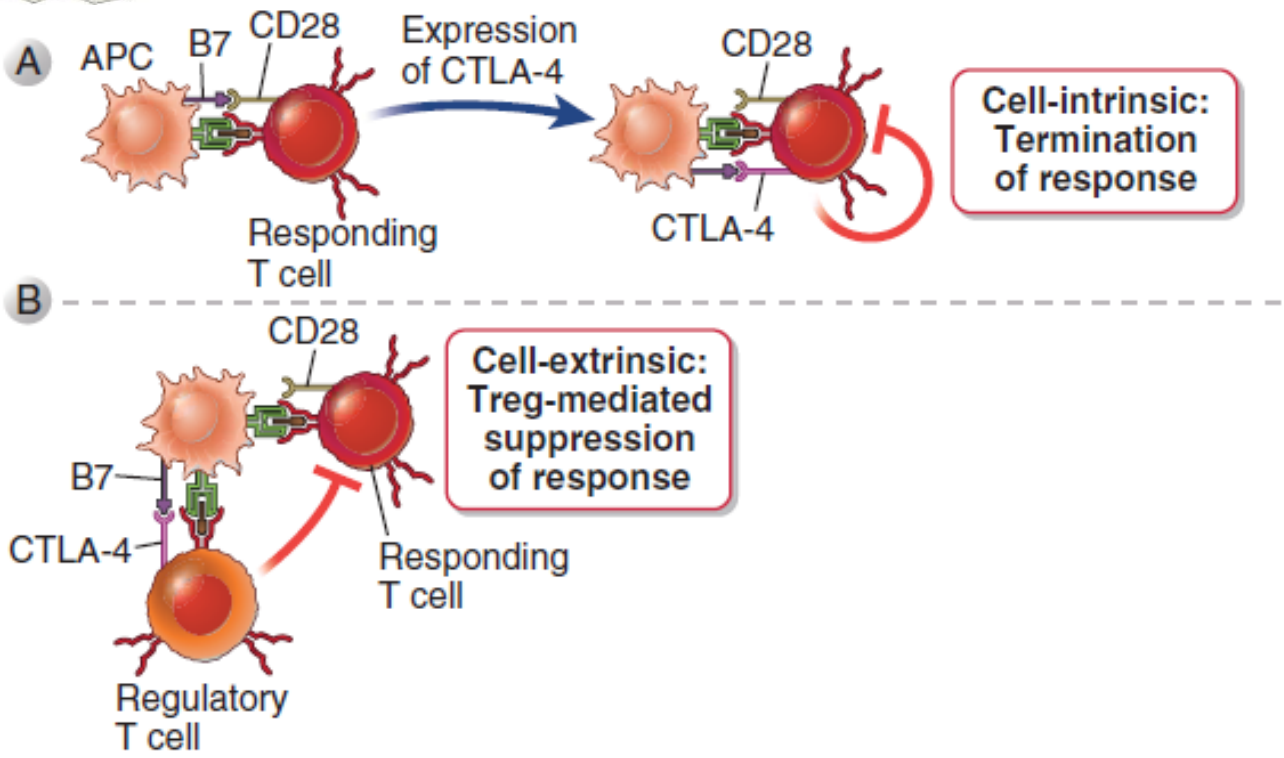


# Control of T cell response by CTLA-4

*Contact-dependent inhibition*




Treg cells constitutively express CTLA-4



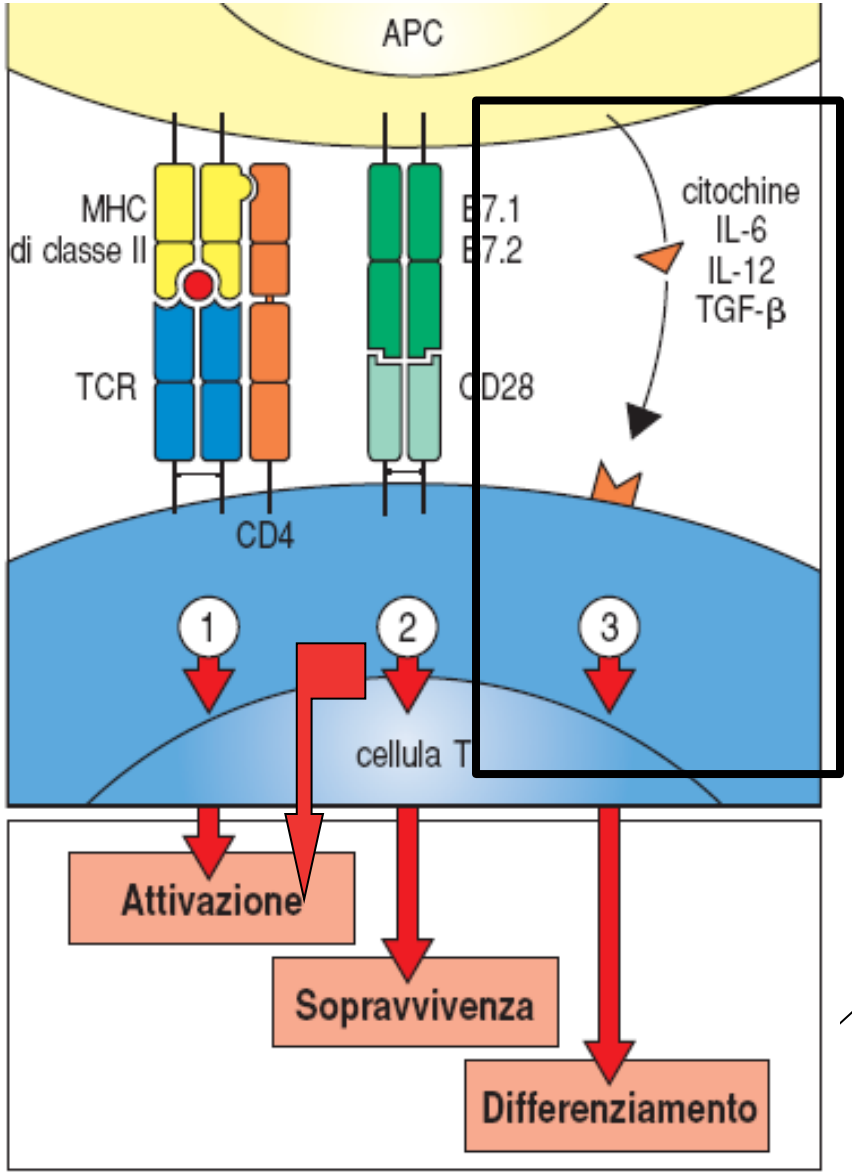
# CITOCHINE DELL'IMMUNITA' ADATTATIVA

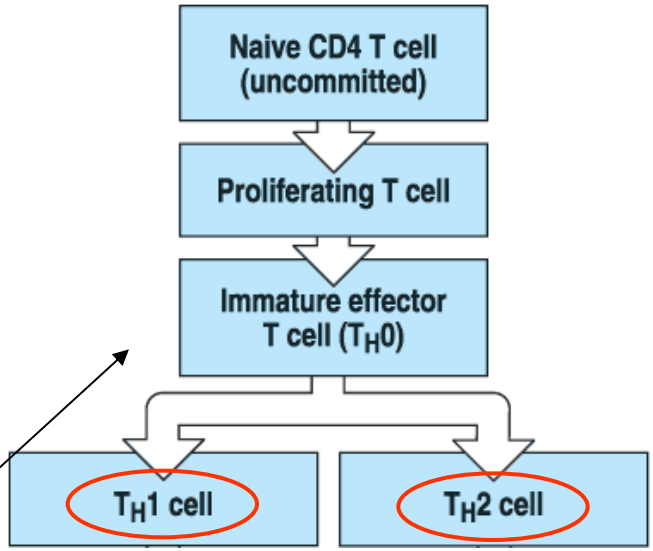
| Cytokine | Size | Principal cell source | Principal cell targets and biologic effects |
|---|---|---|---|
| Interleukin-2 (IL-2) | 14–17 kD | T cells | T cells: proliferation, increased cytokine synthesis; potentiates Fas-mediated apoptosis<br>NK cells: proliferation, activation<br>B cells: proliferation, antibody synthesis (*in vitro*) |
| Interleukin-4 (IL-4) | 18 kD | $CD4^+$ T cells ($T_H2$), mast cells | B cells: isotype switching to IgE<br>T cells: $T_H2$ differentiation, proliferation<br>Macrophages: inhibition of IFN-γ–mediated activation<br>Mast cells: proliferation (*in vitro*) |
| Interleukin-5 (IL-5) | 45–50 kD; homodimer of 20-kD subunits | $CD4^+$ T cells ($T_H2$) | Eosinophils: activation, increased production<br>B cells: proliferation, IgA production |
| Interferon-γ (IFN-γ) | 50 kD (glycosylated); homodimer of 21- to 24-kD subunits | T cells ($T_H1$, $CD8^+$ T cells), NK cells | Macrophages: activation (increased microbicidal functions)<br>B cells: isotype switching to opsonizing and complement-fixing IgG subclasses<br>T cells: $T_H1$ differentiation<br>Various cells: increased expression of class I and class II MHC molecules, increased antigen processing and presentation to T cells |
| Transforming growth factor-β (TGF-β) | 25 kD; homodimer of 12.5-kD subunits | T cells, macrophages, other cell types | T cells: inhibition of proliferation and effector functions<br>B cells: inhibition of proliferation; IgA production<br>Macrophages: inhibition |
| | | | |
| Interleukin-13 (IL-13) | 15 kD | $CD4^+$ T cells ($T_H2$) | B cells: isotype switching to IgE<br>Epithelial cells: increased mucus production<br>Macrophages: inhibition |

