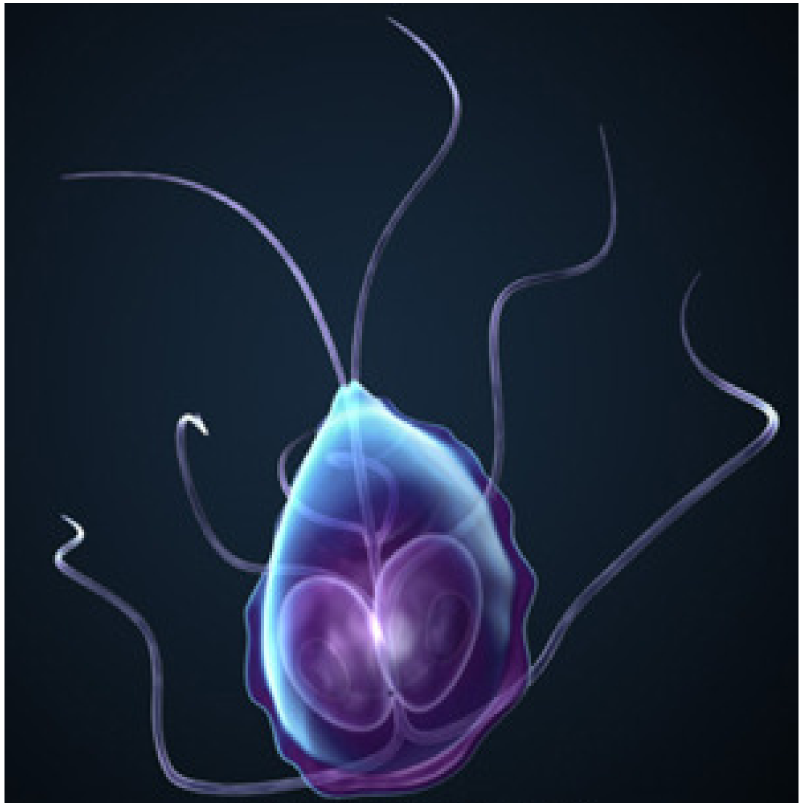
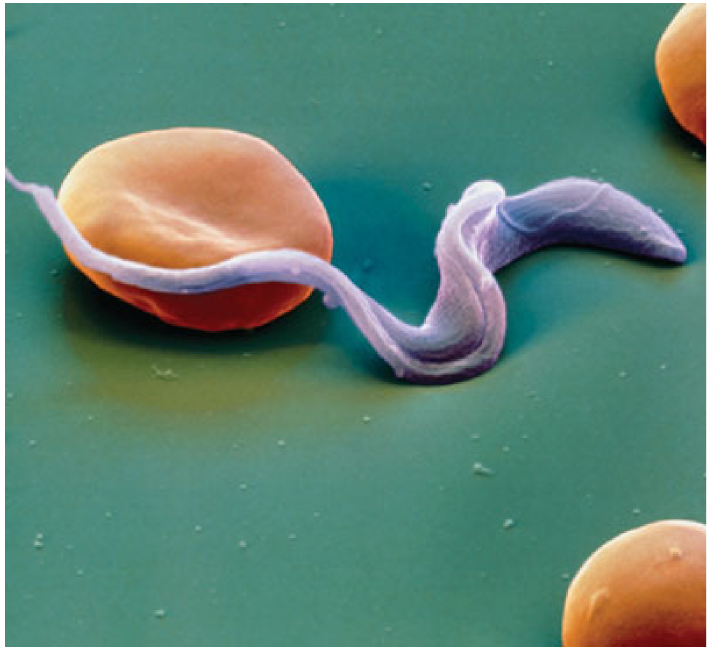
INMUNOPATOLOGÍA

Inmunología de las infecciones parasitarias

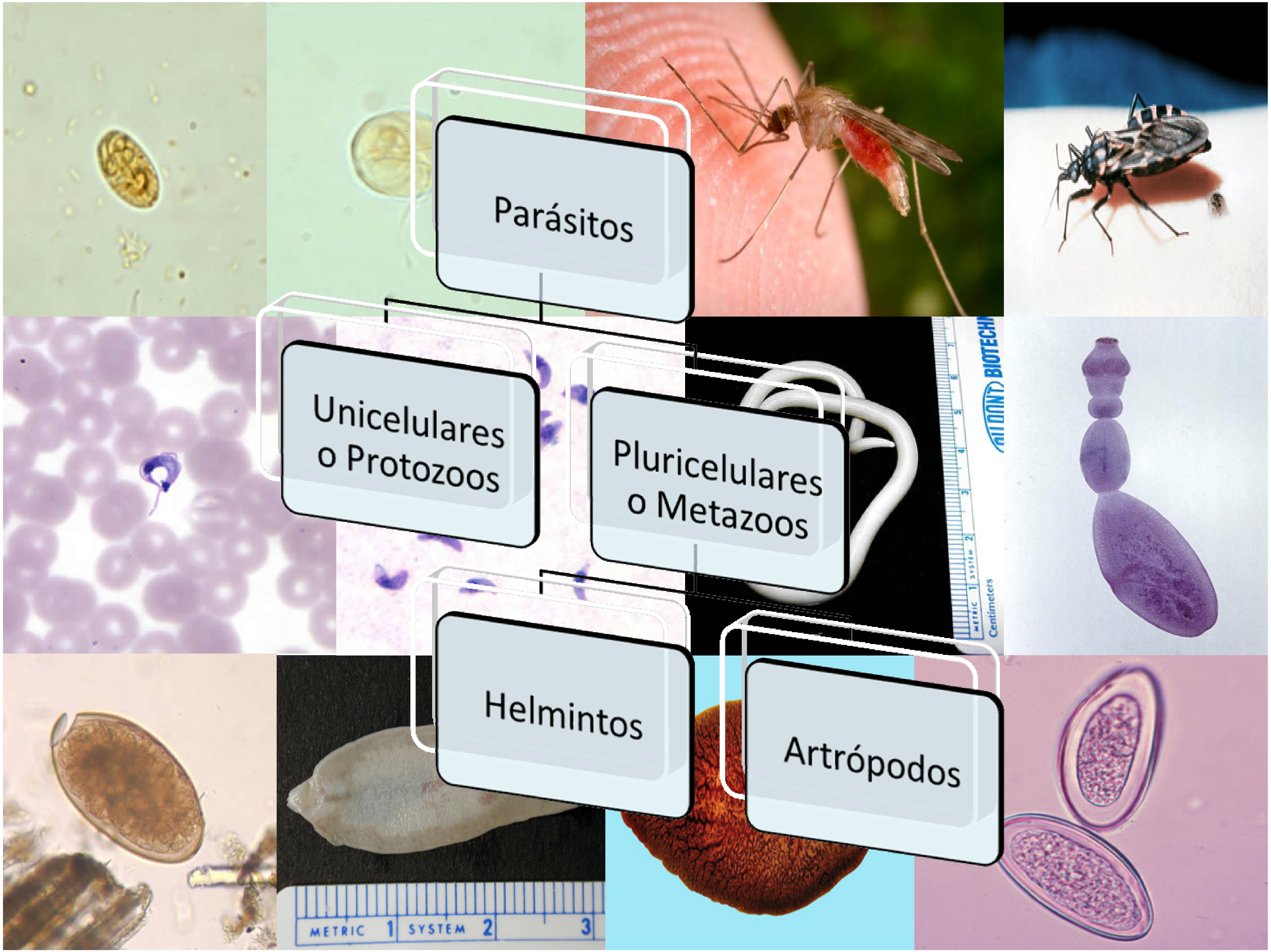
2010



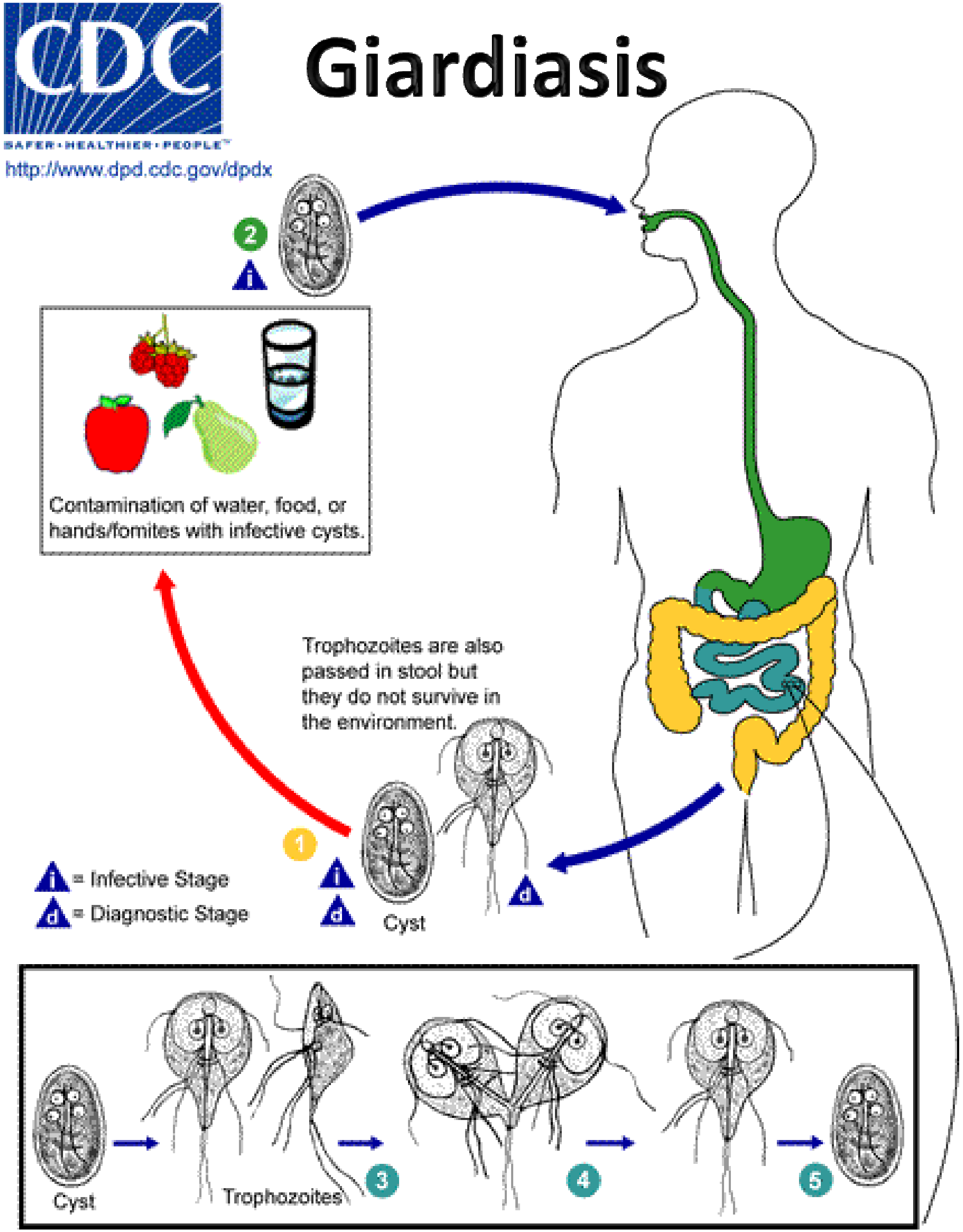


Elisa Beraja

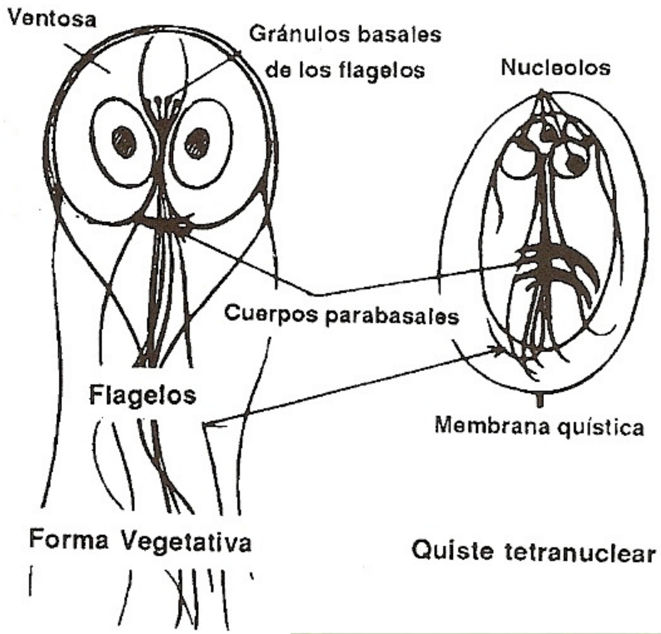

Mutualismo
Asociaciones biológicas entre individuos de distintas especies
Parasitismo
Comensalismo


Parásitos
Unicelulares o Protozoos
Pluricelulares o Metazoos
Helmintos
Artrópodos
METRIC 1 SYSTEM 2 3

Giardiasis

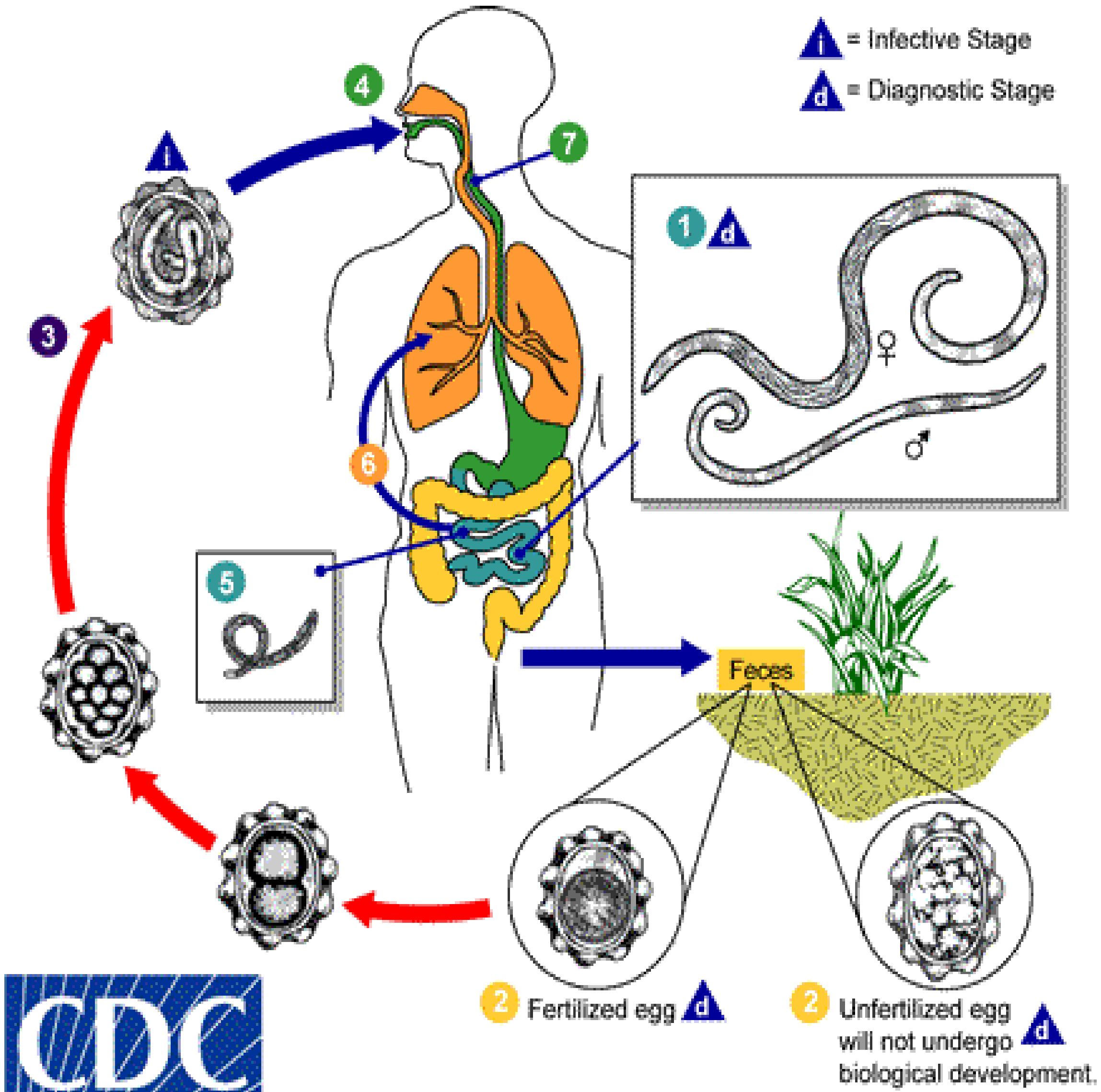


CDC
SAFER • HEALTHIER • PEOPLE™
http://www.dpd.cdc.gov/dpdx
Contamination of water, food, or hands/fomites with infective cysts.
Trophozoites are also passed in stool but they do not survive in the environment.
= Infective Stage
= Diagnostic Stage
Cyst
Cyst
Trophozoites



Ventosa
Gránulos basales de los flagelos
Nucleolos
Cuerpos parabasales
Flagelos
Membrana quística
Forma Vegetativa
Quiste tetranuclear