- What are the functions of helper T lymphocytes?
- How are their functions accomplished?
- How are their functions acquired?

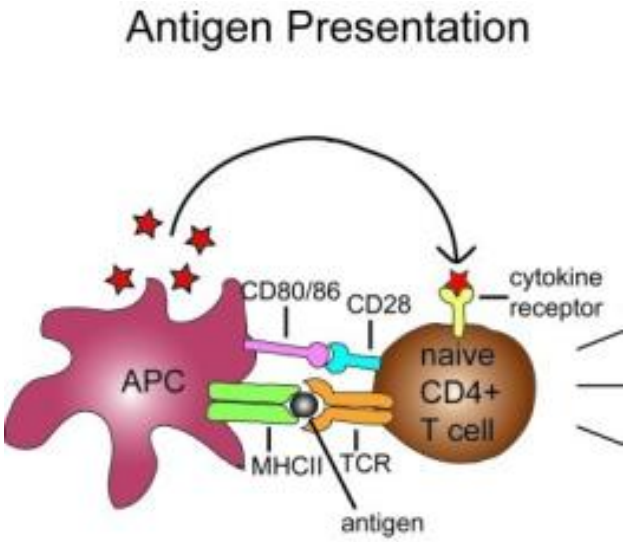
Quali segnali determinano il differenziamento delle diverse sottopopolazioni T?

# Le DC promuovono la piena attivazione dei linfociti $T_H$ vergini $CD4^+$ e il loro differenziamento in linfociti T con funzioni specifiche tipo $T_H1$ e $T_H2$ e T……



# Cytokines in adaptive immunity




-To stimulate the growth and differentiation of lymphocytes in the early stages (in peripheral lymphoid tissue)

Perché la produzione di citochine viene indotta nelle APC?

# Third signal

T lymphocyte differentiation into different effector populations is driven by cytokines.

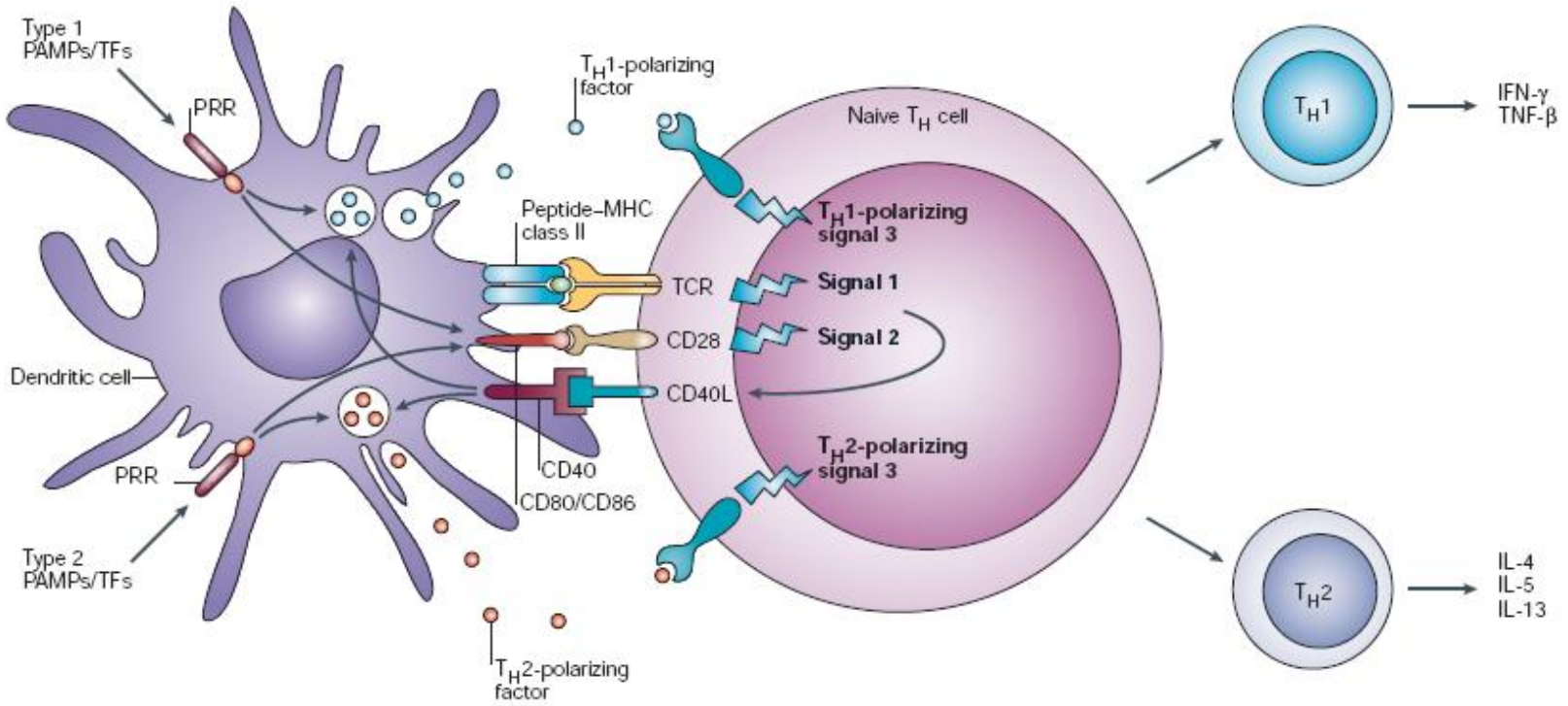



Figure 1 | **T-cell stimulation and T helper 1 ($T_H1$)/$T_H2$-cell polarization require three dendritic cell-derived signals.**

# Dopo la fase di attivazione …….

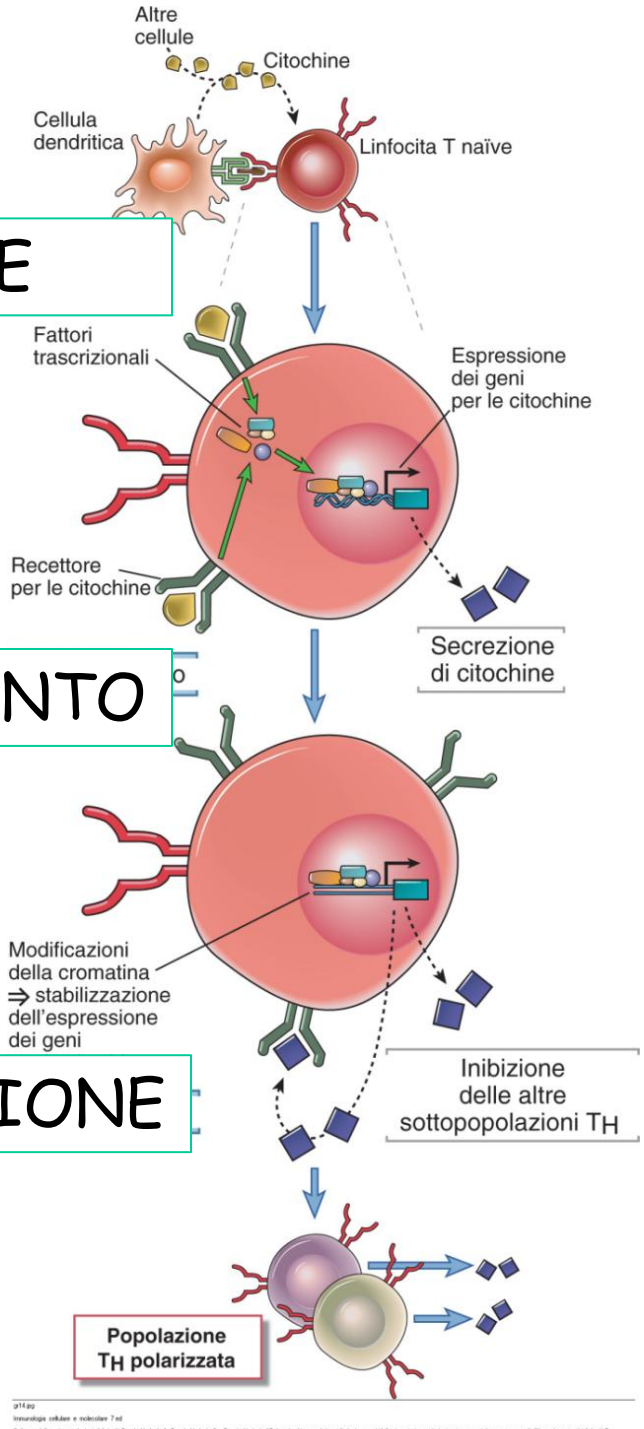
Il differenziamento è influenzato sia dalla forza dello stimolo antigenico che da fattori ambientali (citochine prodotte da cellule APC o da cellule limitrofe)