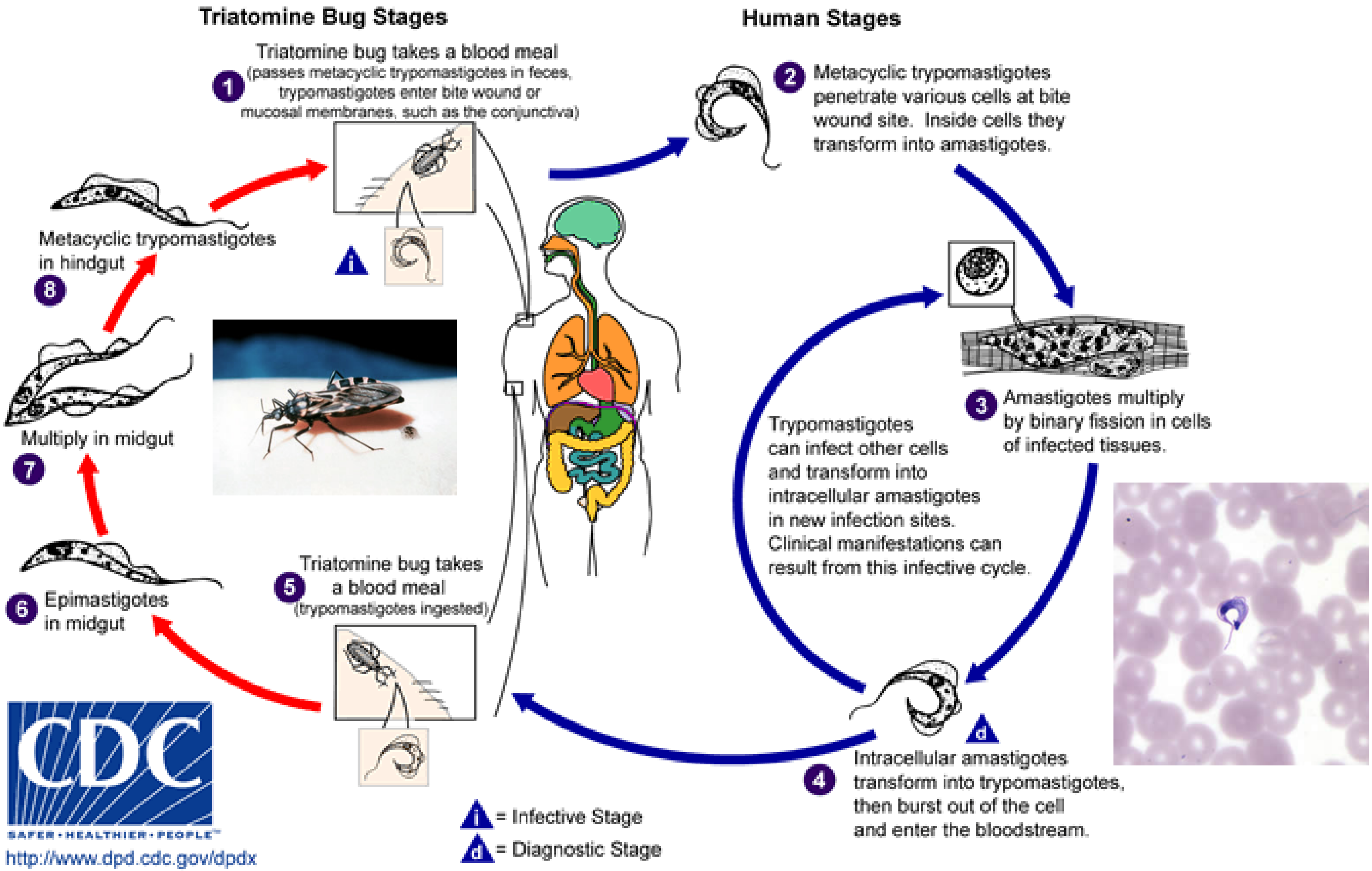
Ascariasis



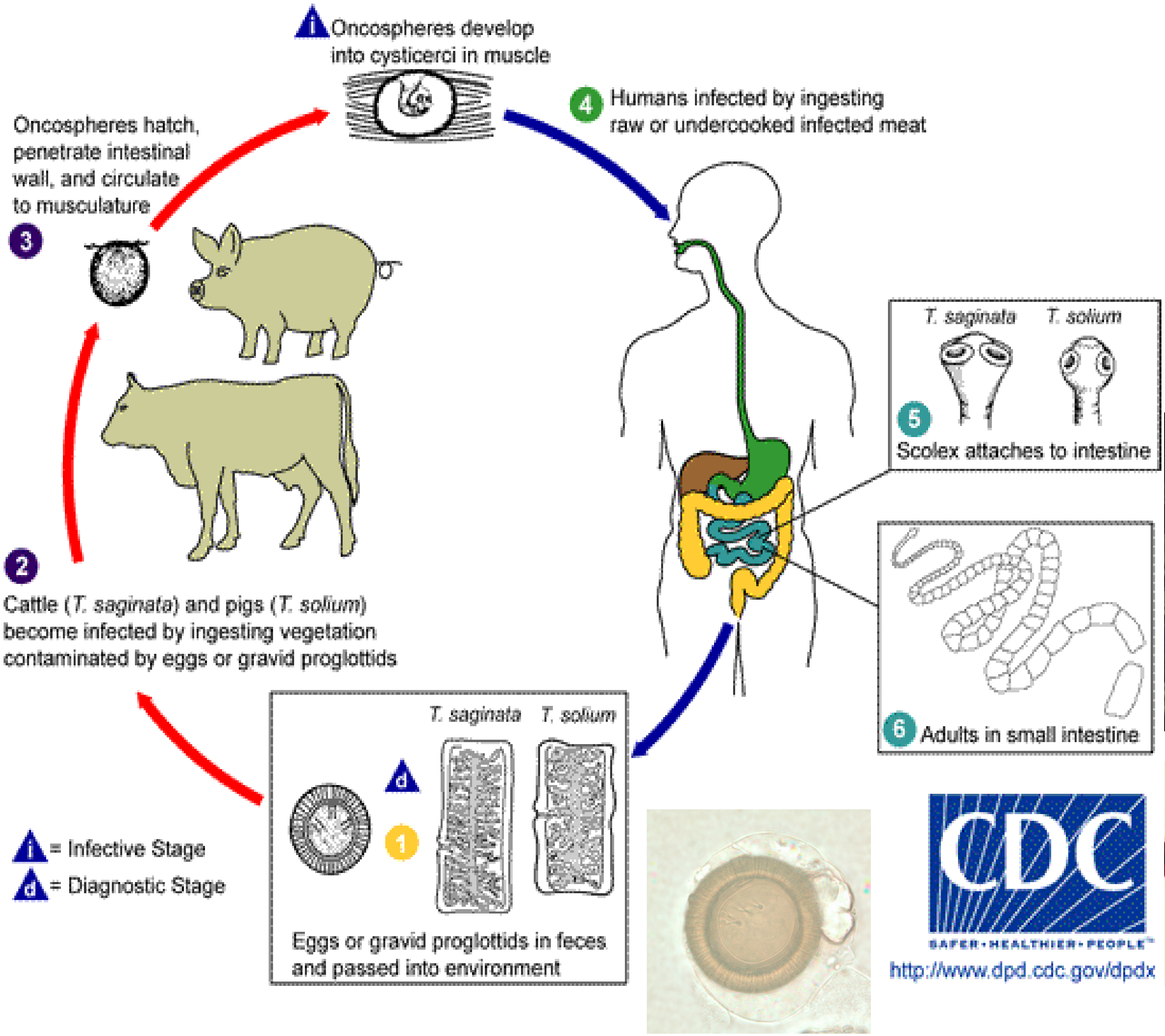
SAFER·HEALTHIER·PEOPLE™

http://www.dpd.cdc.gov/dpdx

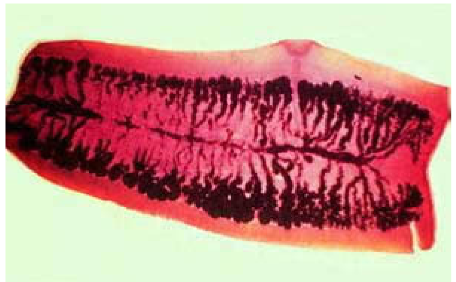
Enfermedad de Chagas



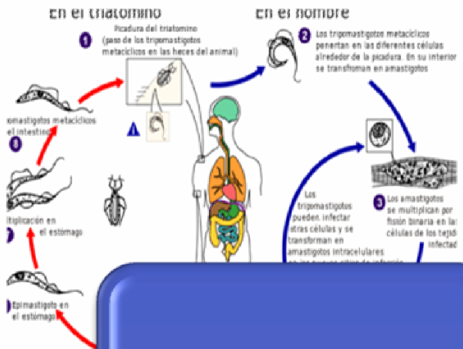
Teniasis



Oncospheres develop into cysticerci in muscle
4 Humans infected by ingesting raw or undercooked infected meat
Oncospheres hatch, penetrate intestinal wall, and circulate to musculature
3
T. saginata
T. solium
5 Scolex attaches to intestine
6 Adults in small intestine
2
Cattle (T. saginata) and pigs (T. solium) become infected by ingesting vegetation contaminated by eggs or gravid proglottids
T. saginata
T. solium
d
1
Eggs or gravid proglottids in feces and passed into environment
i = Infective Stage
d = Diagnostic Stage
http://www.dpd.cdc.gov/dpdx



Infección parasitaria



Relación Huésped-Parásito

Enfermedad parasitaria

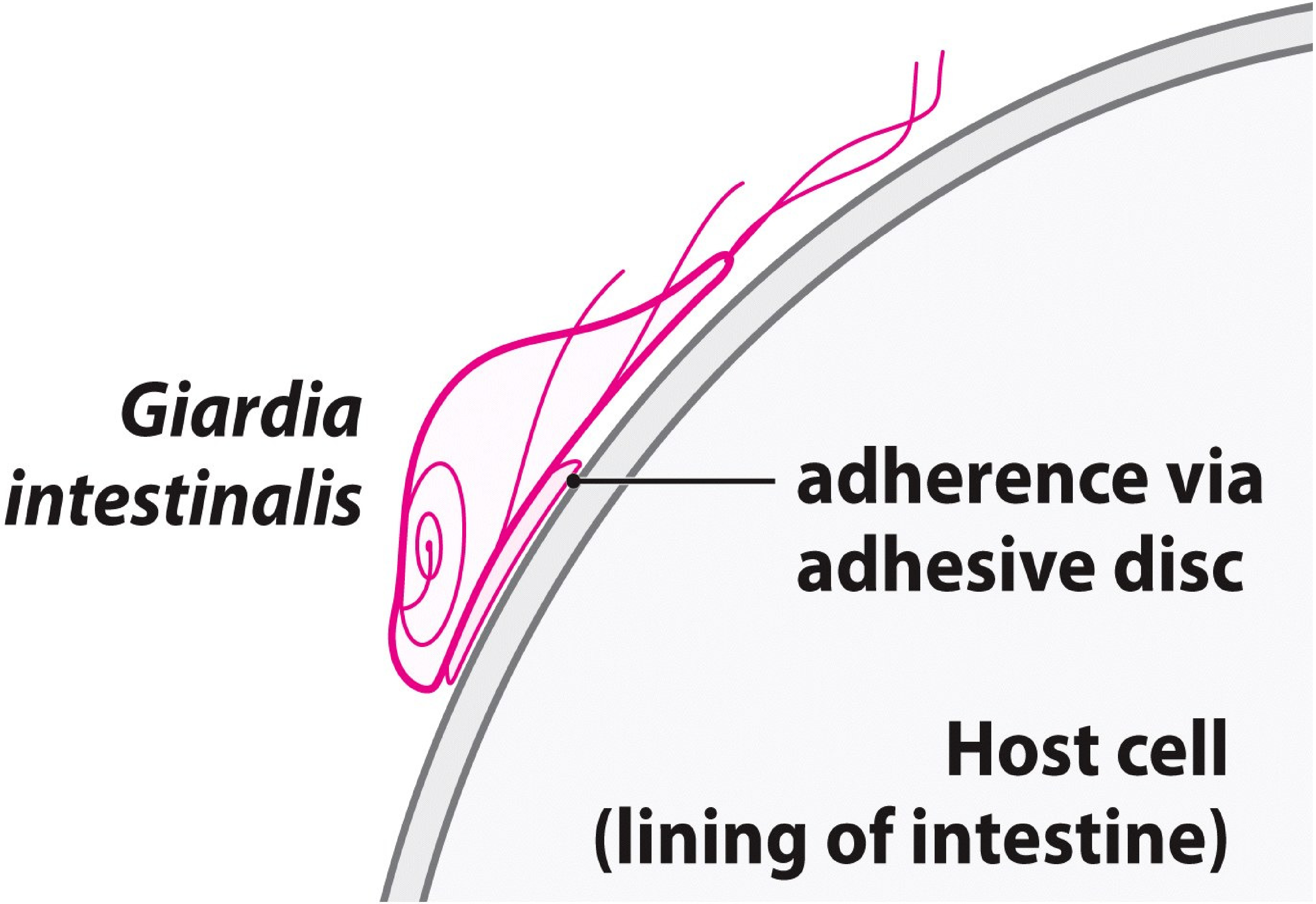


Figure 10.13d Living in a Microbial World (© Garland Science)

Clasificación clínica de las parasitosis

Morfología

- Protozoosis
- Helmintosis
- Artrópodos

Grado de parasitismo

- Temporarias o facultativas
- Permanentes y obligatorias

Topografía

- Ectoparasitosis
- Endoparasitosis

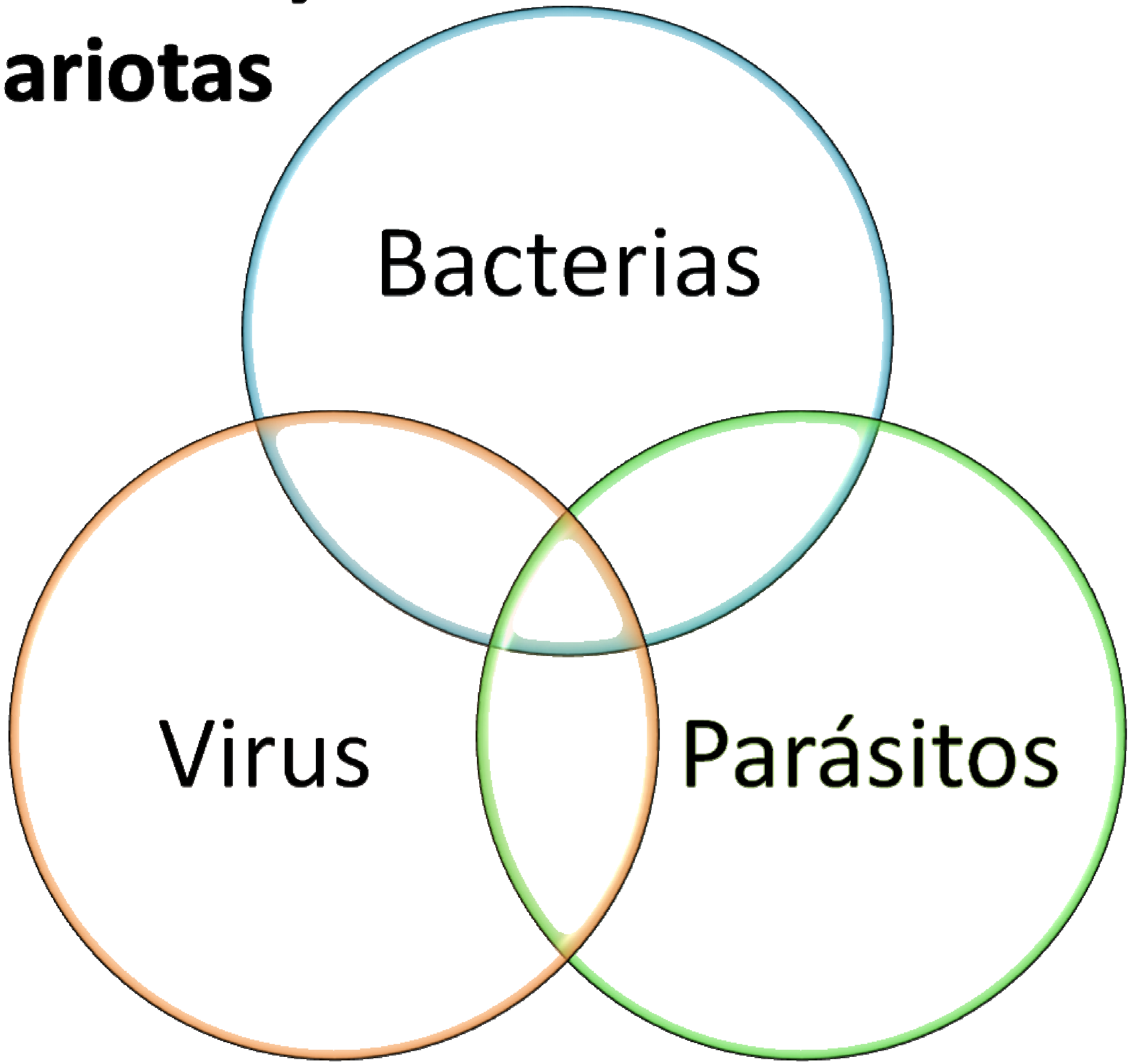
Localización

- Enteroparasitosis
- Histoparasitosis
- Hemoparasitosis
- Ectoparasitosis


Perfil epidemiológico
Países con clima tropical
Deficiente cobertura de agua potable y saneamiento ambiental
Precaria higiene ambiental, laboral, personal
Falta de programas específicos de prevención
Falta de políticas nacionales y de salud
Malnutrición
Pobreza

La respuesta inmune y su efecto sobre los parásitos

Procariotas y Eucariotas



Complejidad antigénica

- Ag metabólicos
- Ag somáticos
- Ag heterófilos

Complejidad fisiológica

- Isozimas

Complejidad estructural

Complejidad biológica

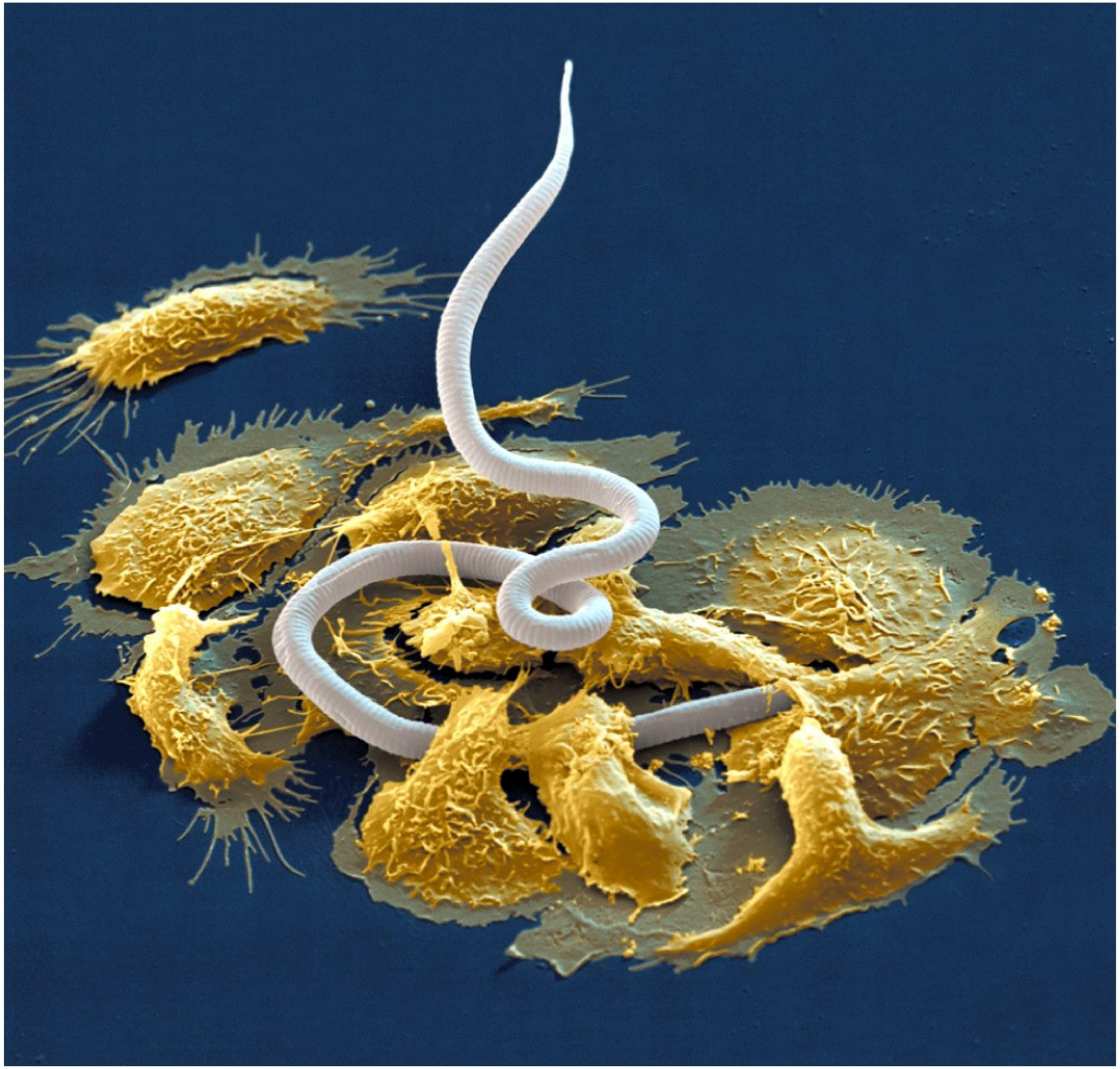


Figure 1-5d
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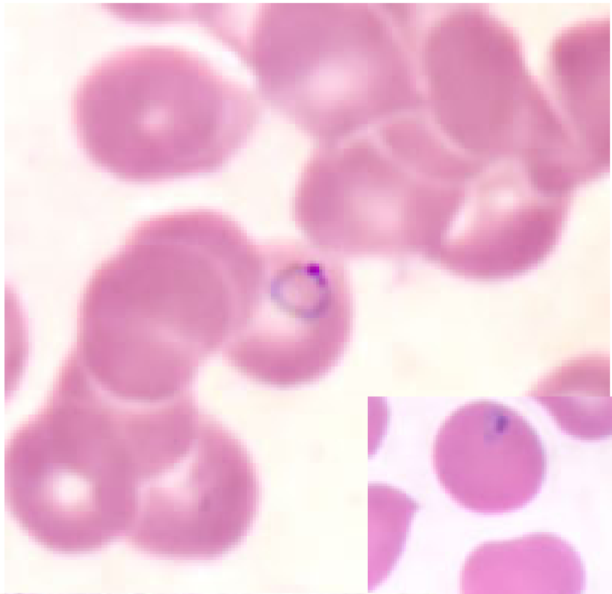
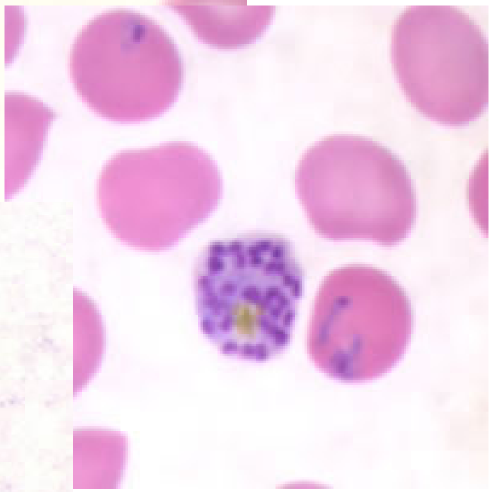
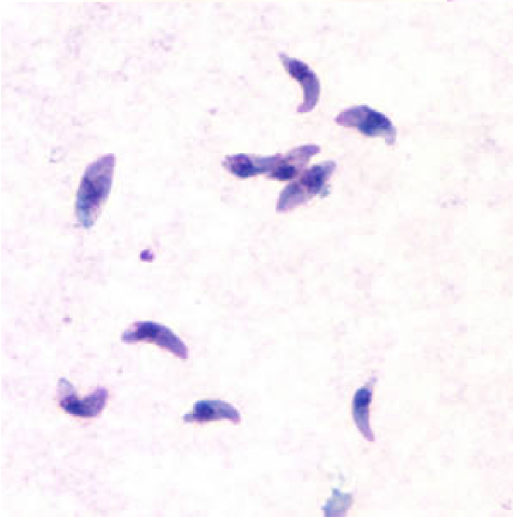
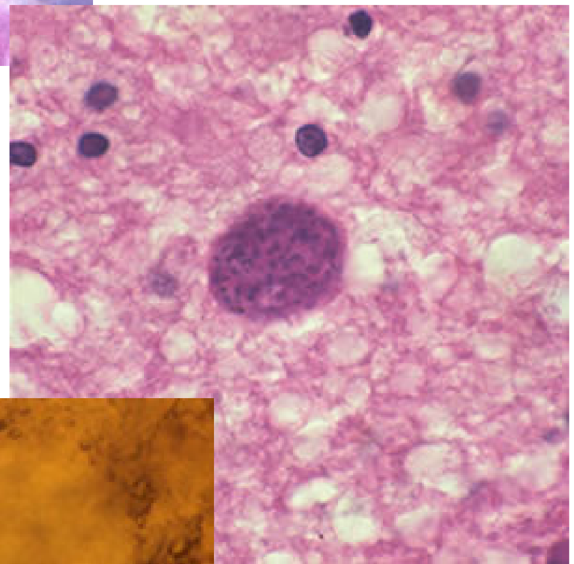
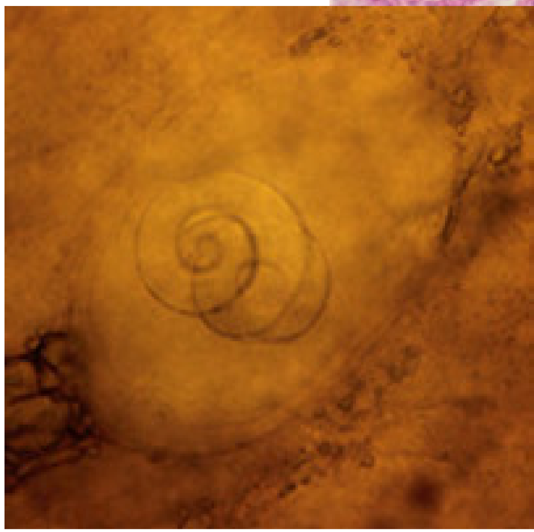
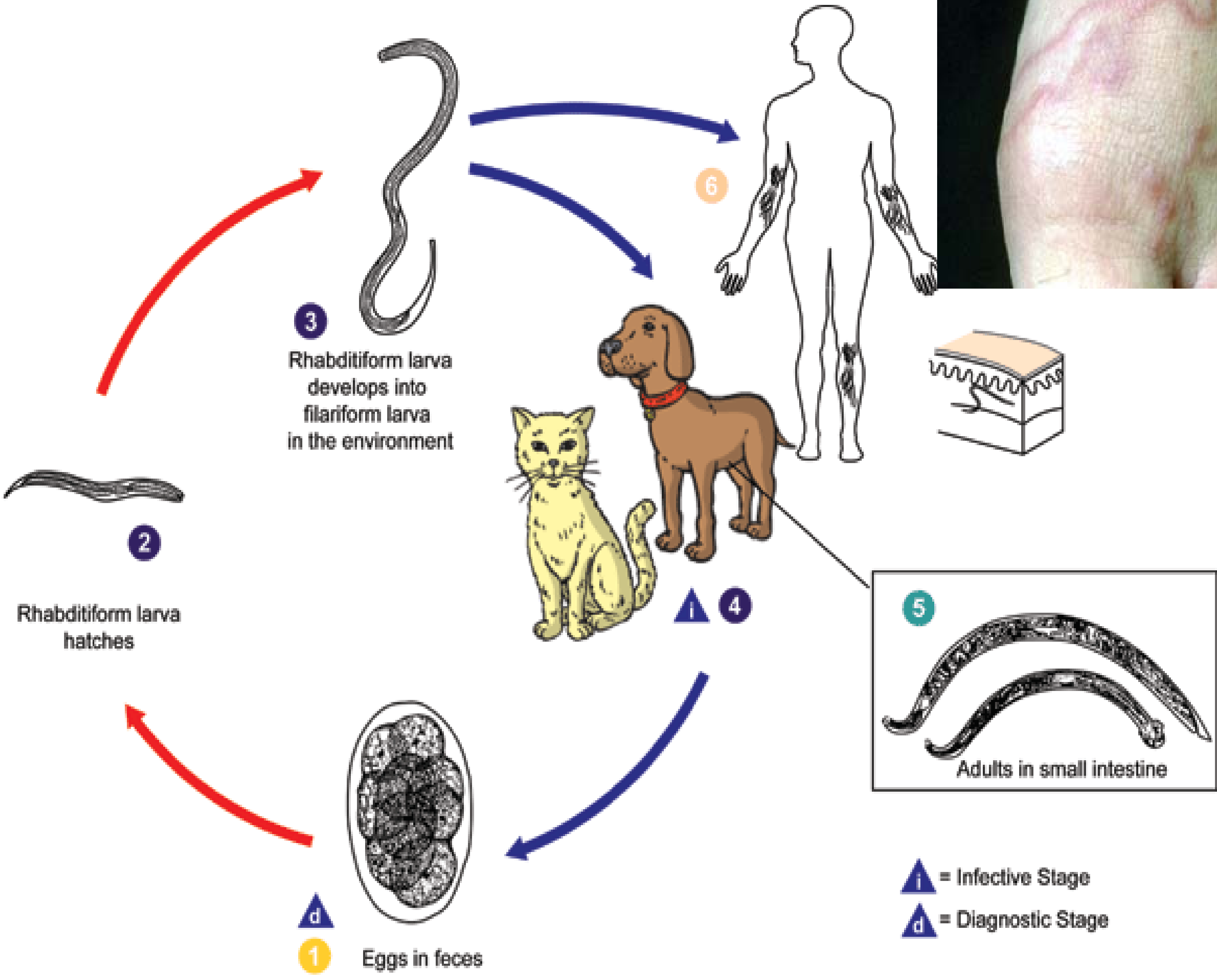
Localización

Movilidad



3
Rhabditiform larva
develops into
filariform larva
in the environment
6
2
Rhabditiform larva
hatches
i 4
5
Adults in small intestine
d
1
Eggs in feces
i = Infective Stage
d = Diagnostic Stage

Presentación de Ag → Hipobiosis → Modulación de la inmunidad

INMUNIDAD INNATA

Mecanismos humorales

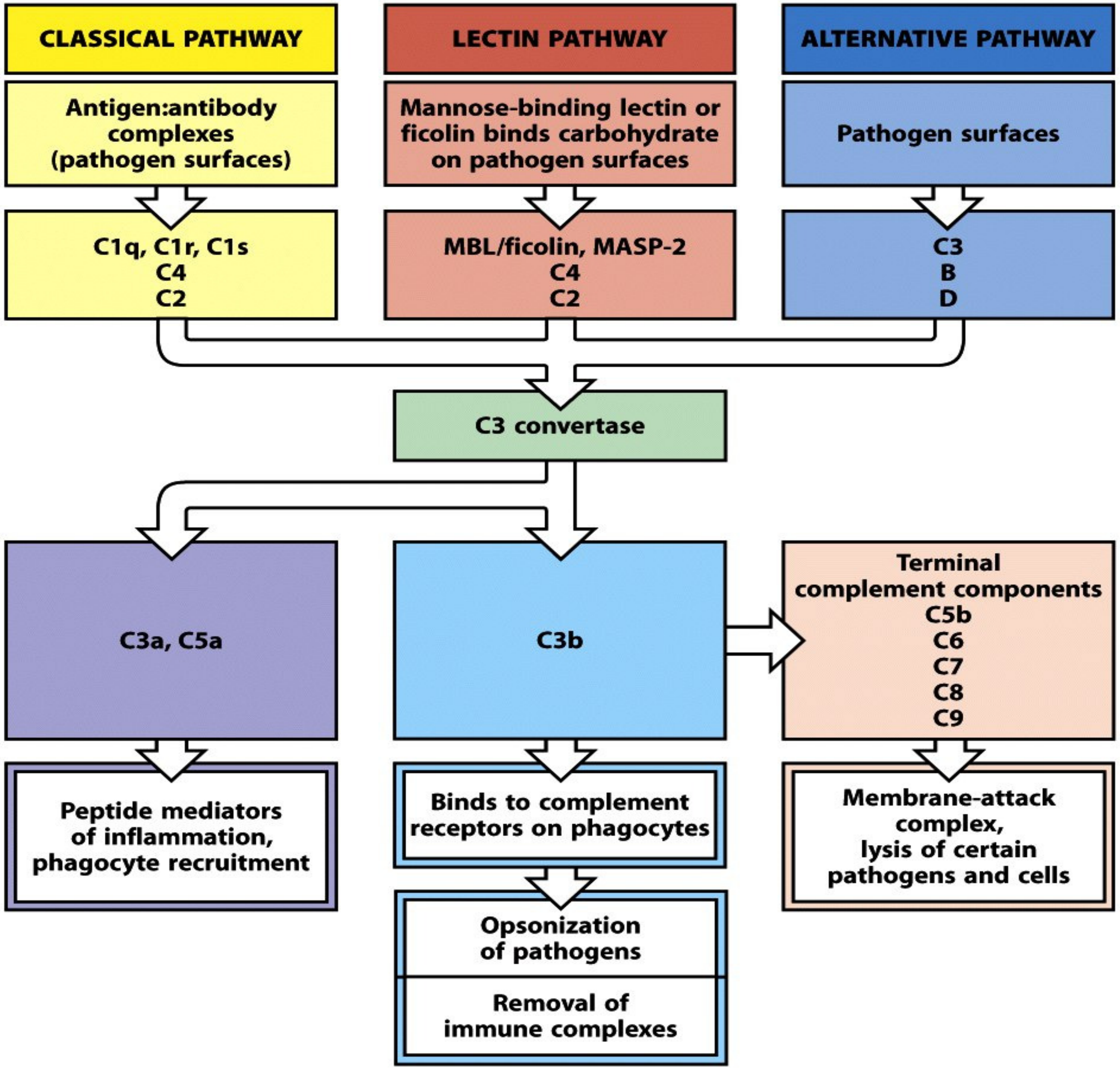


Figure 2-25 Immunobiology, 7ed. (© Garland Science 2008)

TFL (factores líticos específicos para tripanosomas)

- TFL 1
- TFL 2

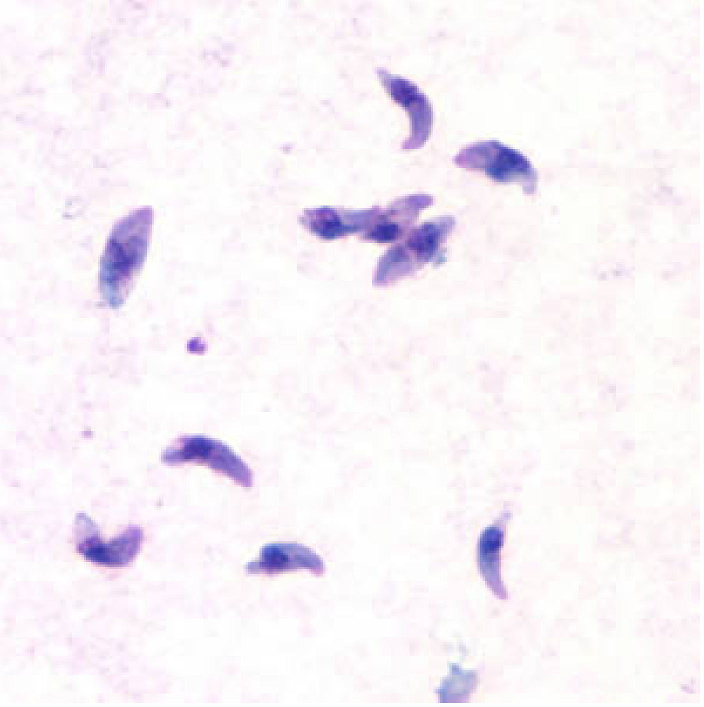
Resistencia innata en humanos contra T. brucei

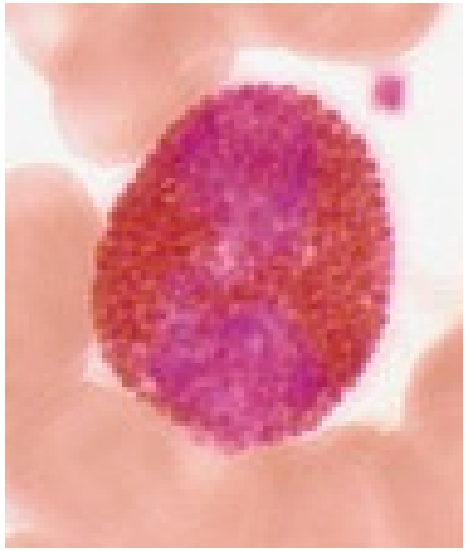
Daño oxidativo

Mecanismos celulares

- **Fagocitosis por macrófagos:**

- Opsonización por el C'
- RLC



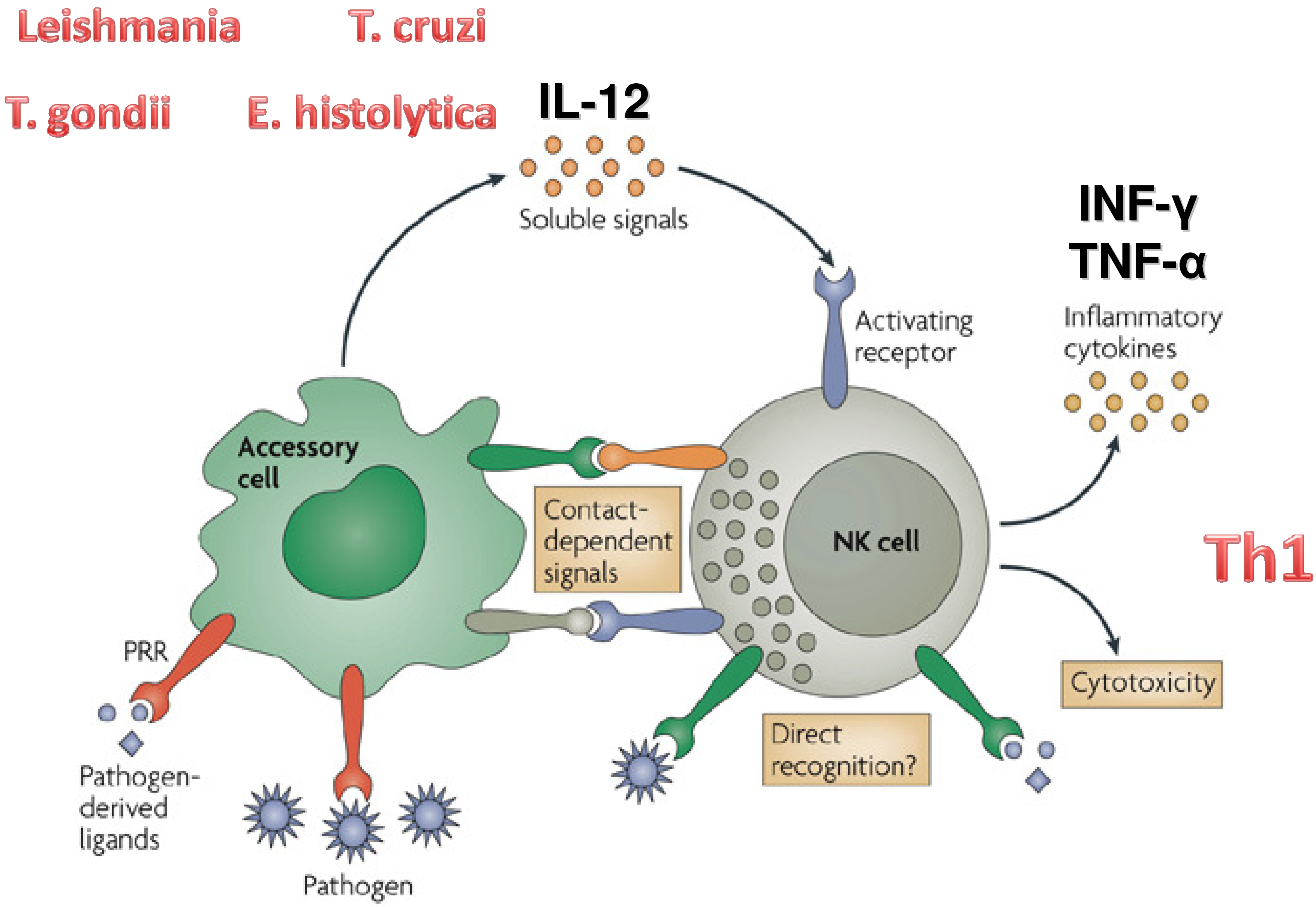


- Liberación de sus gránulos, que contienen proteínas tóxicas

- IRO

Schistosoma

Trichuris



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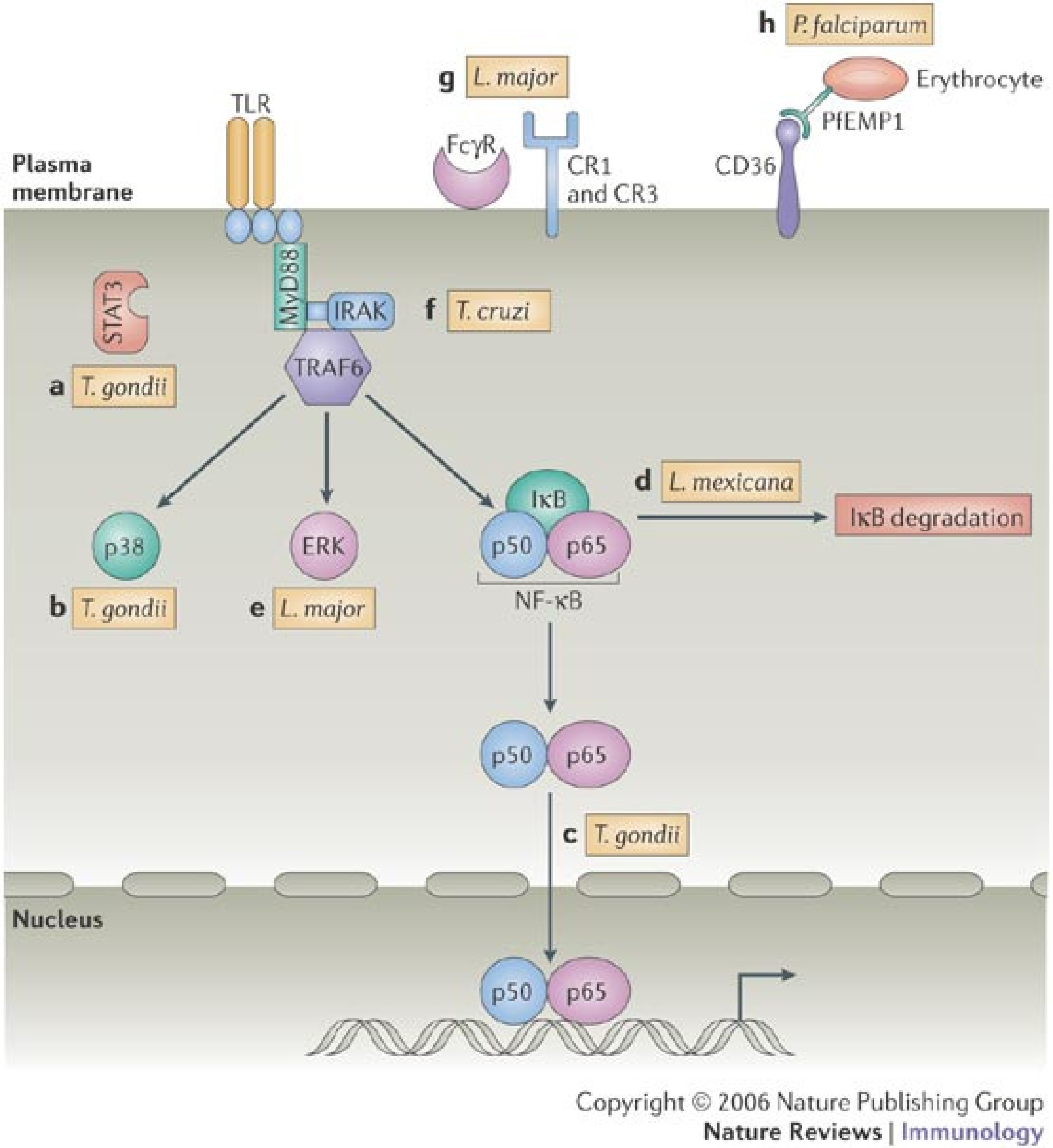
NKT y los Tγδ

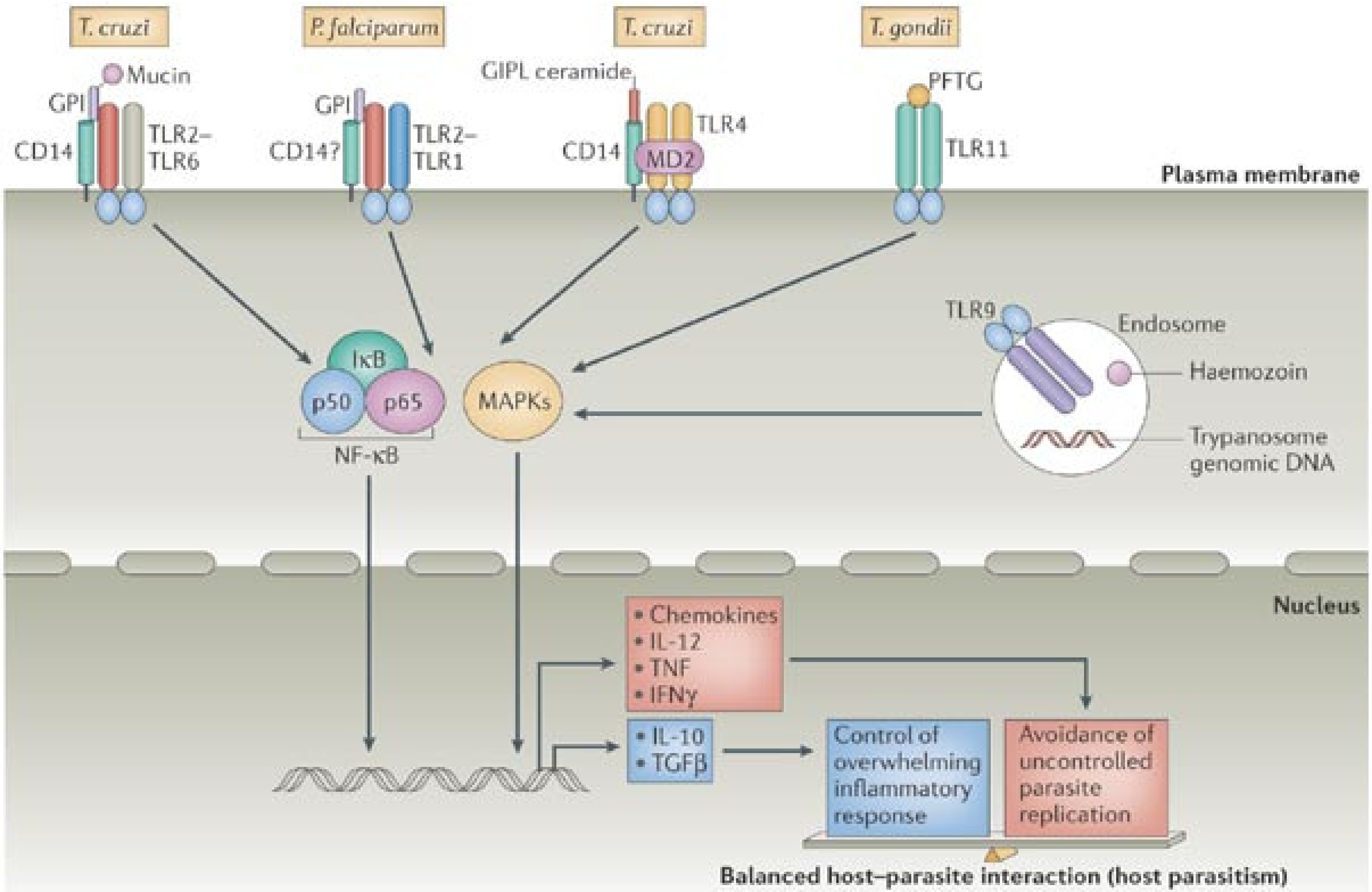
- **NKT:** Resistencia a la infección por L. major. No median efecto protector en infección por Trichuris muris