## INDUZIONE

## INDIRIZZAMENTO

polarizzazione guidata da citochine

## AMPLIFICAZIONE



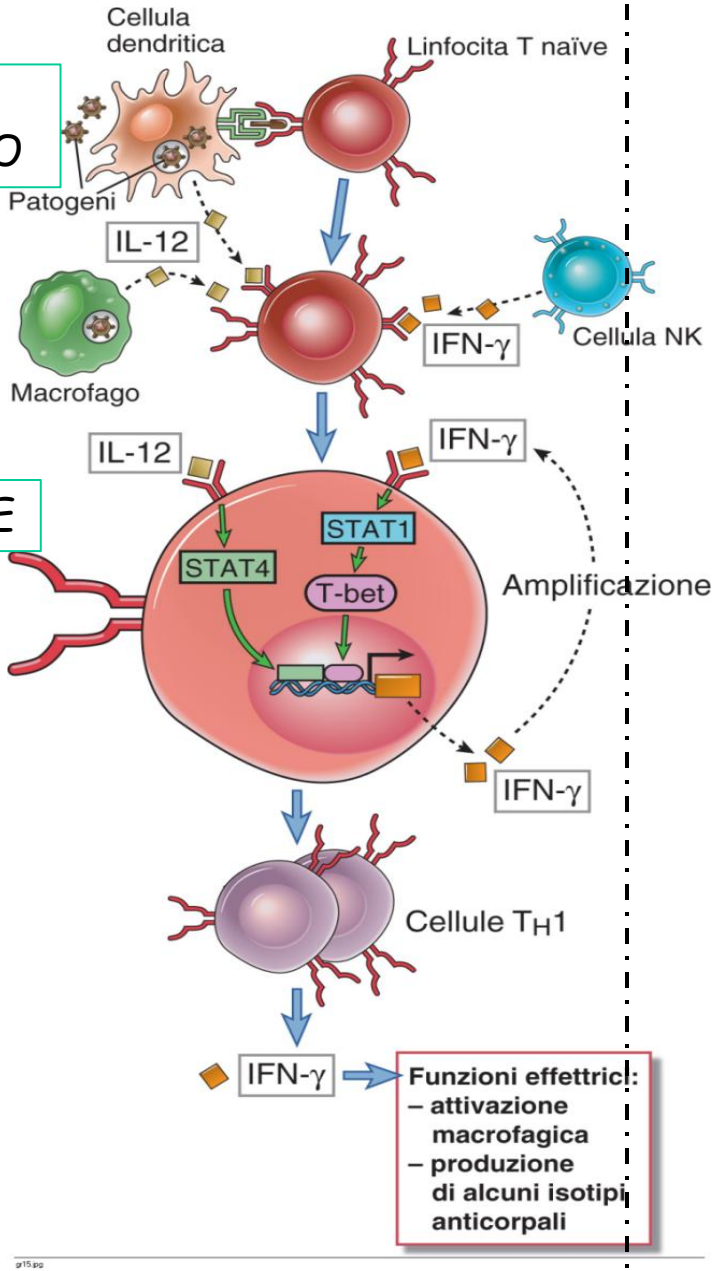
I diversi fattori di trascrizione associati alle diverse popolazioni di linfociti T determinano l'espressione delle citochine e le modificazioni della cromatina