- **Tγδ:** Se incrementan en sangre de individuos infectados por protozoos y helmintos (IFN-γ, TNF-α, HSP65 en Toxoplasma y Plasmodium)

CPA

- RRP: TLR (TLR-2)
- PAMP: GPI (protozoos: Toxoplasma, Leishmania, Plasmodium)





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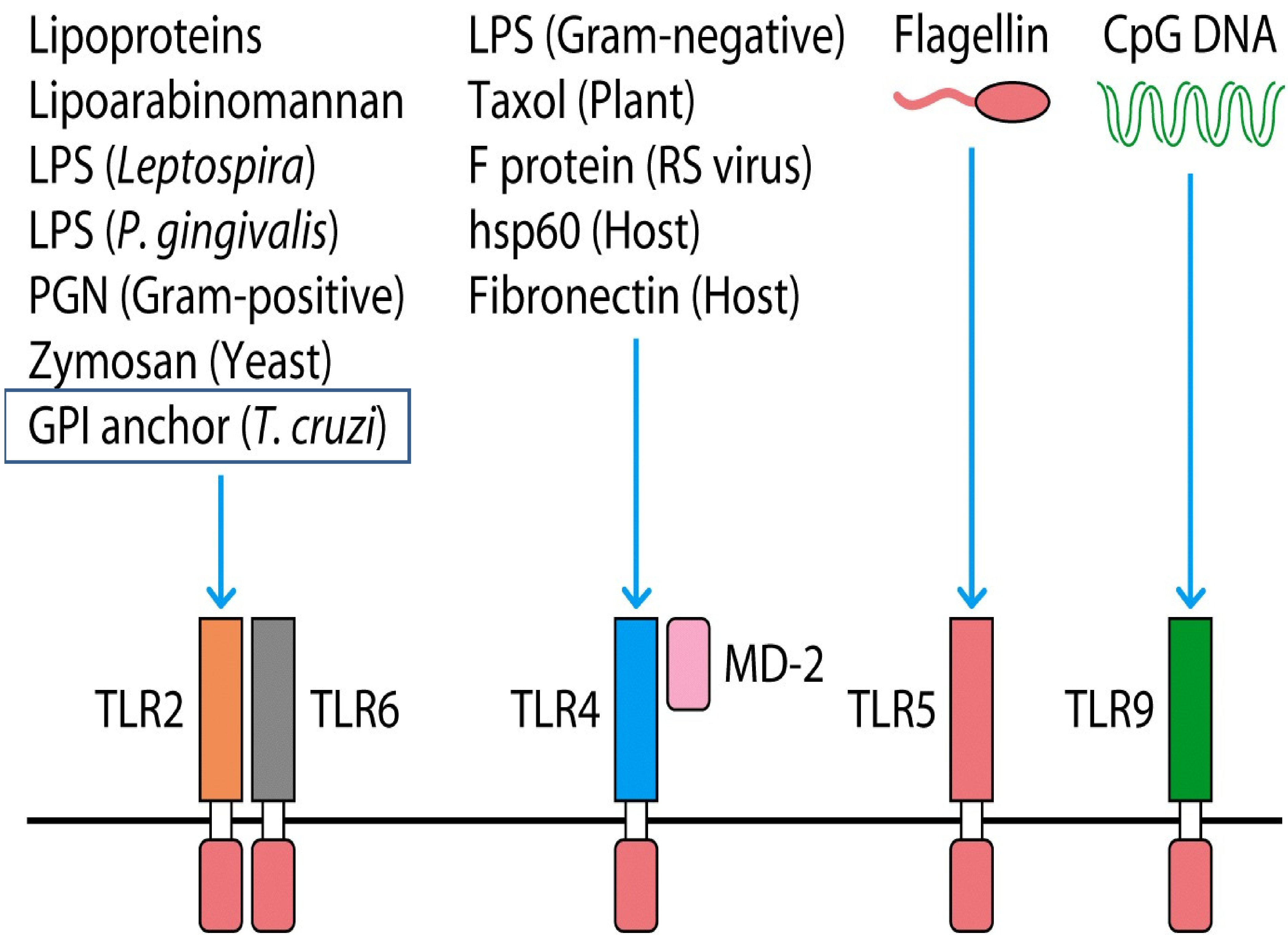
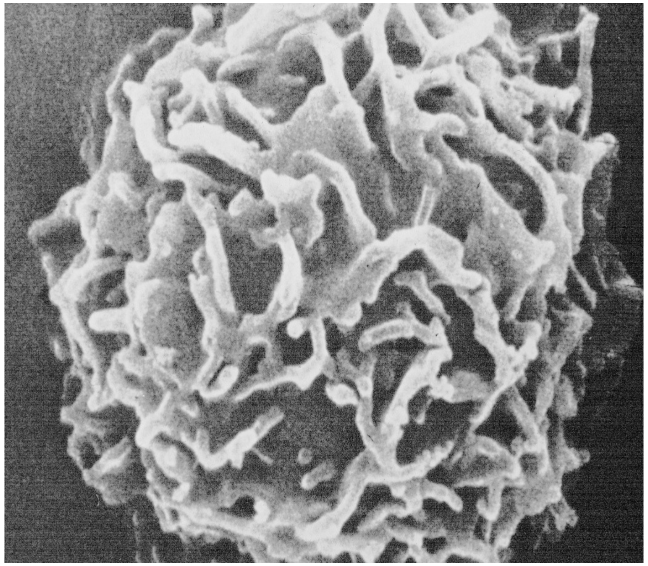

Lipoproteins
Lipoarabinomannan
LPS (*Leptospira*)
LPS (*P. gingivalis*)
PGN (Gram-positive)
Zymosan (Yeast)
GPI anchor (*T. cruzi*)
LPS (Gram-negative)
Taxol (Plant)
F protein (RS virus)
hsp60 (Host)
Fibronectin (Host)
Flagellin
CpG DNA
TLR2
TLR6
TLR4
MD-2
TLR5
TLR9

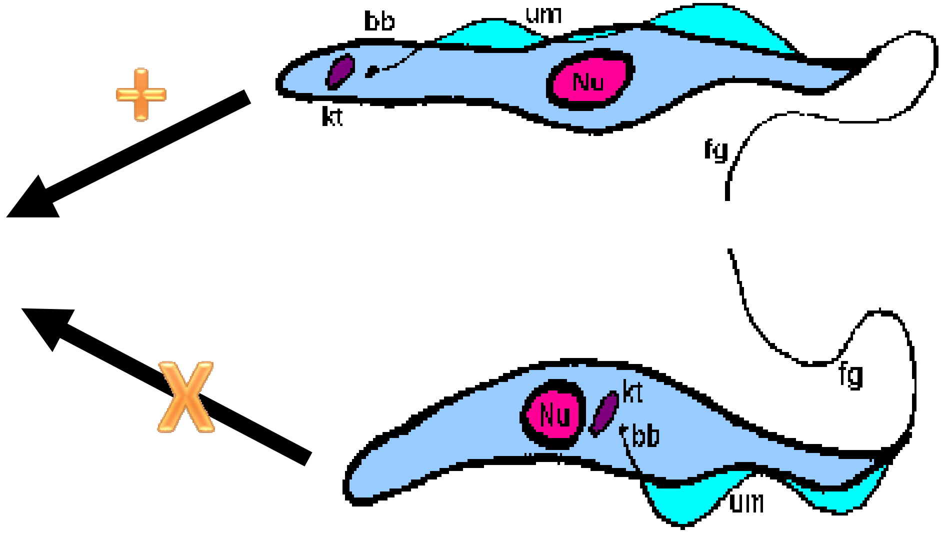


iNOS

TNF-α

IL-1

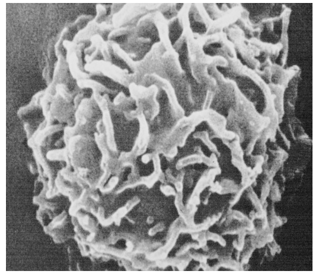
IL-12



Th2

IL-10

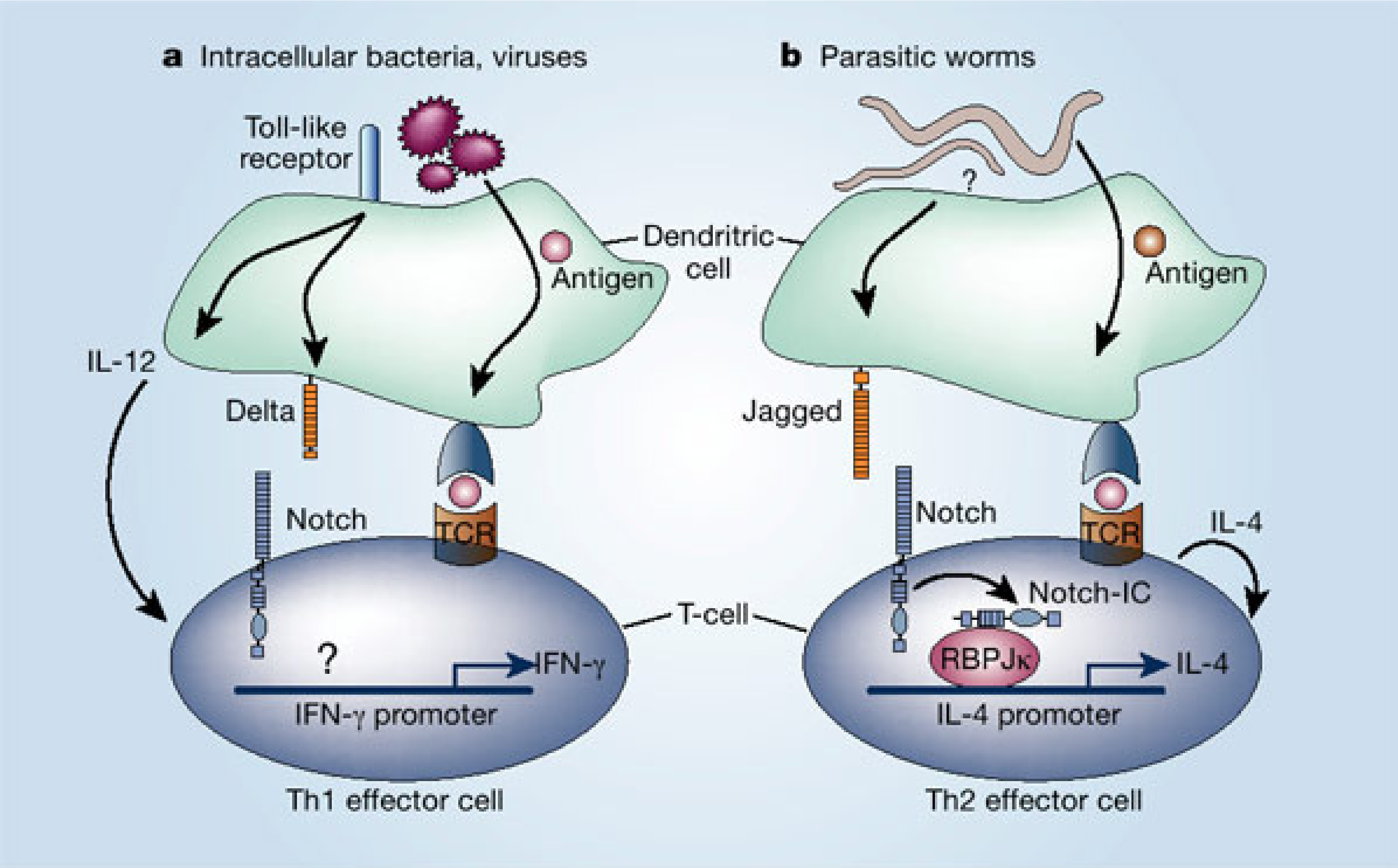
PG E-2



LB 1

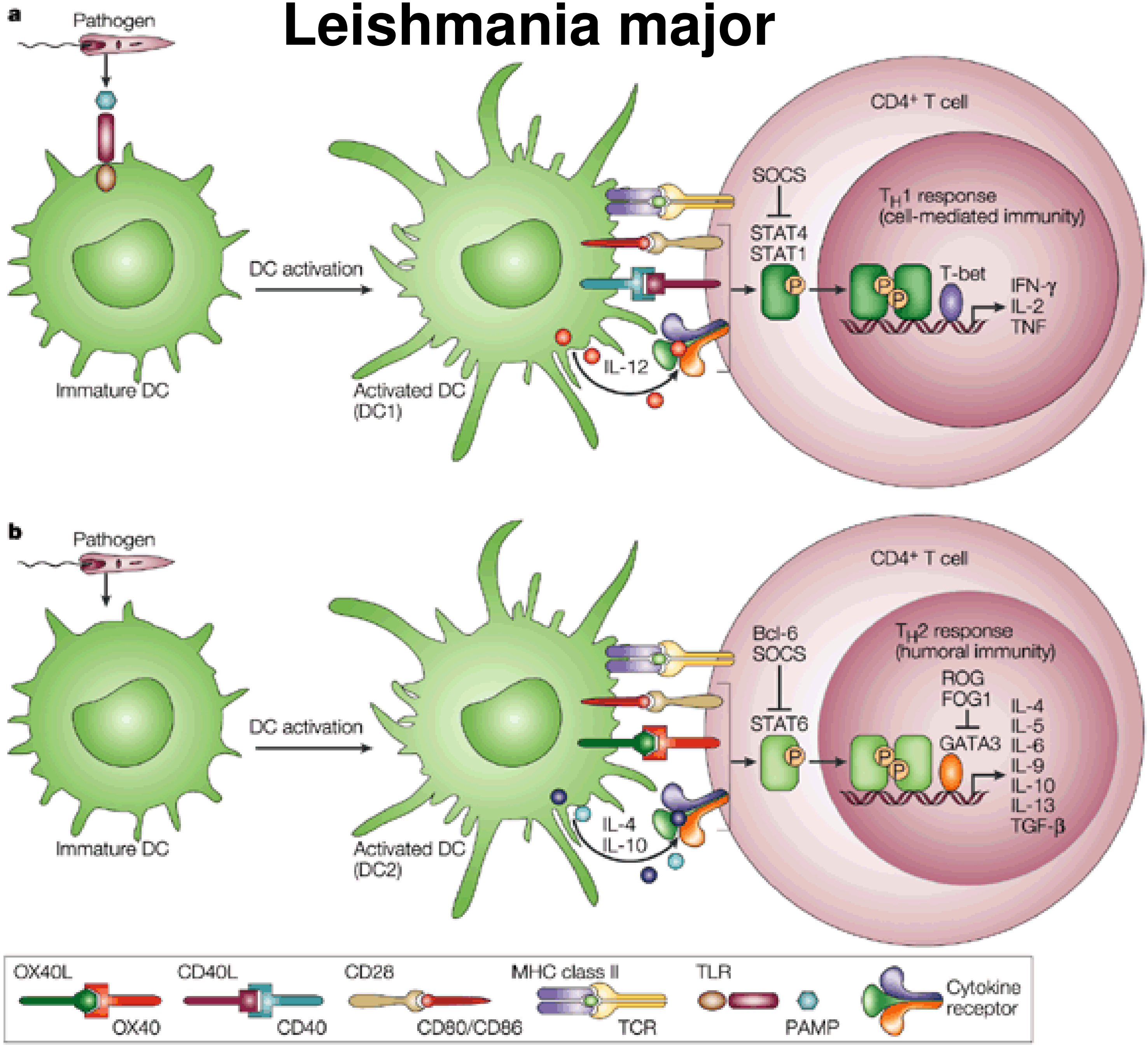
CPA: Presentan un aumento en la expresión de CD40, CD54 y CD86

LT



- **Helmintos:** Th2, IgE, Eo, Mastocitos
- **Protozoos intracelulares:** Th1

Leishmania major



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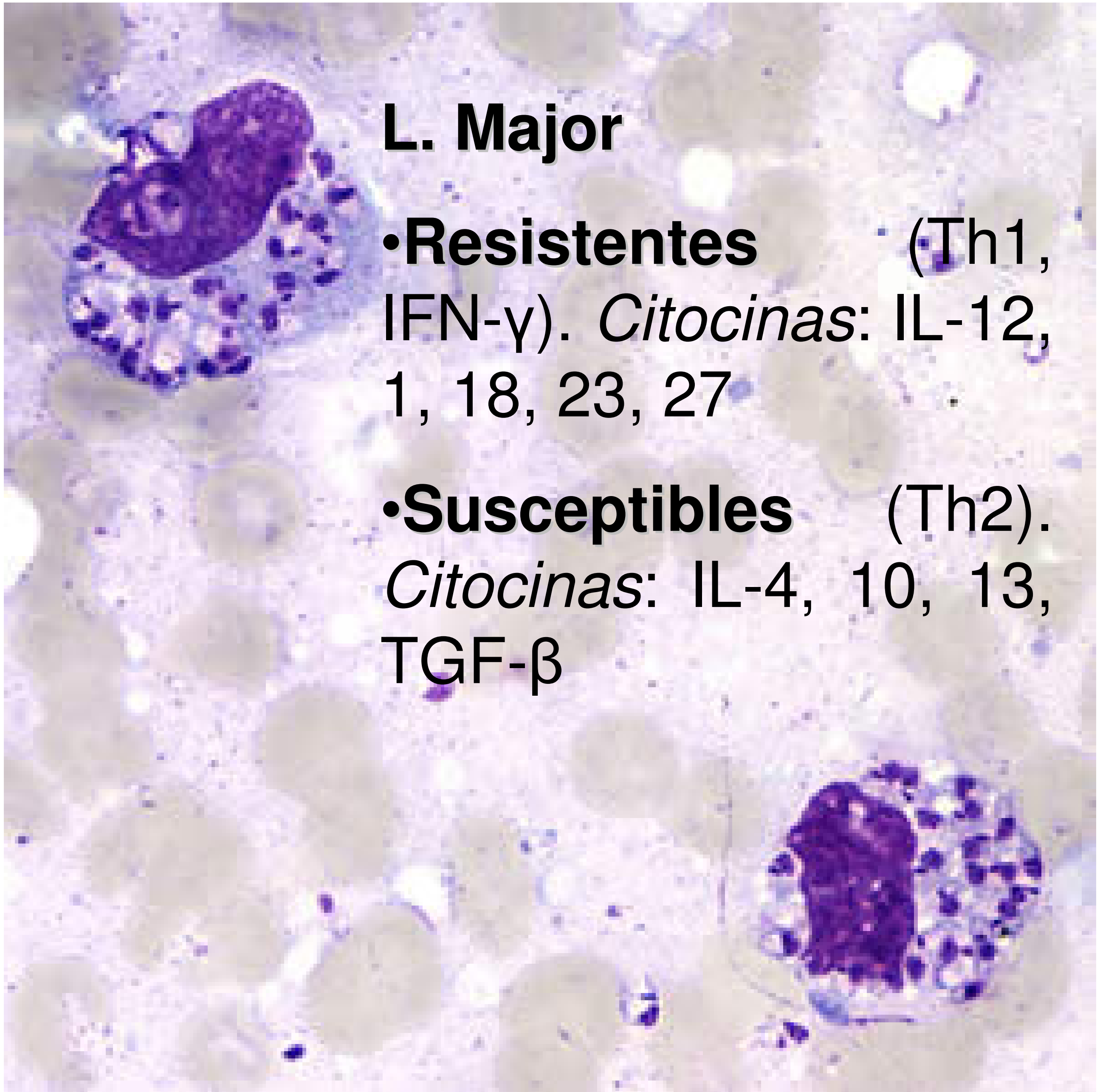
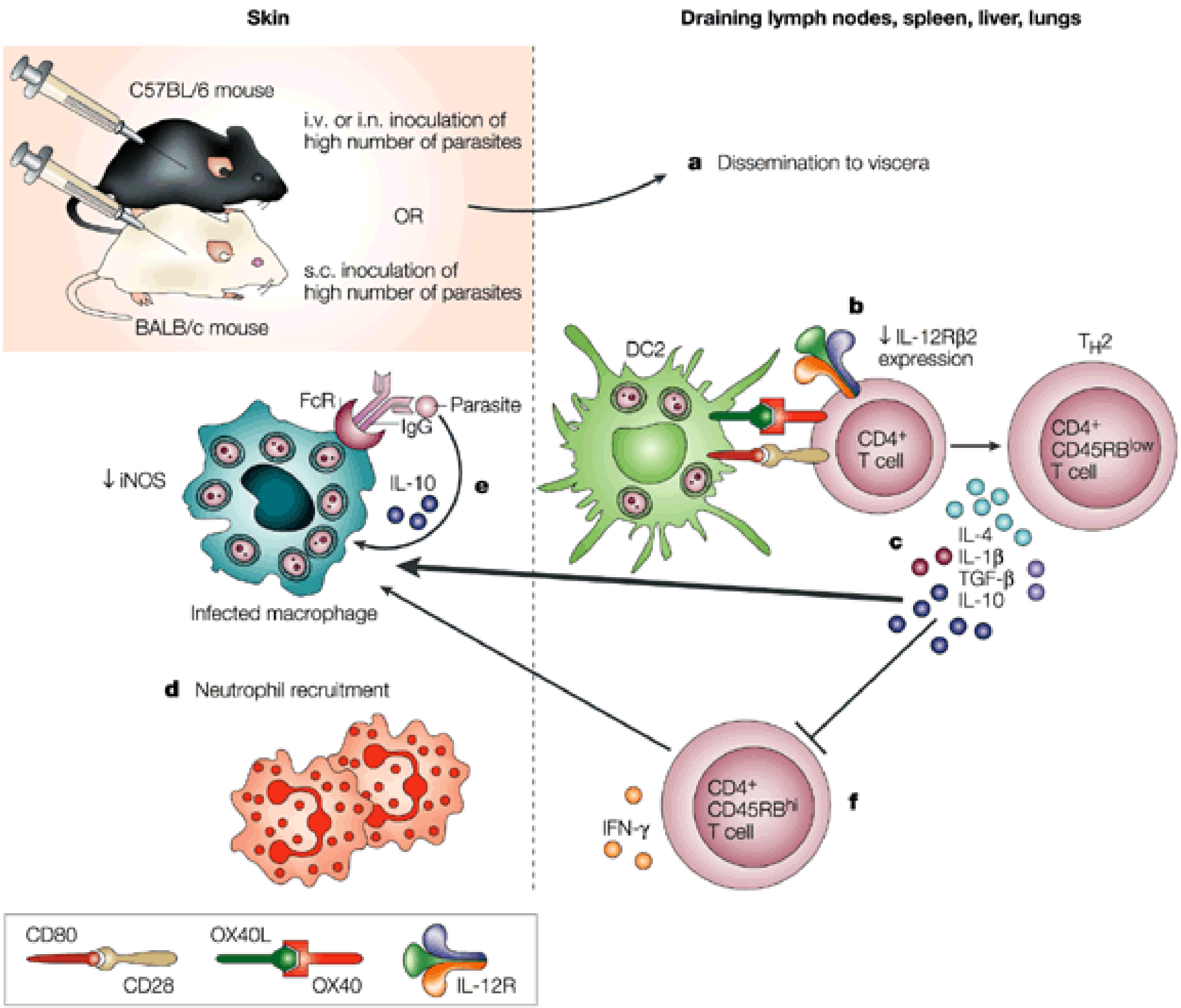


L. Major

•**Resistentes** (Th1, IFN-γ). *Citocinas*: IL-12, 1, 18, 23, 27

•**Susceptibles** (Th2). *Citocinas*: IL-4, 10, 13, TGF-β



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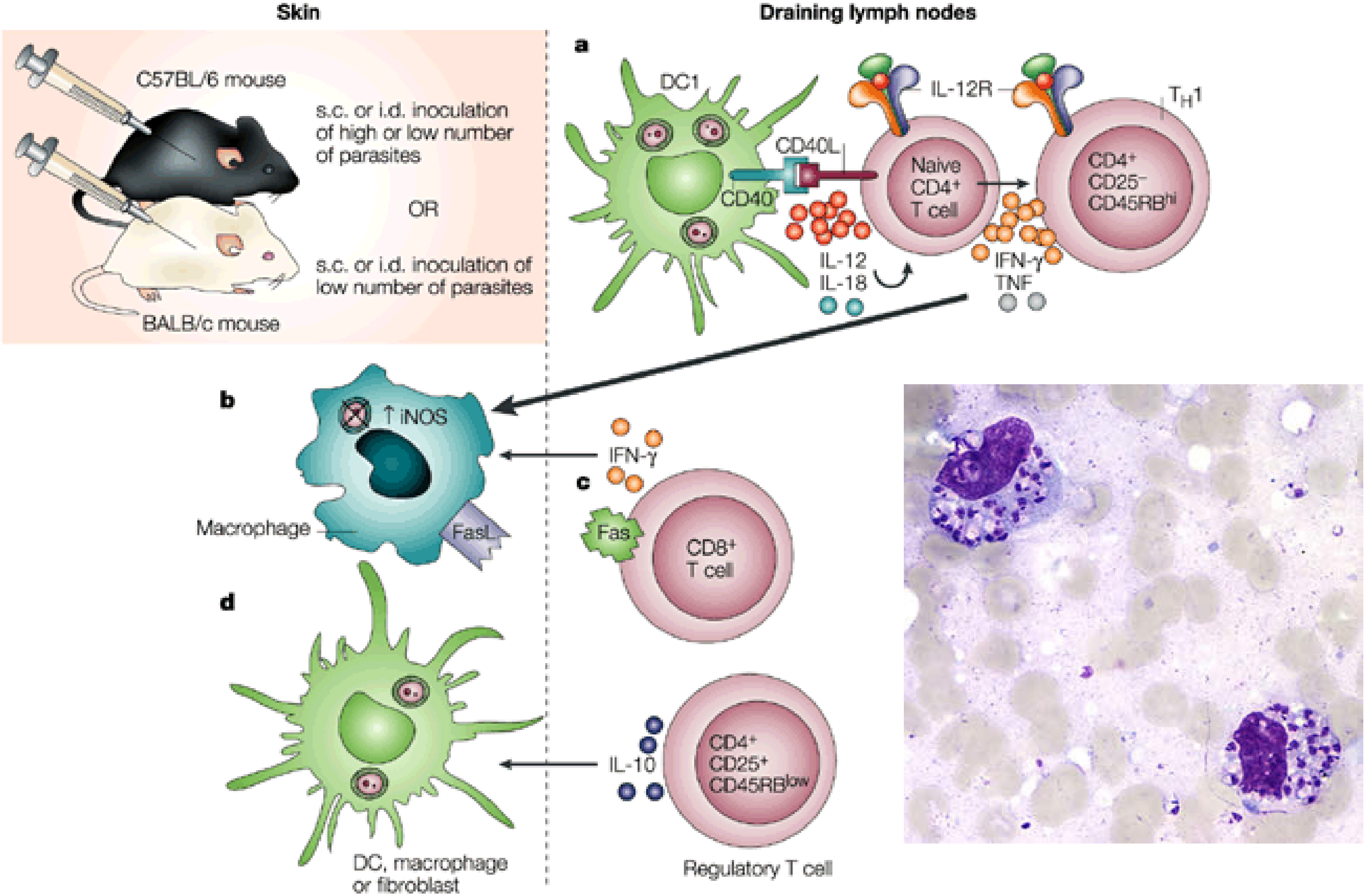

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INMUNIDAD ADAPTATIVA

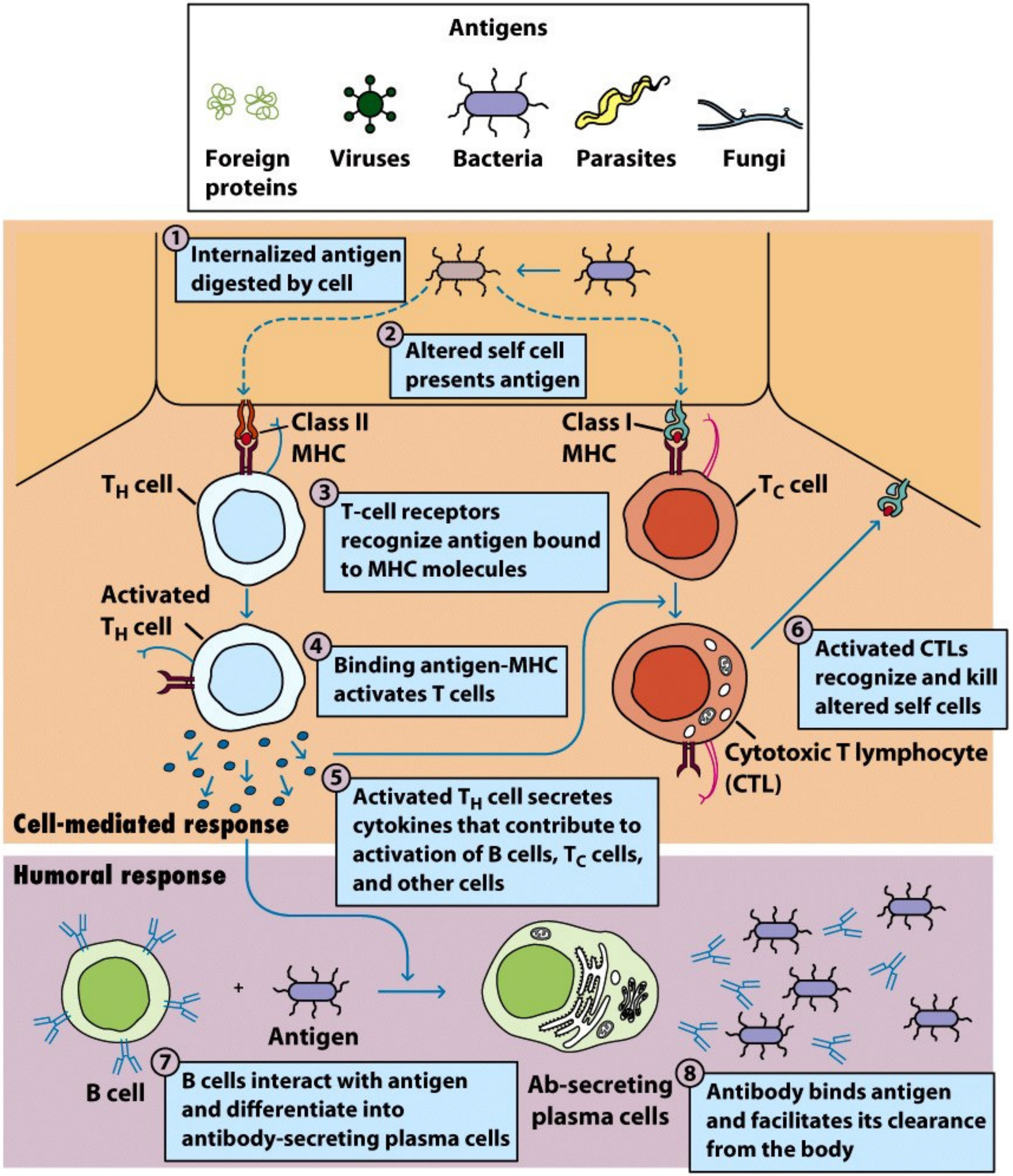

Figure 1-10

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PARÁSITOS INTRACELULARES

- **IFN-γ** (Leishmania, T. cruzi y T. gondii). iNOS → IRN, IRO, ↓ disponibilidad de nutrientes.

- **LT CD8$^+$:** T. gondii, T. cruzi que parasitan células no fagocíticas que expresan MHC I. L. major en Mo. IFN-γ

- **Etapas extracelulares breves:** Ac → Favorecen fagocitosis e impiden invasión de nuevas células.

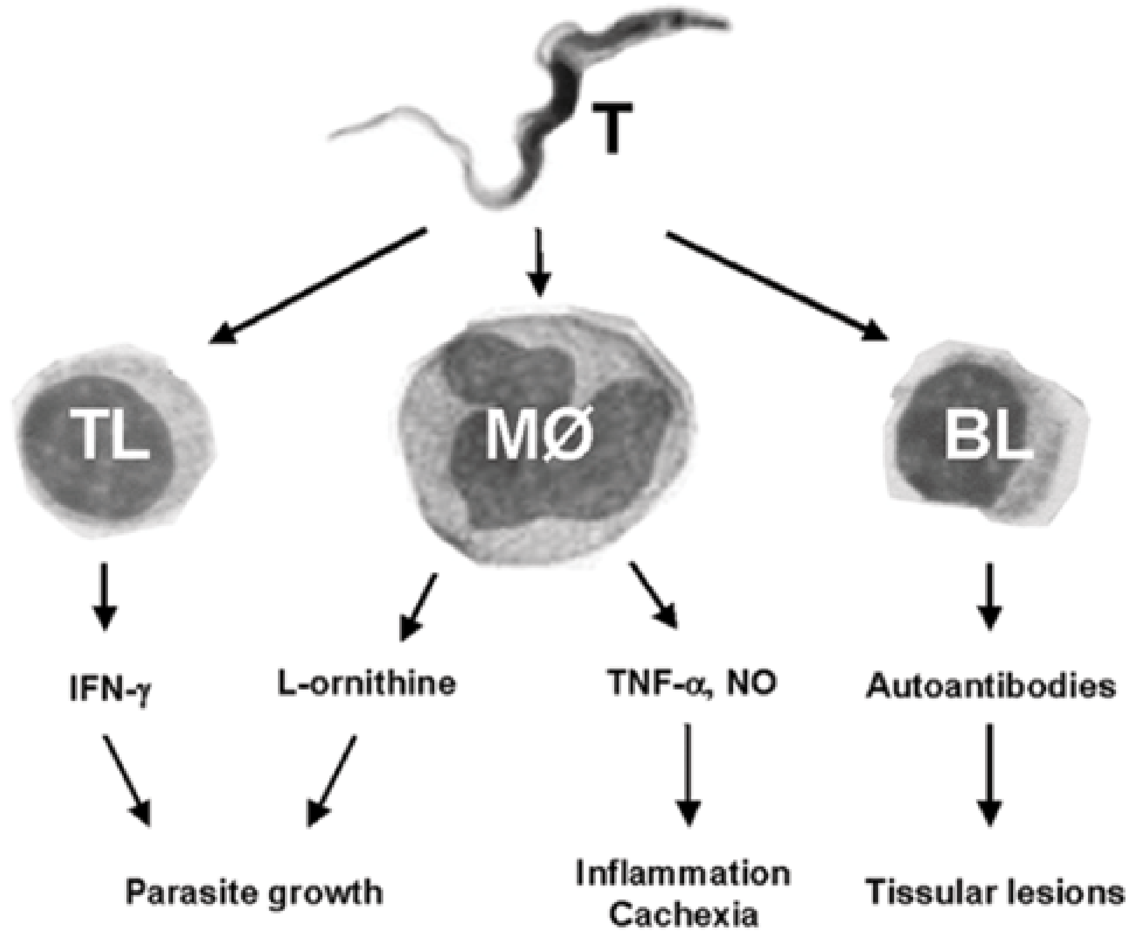


Fig. 2 – Trypanosomes induce secretion of various components from immune cells. Besides their trypanocidal effects, these molecules are also involved in deleterious mechanisms for host tissues and/or favour parasite growth. (T: trypanosome; Mø: macrophage; TL: T lymphocyte; BL: B lymphocyte)

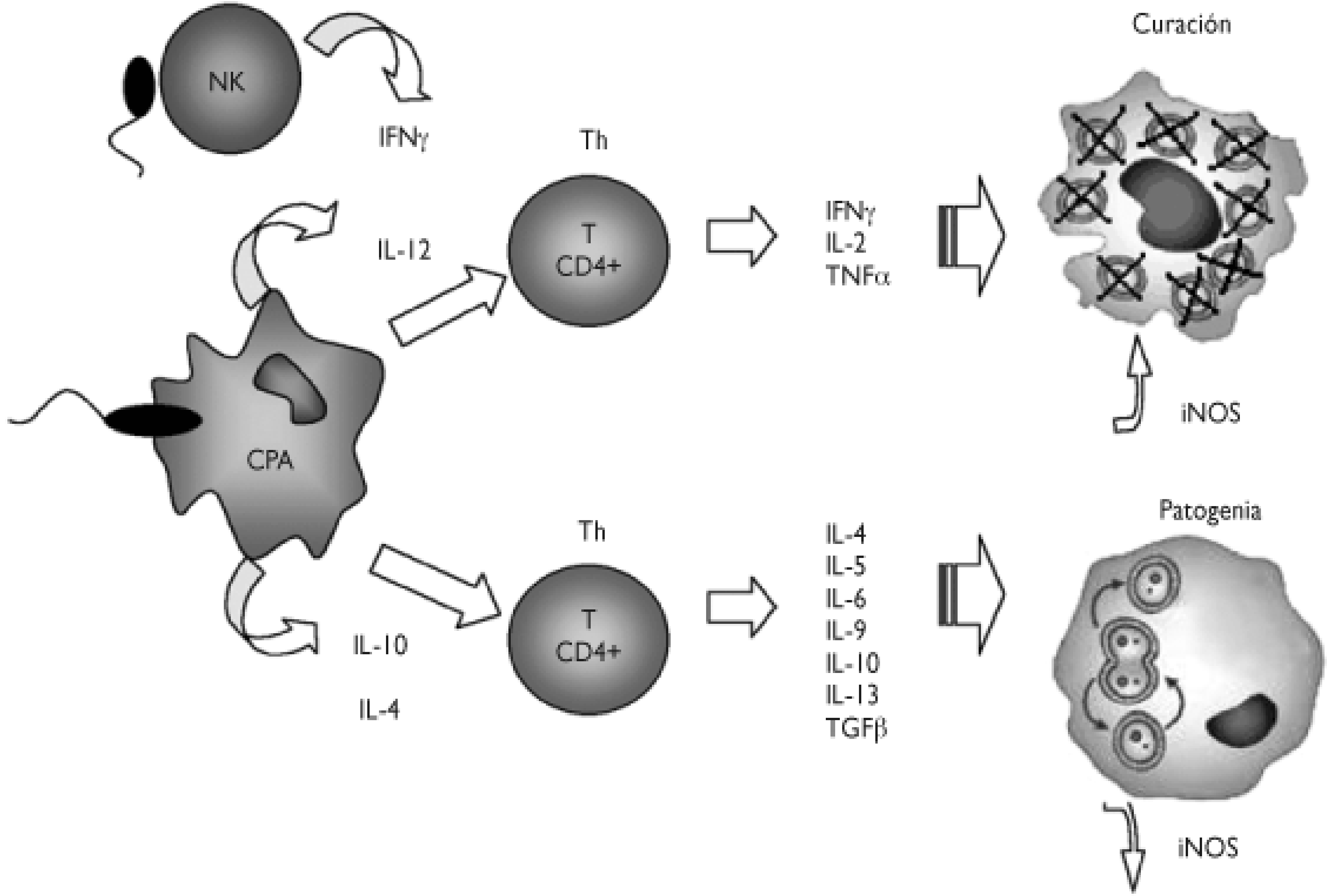
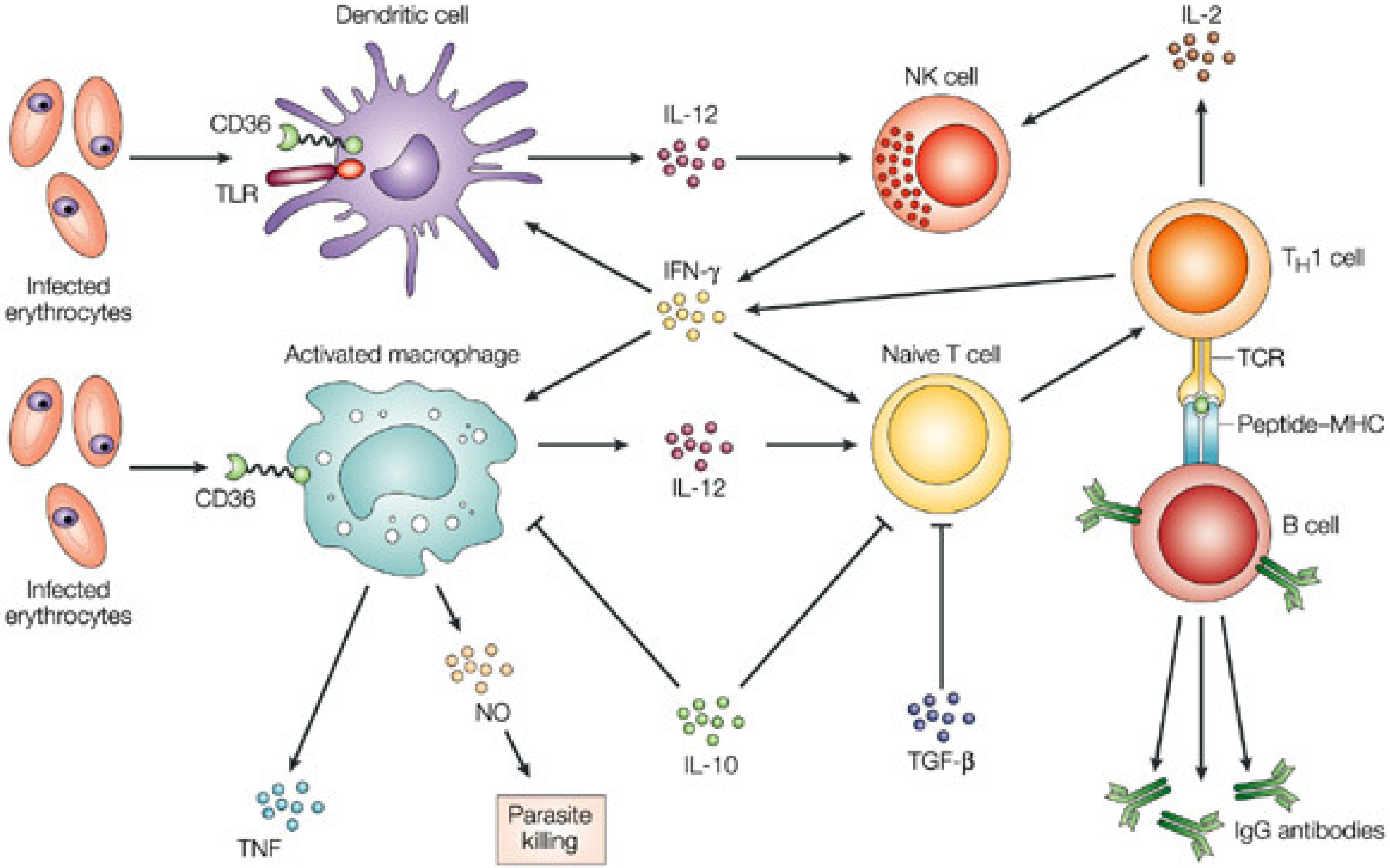
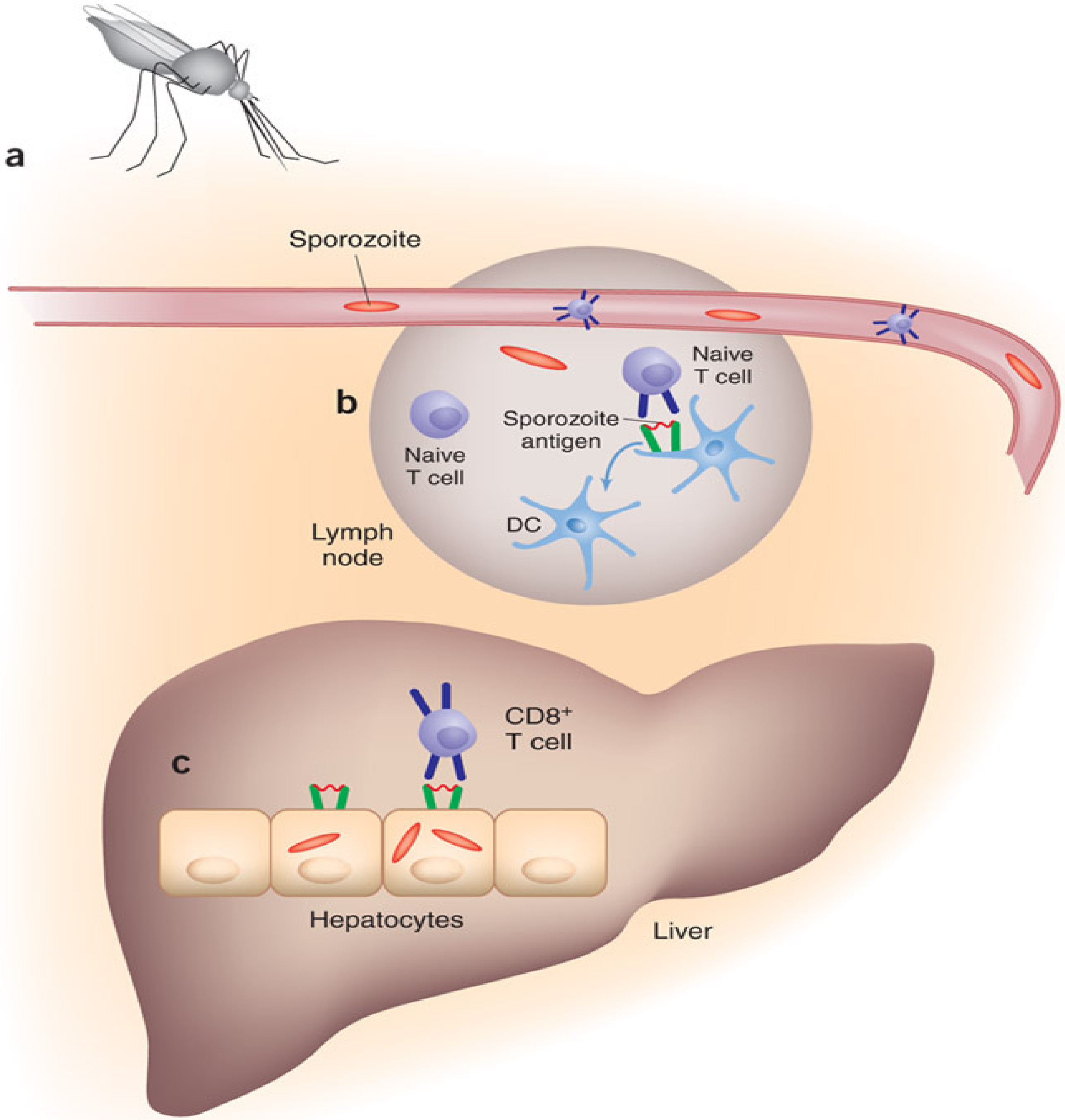
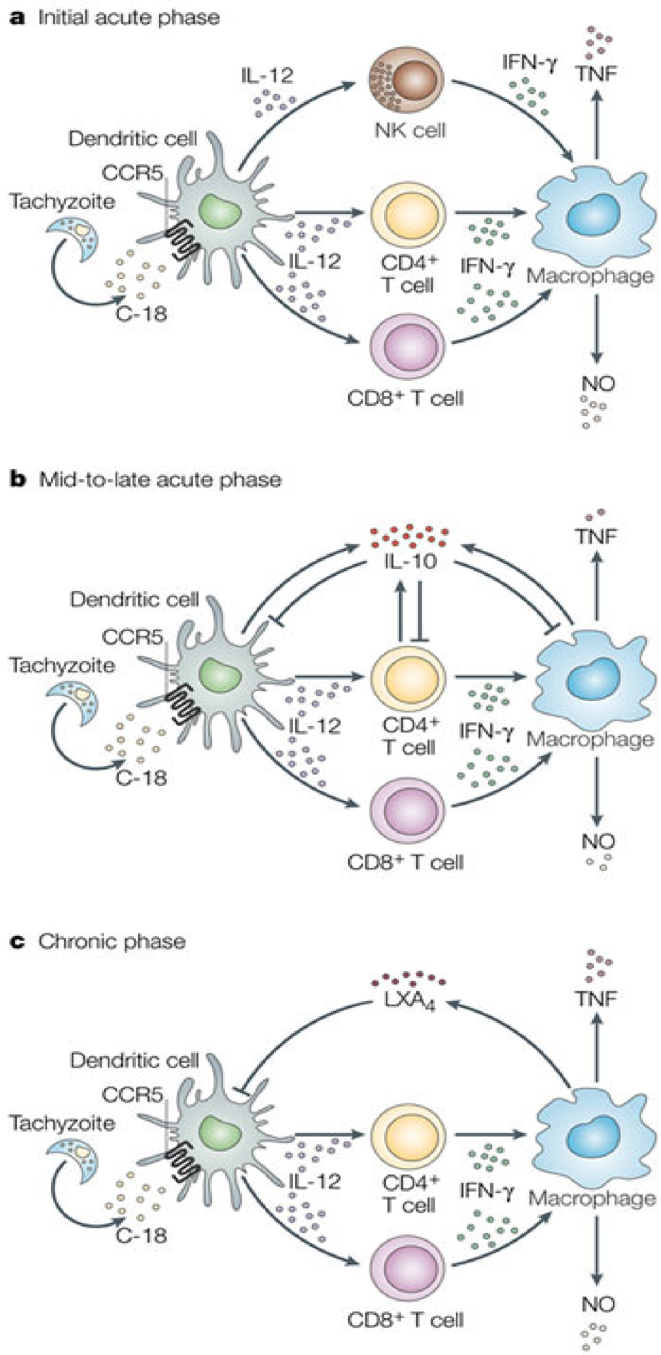