# TH1/TH2 Decision Making

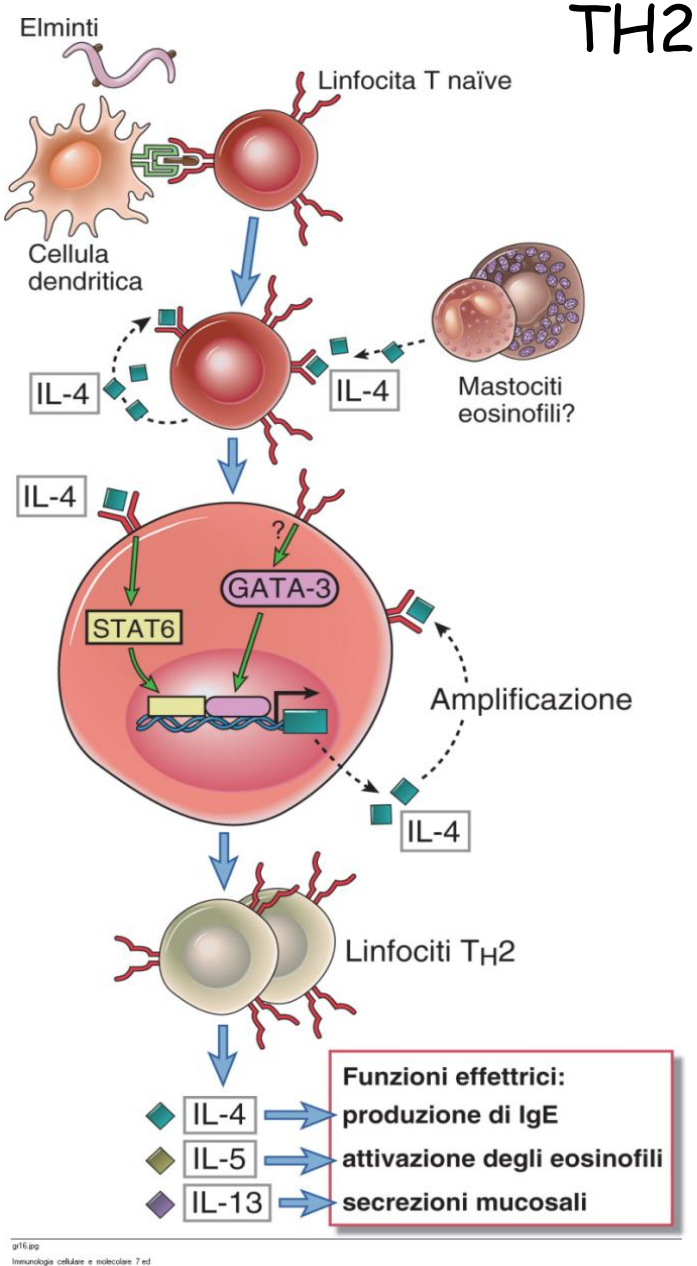
## TH1

INDUZIONE e INDIRIZZAMENTO

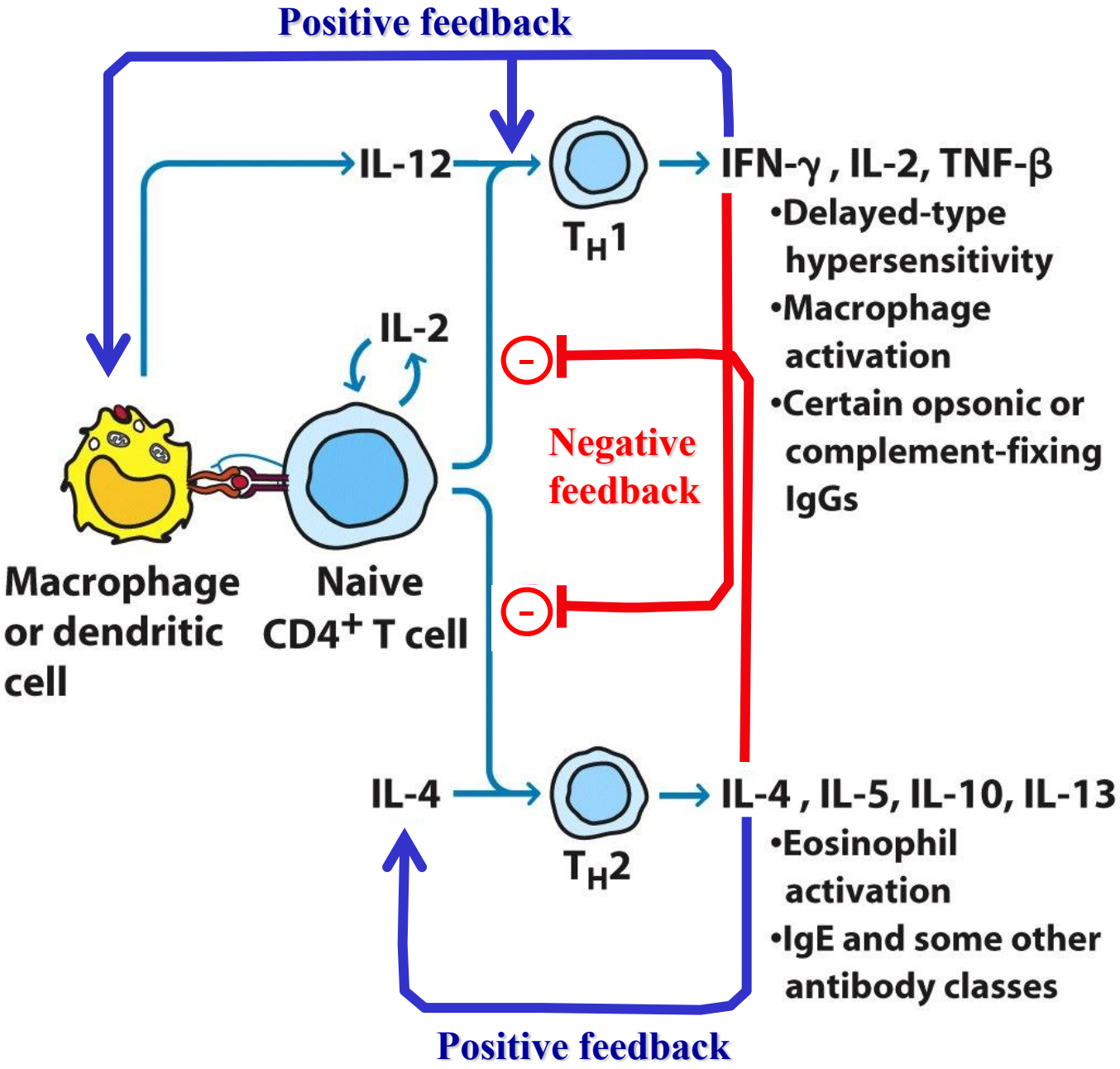