Figura 1. Reacción inmunitaria a *Leishmania*. El modelo murino de la infección señala que la susceptibilidad y resistencia al patógeno dependen del patrón de citocinas expresado por los linfocitos T


Dendritic cell
CD36
TLR
Infected erythrocytes
IL-12
NK cell
IL-2
IFN-γ
TH1 cell
TCR
Peptide–MHC
Activated macrophage
CD36
Infected erythrocytes
IL-12
Naive T cell
B cell
NO
Parasite killing
TNF
IL-10
TGF-β
IgG antibodies


a
Sporozoite
b
Naive
T cell
Sporozoite
antigen
Naive
T cell
DC
Lymph
node
CD8+
T cell
c
Hepatocytes
Liver



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PARÁSITOS EXTRACELULARES

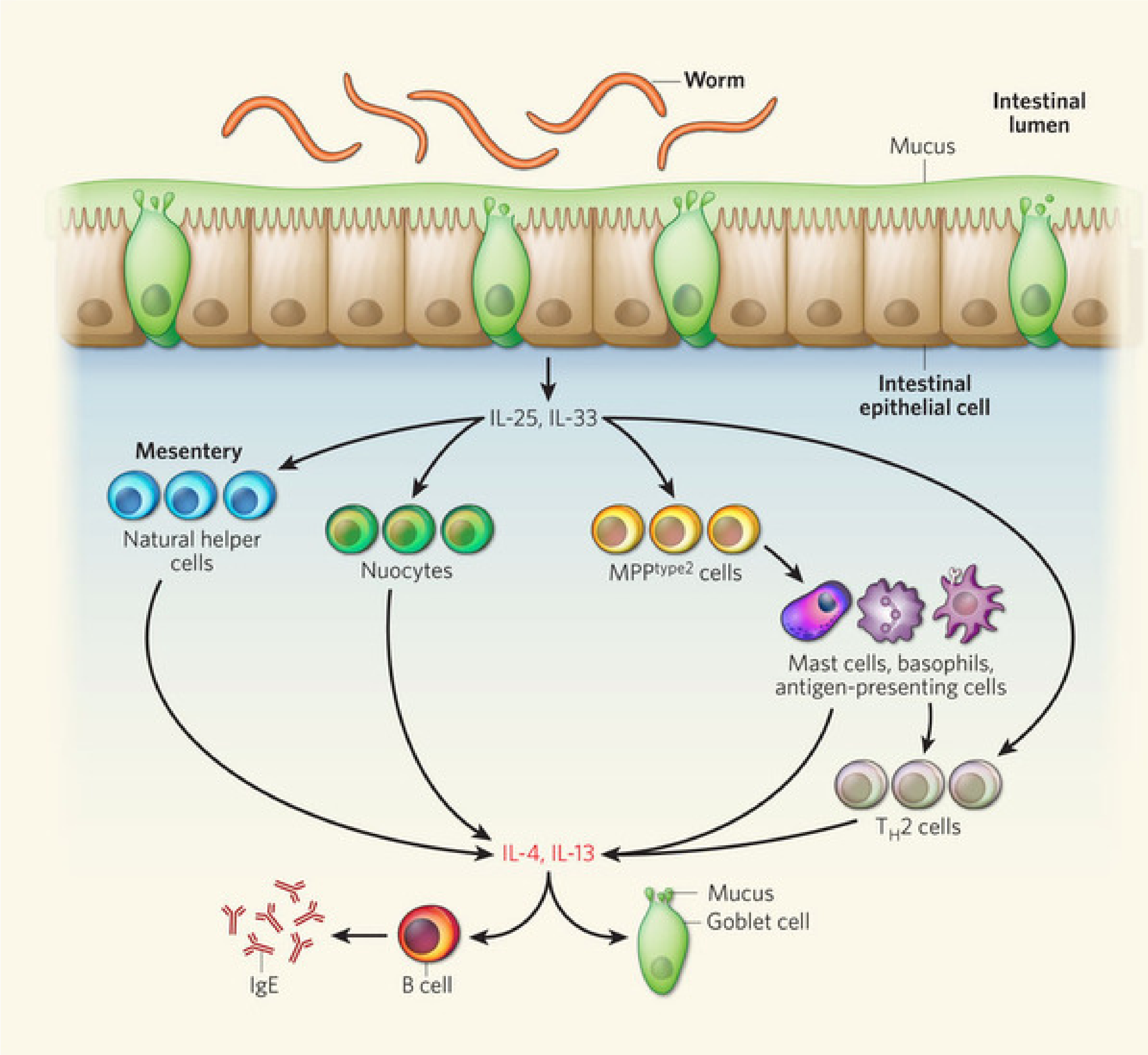
- Muerte directa por mediadores tóxicos
- Alteraciones en la migración parasitaria
- Expulsión de los tejidos
- Inhibición de la producción de huevos

- Th2 (Nematodos Intestinales) → Resistencia = IgE, IgG1, Eosinofilia, Mastocitosis

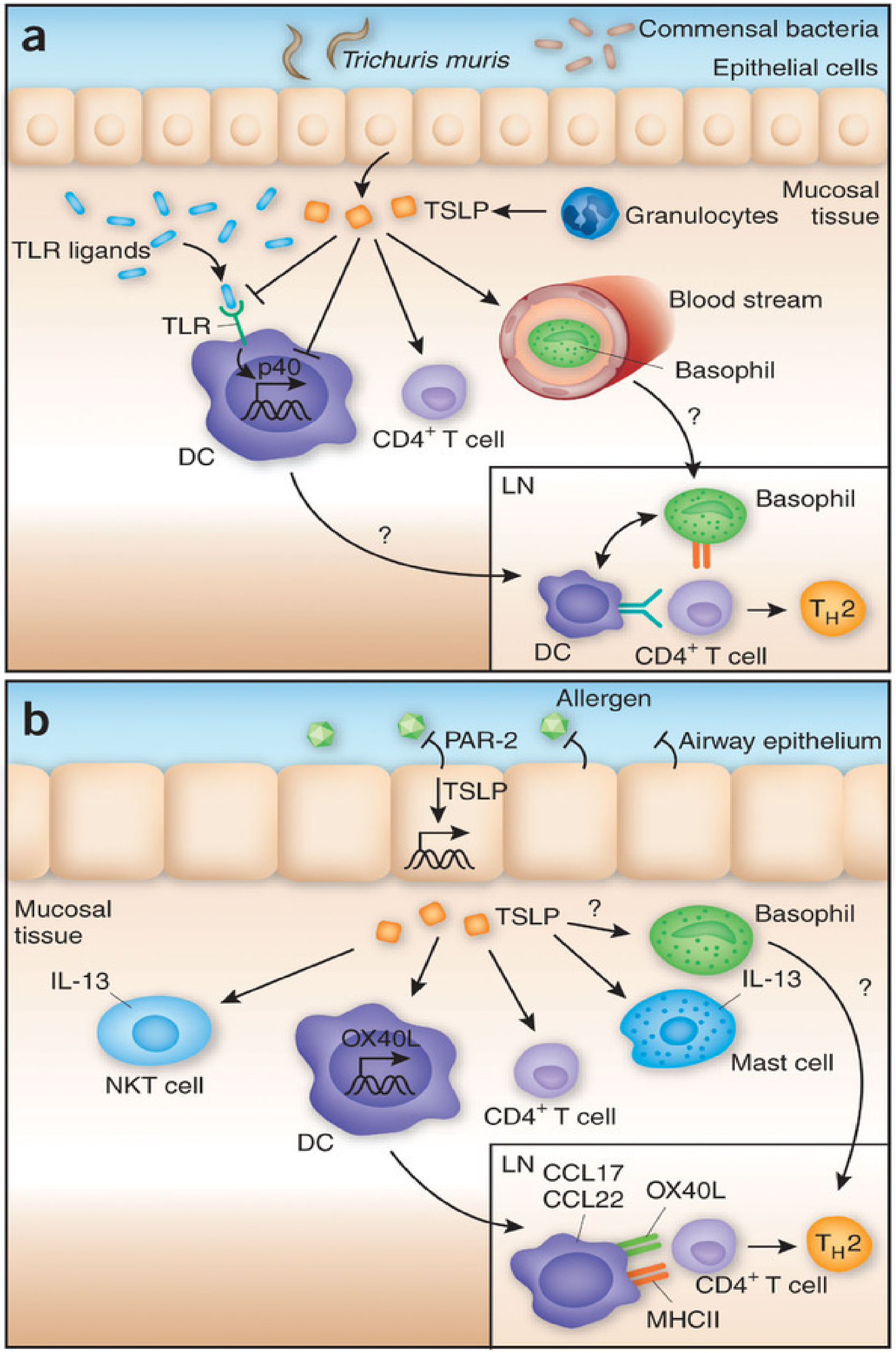
- IL-4 (13, 9, 5, 10) → Expulsión de nematodos intestinales

- Ac anti-IL-4 → Th1 → Susceptibilidad = IFN-γ, IgG2a

- Ac anti-IL-12 → Th2



Worm
Intestinal lumen
Mucus
Intestinal epithelial cell
IL-25, IL-33
Mesentery
Natural helper cells
Nuocytes
MPPtype2 cells
Mast cells, basophils, antigen-presenting cells
TH2 cells
IL-4, IL-13
Mucus
Goblet cell
IgE
B cell



a
Trichuris muris
Commensal bacteria
Epithelial cells
Mucosal tissue
TSLP
Granulocytes
TLR ligands
TLR
p40
DC
CD4+ T cell
Blood stream
Basophil
?
LN
Basophil
?
DC
CD4+ T cell
TH2
b
Allergen
PAR-2
Airway epithelium
TSLP
Mucosal tissue
TSLP
?
Basophil
IL-13
IL-13
?
NKT cell
OX40L
DC
CD4+ T cell
Mast cell
LN
CCL17
CCL22
OX40L
CD4+ T cell
TH2
MHCII

ANTICUERPOS

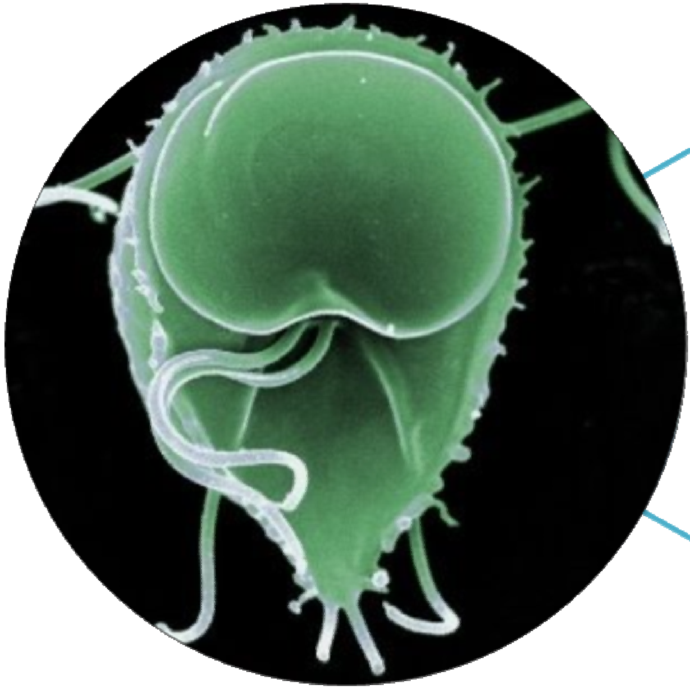
Rol frente a las **reinfecciones**:

- IgA en mucosas → Giardia
- IgG1 e IgE → T. spiralis
- IgE → Schistosoma

Activación de Mastocitos (RFc)

Cooperación con Eo y Mo en ADCC

MECANISMOS DE EVASIÓN DE LA RESPUESTA INMUNE

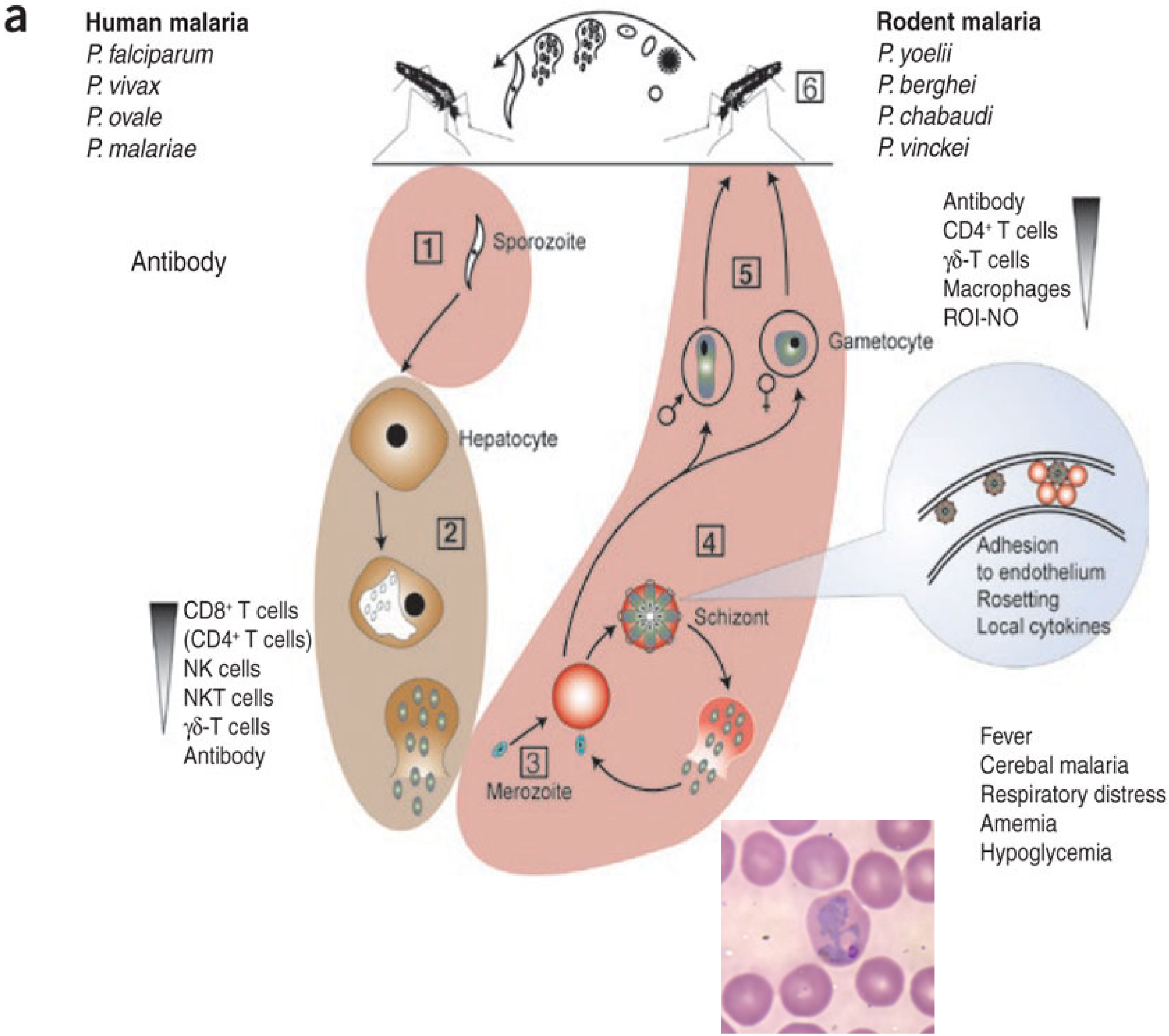


Evasión del reconocimiento específico

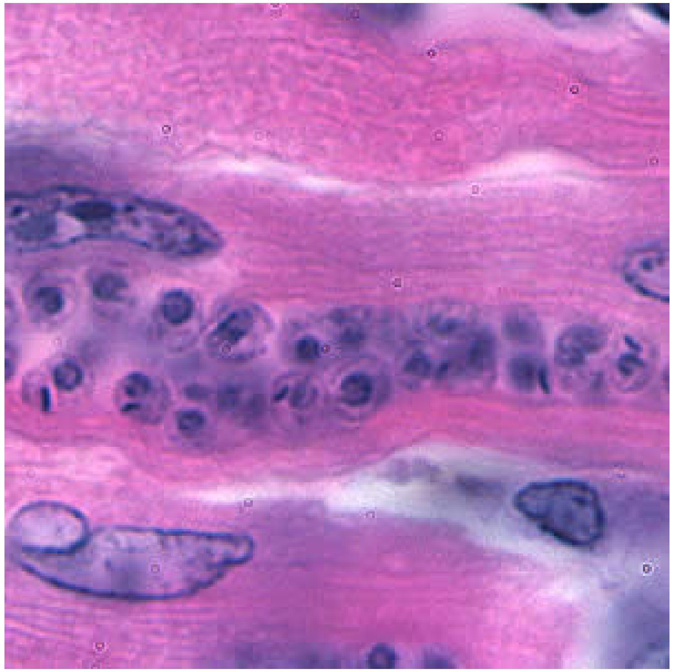
- Seclusión física
- Enmascarándose con Ag del huésped
- Liberando de su superficie, Ag que son blancos de la respuesta inmune
- Variación antigénica
- Alteración de la presentación antigénica

Supresión de la respuesta inmune del huésped

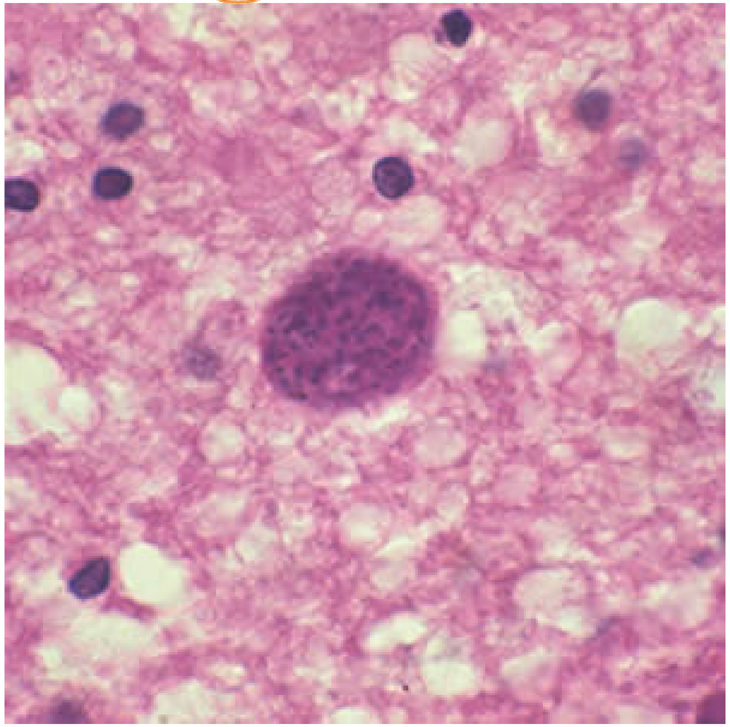
- Resistencia al C’
- Control de la disponibilidad, número y función de células efectoras


a
Human malaria
P. falciparum
P. vivax
P. ovale
P. malariae
Rodent malaria
P. yoelii
P. berghei
P. chabaudi
P. vinckei
6
1
Sporozoite
Antibody
5
Antibody
CD4⁺ T cells
γδ-T cells
Macrophages
ROI-NO
Gametocyte
♂
♀
Hepatocyte
2
4
Adhesion
to endothelium
Rosetting
Local cytokines
Schizont
CD8⁺ T cells
(CD4⁺ T cells)
NK cells
NKT cells
γδ-T cells
Antibody
3
Merozoite
Fever
Cerebal malaria
Respiratory distress
Amemia
Hypoglycemia

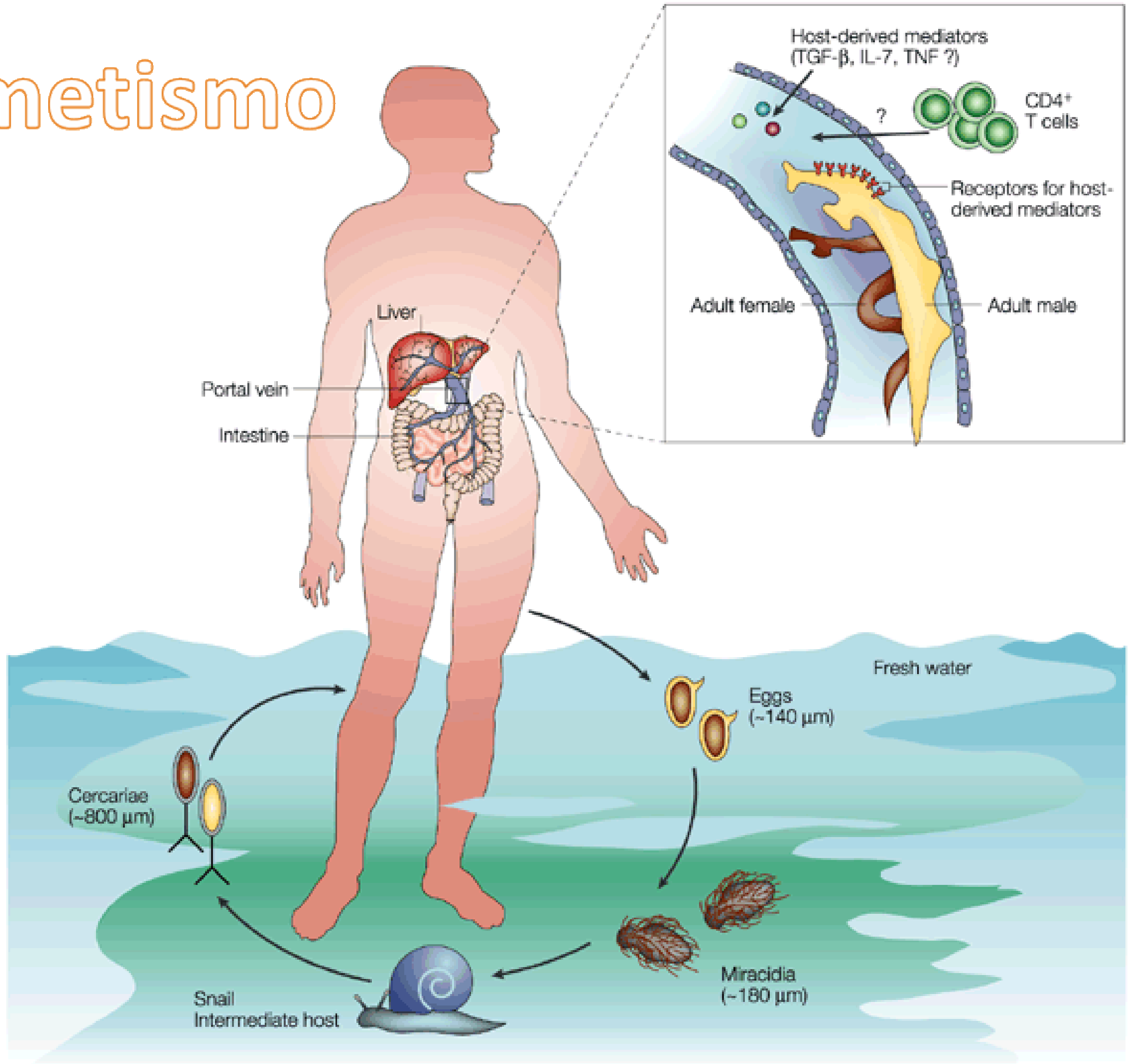
T. cruzi



T. gondii



Mimetismo



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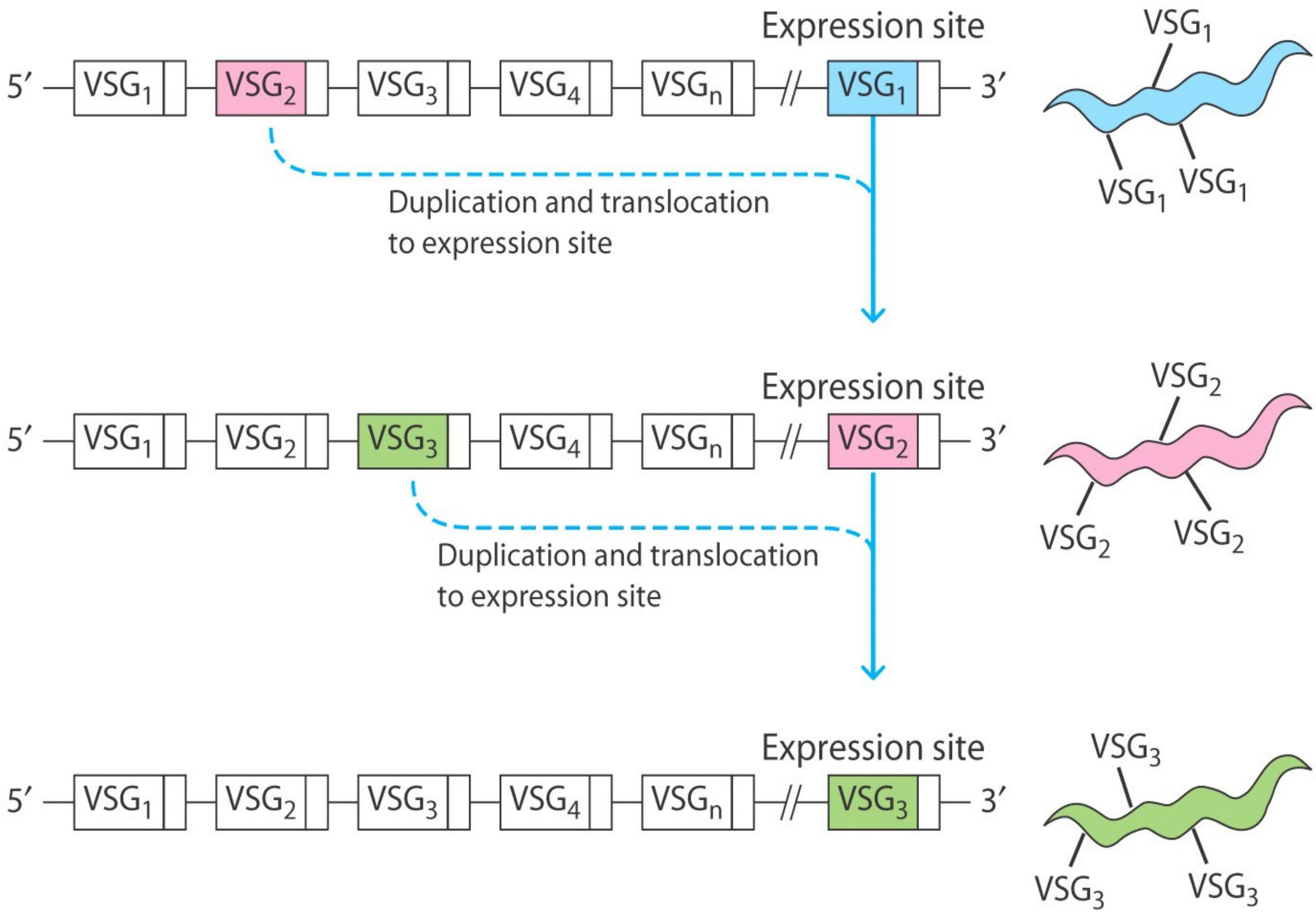
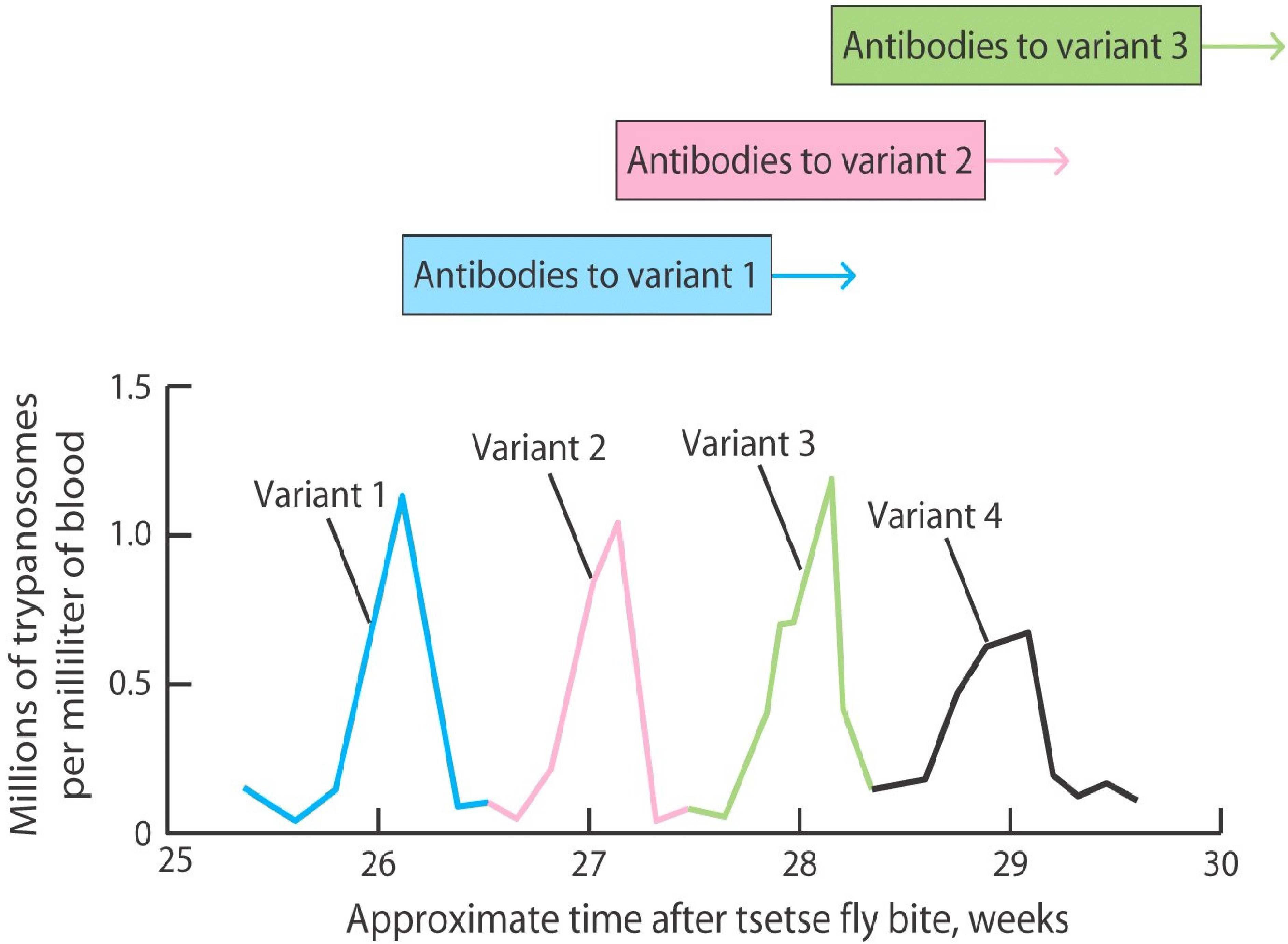
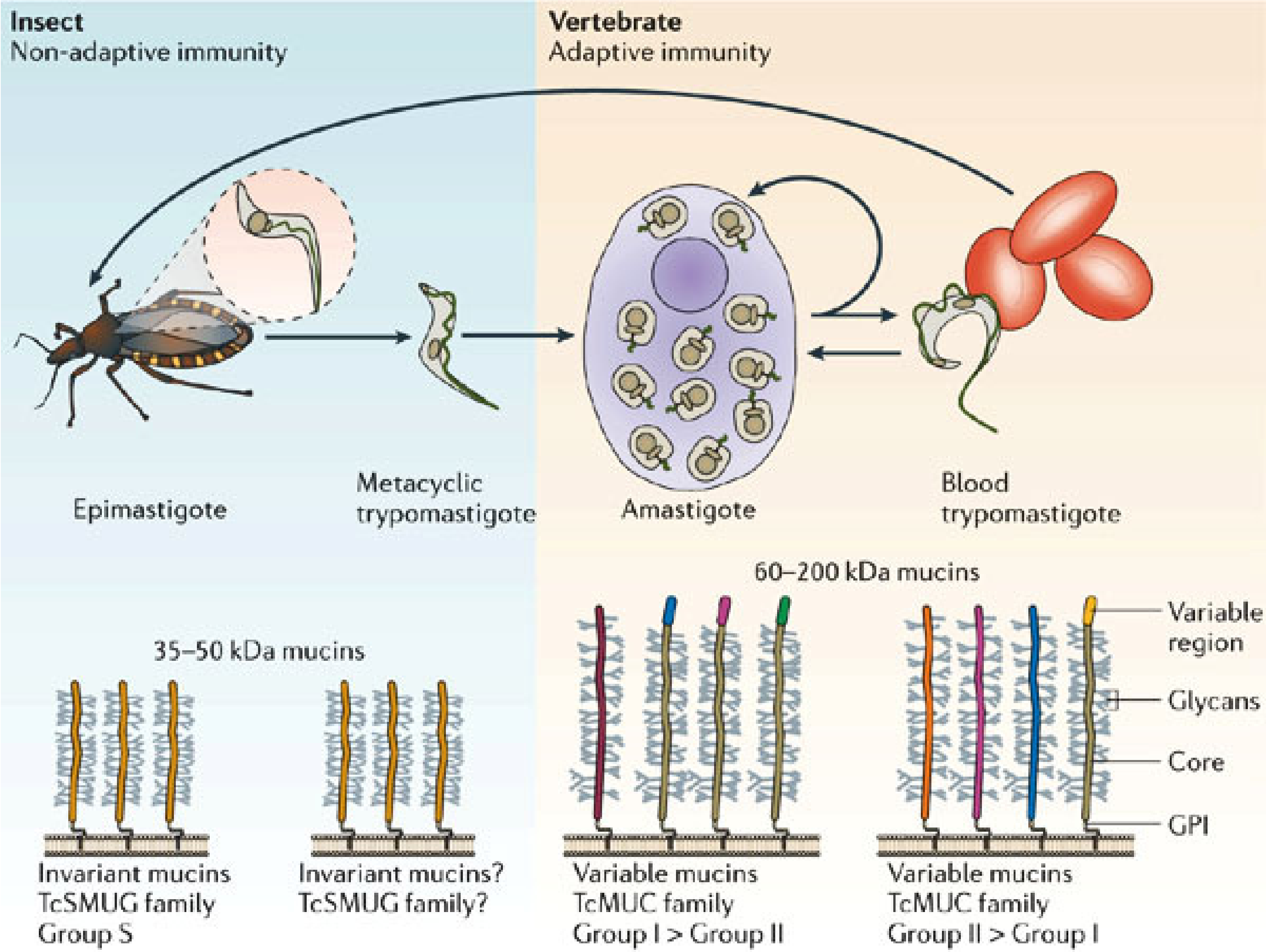
Variación antigénica





Antibodies to variant 3
Antibodies to variant 2
Antibodies to variant 1
Variant 1
Variant 2
Variant 3
Variant 4
1.5
1.0
0.5
0
25
26
27
28
29
30
Millions of trypanosomes per milliliter of blood
Approximate time after tsetse fly bite, weeks