AMPLIFICAZIONE




## TH2



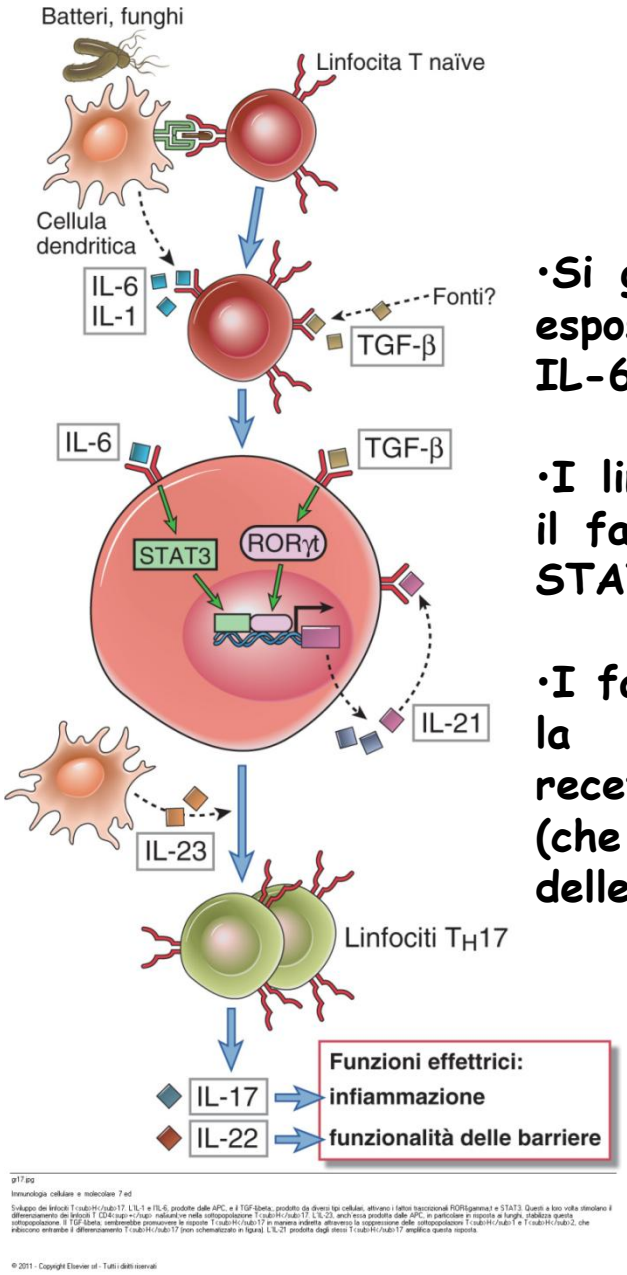
# Positive and negative feedback of helper T cell polarization



# TH17 Decision Making

INDIRIZZAMENTO e INDUZIONE

AMPLIFICAZIONE

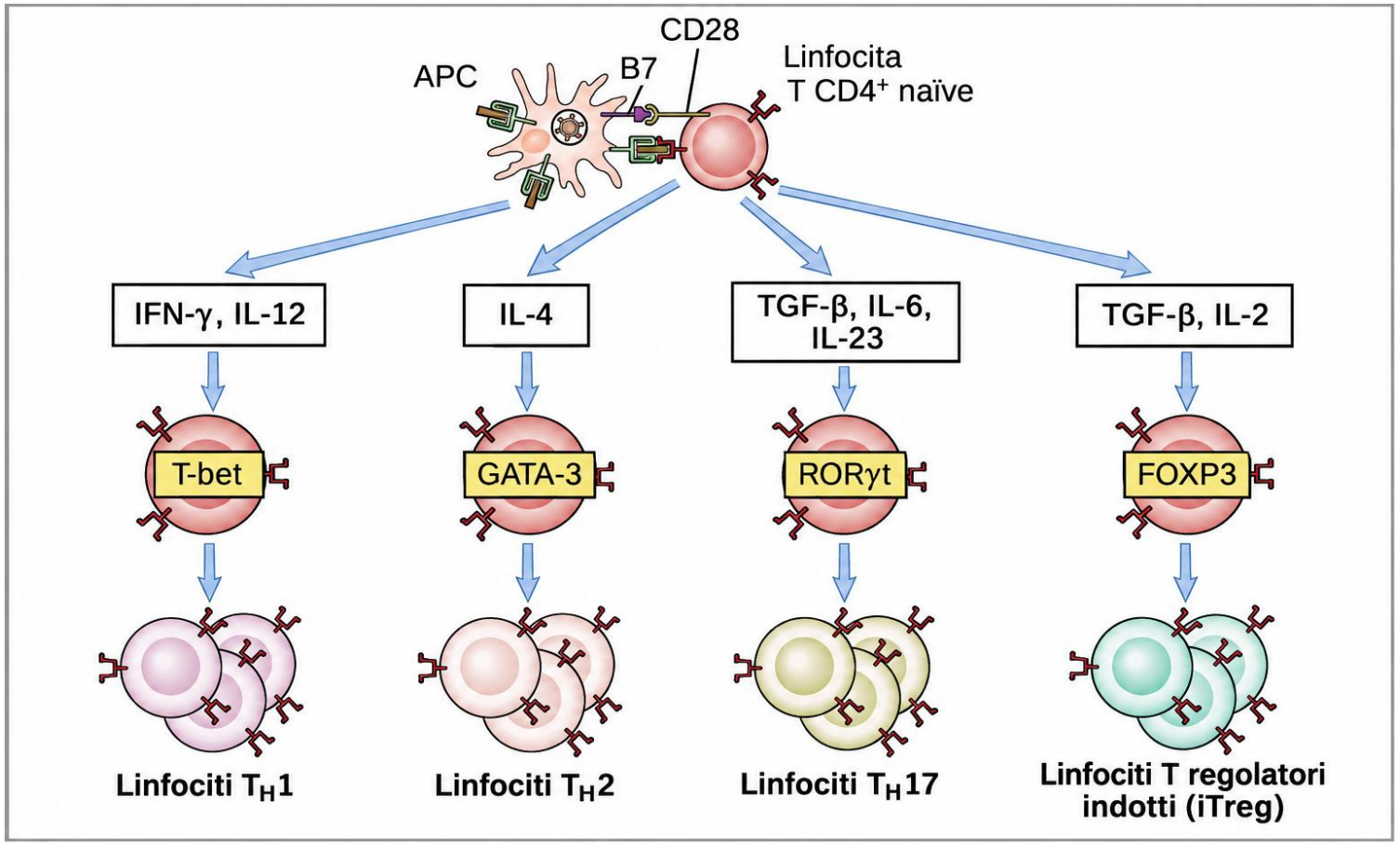



- **Si generano da linfociti T naive esposti a TGF-β in presenza di IL-6**

- **I linfociti rispondono esprimendo il fattore trascrizionale RORγt e STAT3 e la citochina IL-21**

- **I fattori di trascrizione attivano la sintesi di IL-17 e del recettore di membrana per IL-23 (che consente la proliferazione delle cellule Th17)**

# Generazione di sottopopolazioni di linfociti T CD4+




gr17.jpg

**Le citochine prodotte dai linfociti T CD4+ mediano molte delle loro funzioni, ma consentono anche di identificare specifiche sottopopolazioni effettrici**

# Produzione di citochine da Th1/Th2