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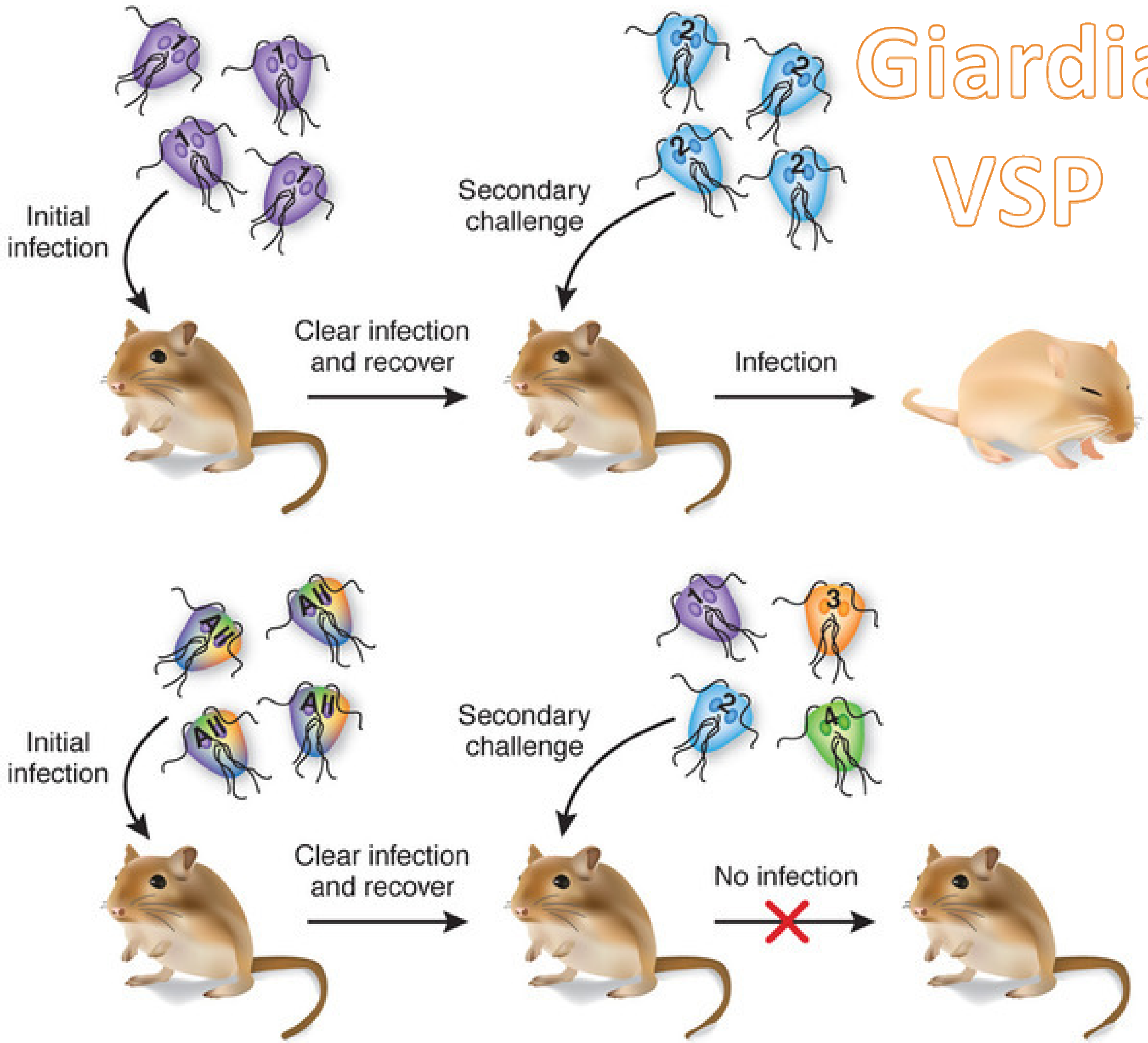
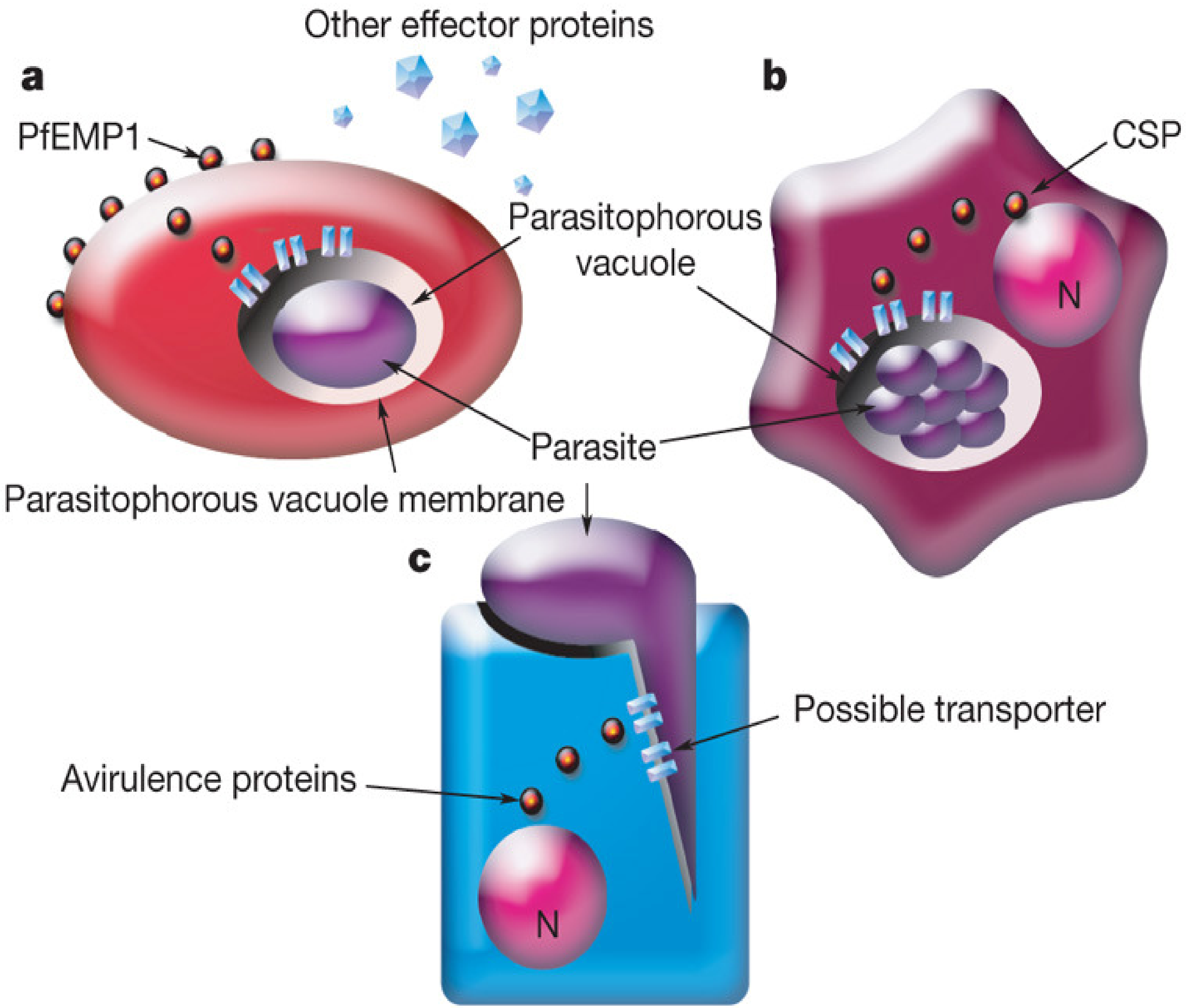
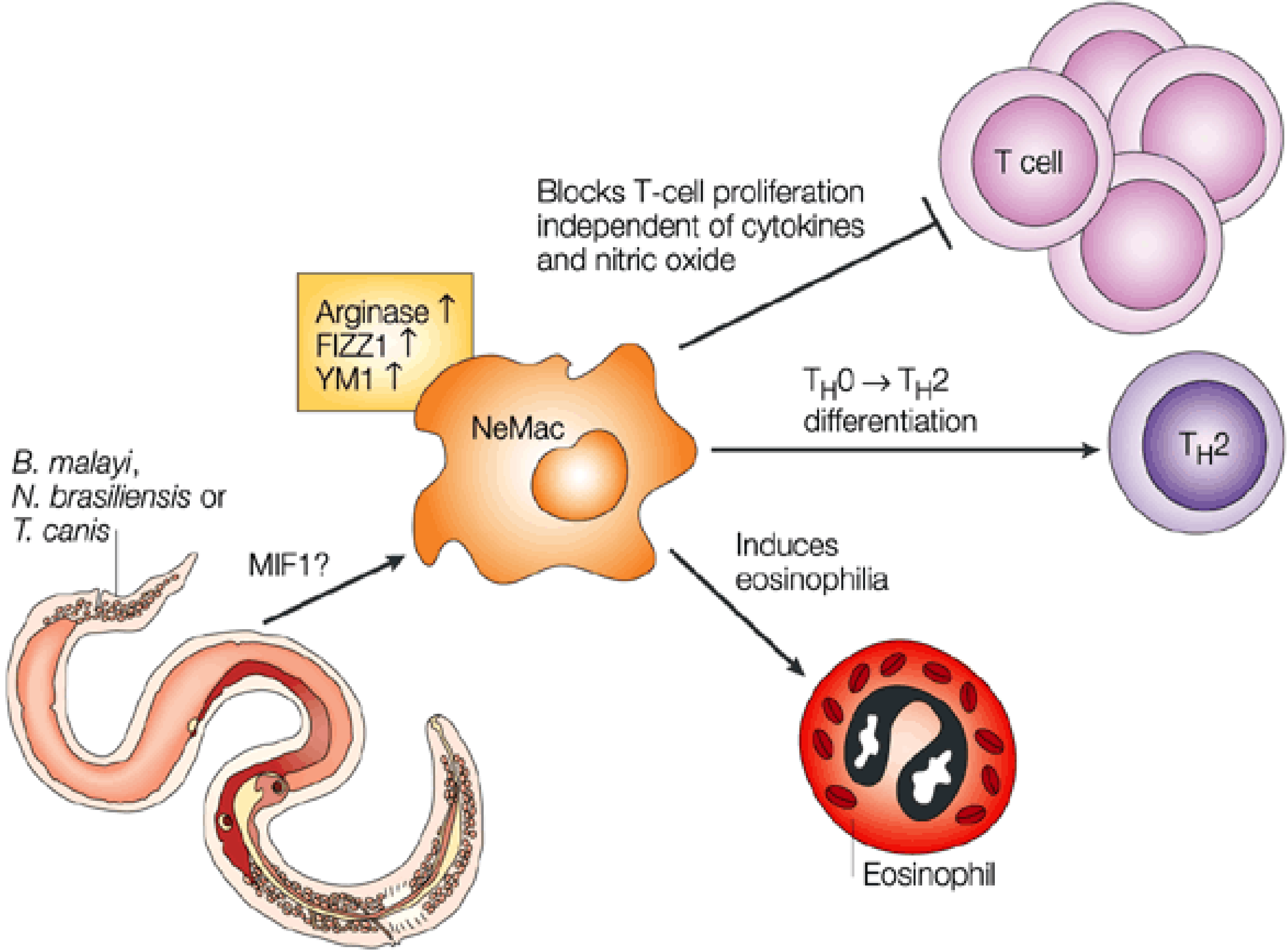
Giardia VSP


Initial infection
Secondary challenge
Clear infection and recover
Infection
Initial infection
Secondary challenge
Clear infection and recover
No infection

Plasmodium



Other effector proteins
a
PfEMP1
Parasitophorous
vacuole
Parasite
Parasitophorous vacuole membrane
b
CSP
N
c
Possible transporter
Avirulence proteins
N



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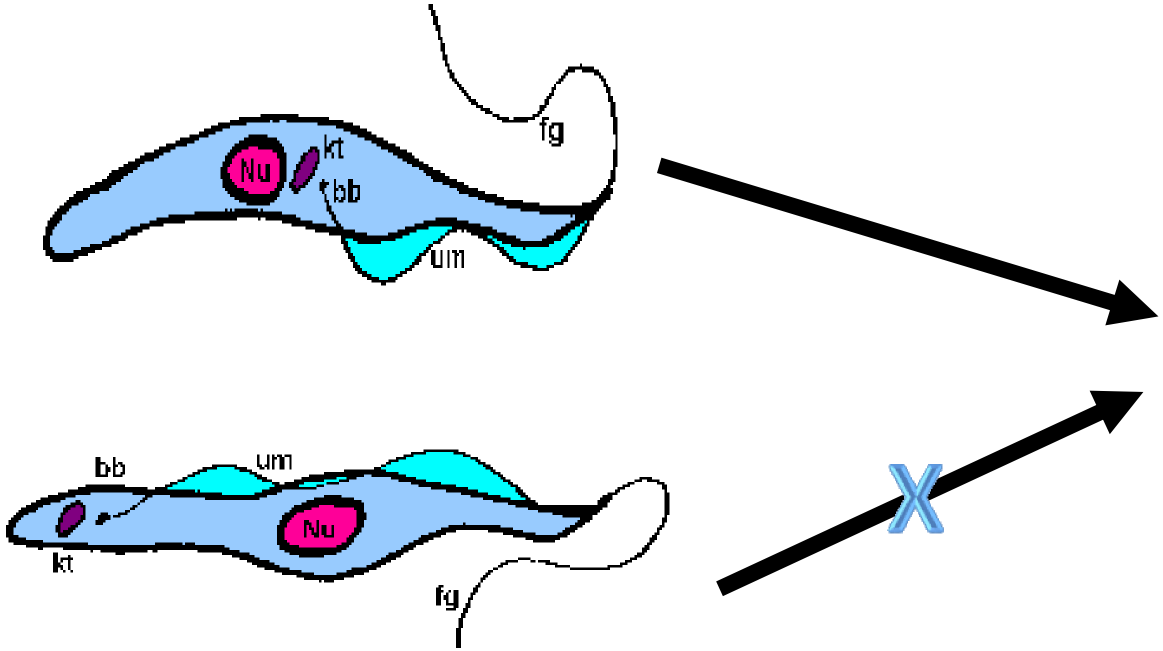
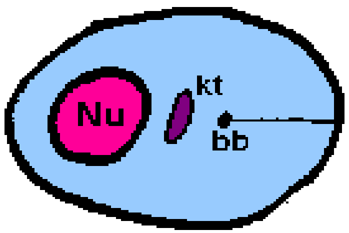
Resistencia al ataque del complemento

- Leishmania → gp63 (C3b → C3bi)



Vía alterna

gp160 = DAF



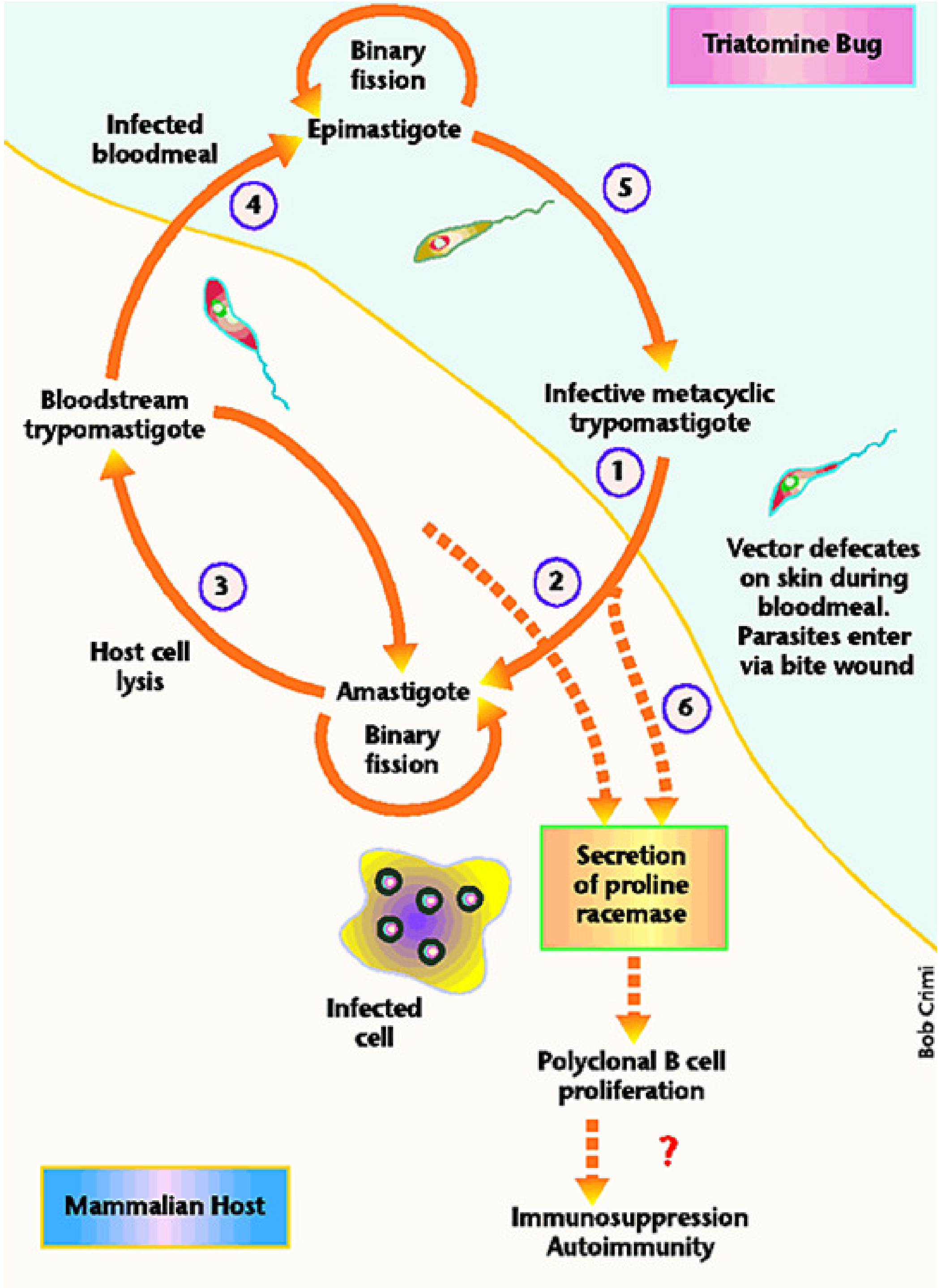
Expresan un proteína homóloga al componente C9 del C’ que le permite romper la membrana del fagosoma y

En T. cruzi…

- Luego de la activación de T $CD4^+$, una fracción de éstas sufre AICD

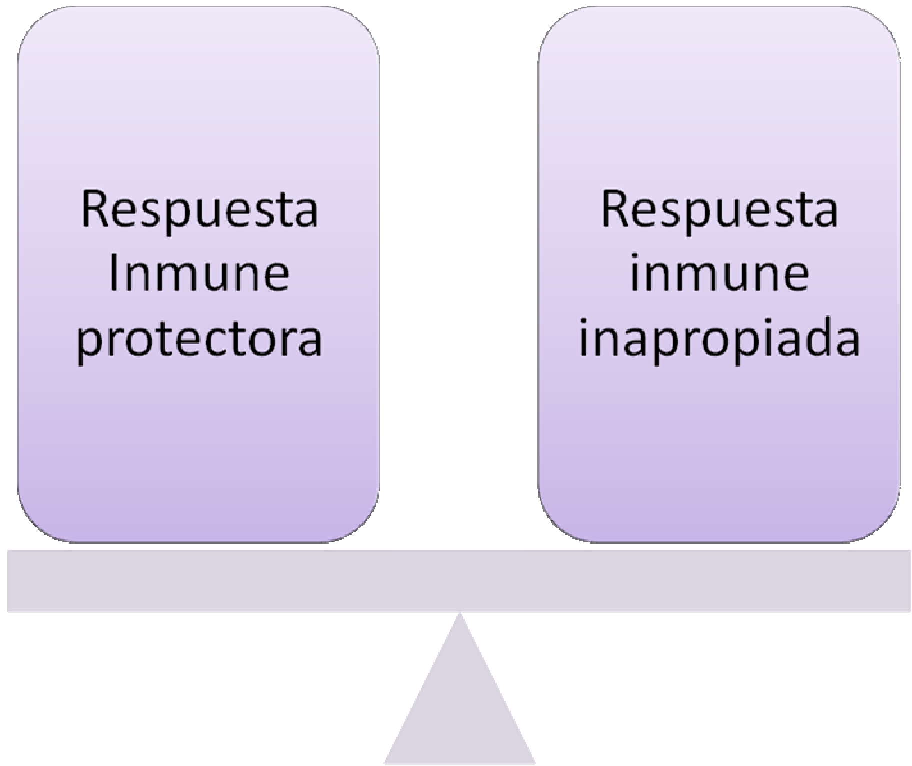
- Favorece expresión de Fas y FasL en LT y B

- Enzima transialidasa puede inducir apoptosis en timocitos y linfocitos en bazo y ganglios periféricos

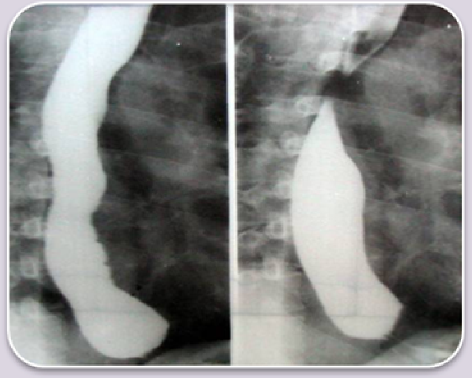


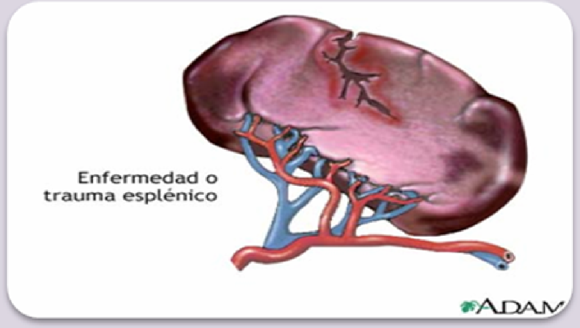
- Alta frecuencia de LT $CD4^{+}CD25^{+}$
- Activación de linfocitos en forma inespecífica → Activación policlonal

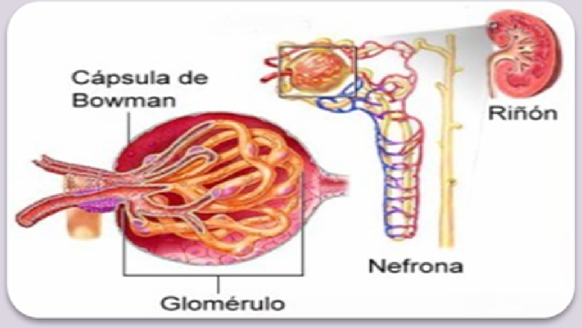
INMUNOPATOLOGÍA



INMUNOPATOLOGÍA







T. cruzi

S. mansoni

P. malarie