

Biología celular de la inmunidad - II



VACCINATION.
DR. JENNER PERFORMING HIS FIRST
VACCINATION (W. JAMES SURIER,
A BOY OF EIGHT, MAY 14, 1774)



FACULTAD DE
CIENCIAS

UDELAR fcien.edu.uy

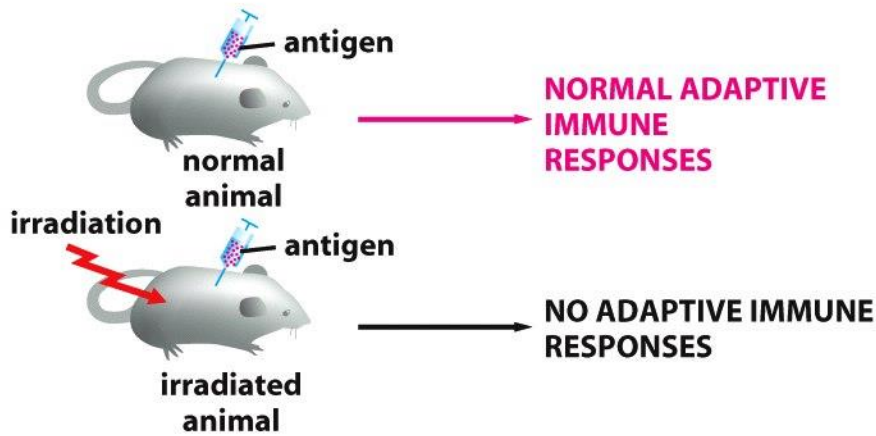
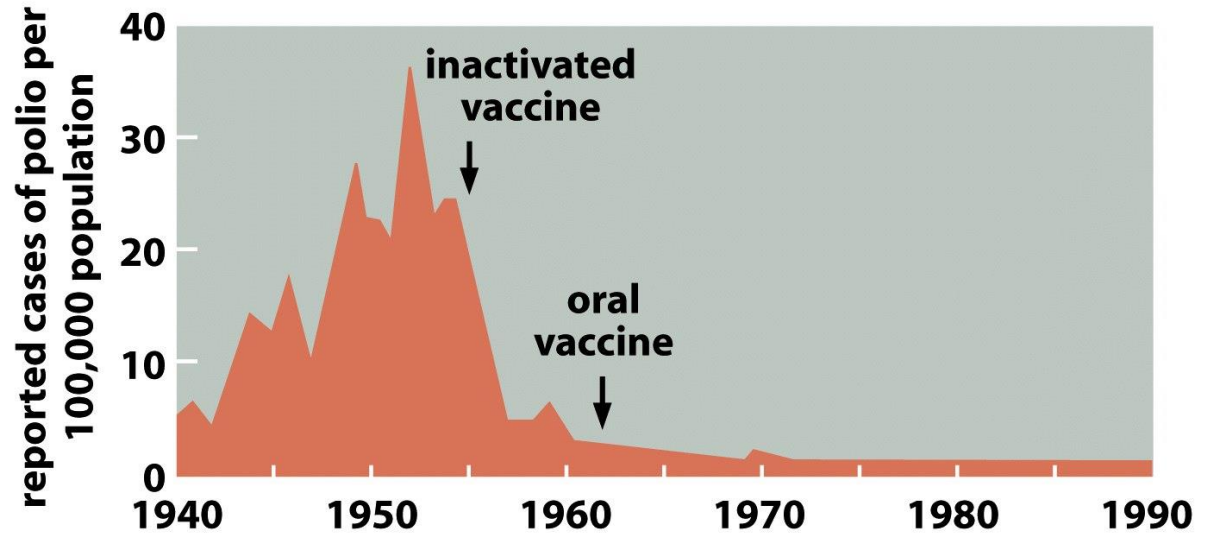
Flavio Zolessi

fzolessi@fcien.edu.uy

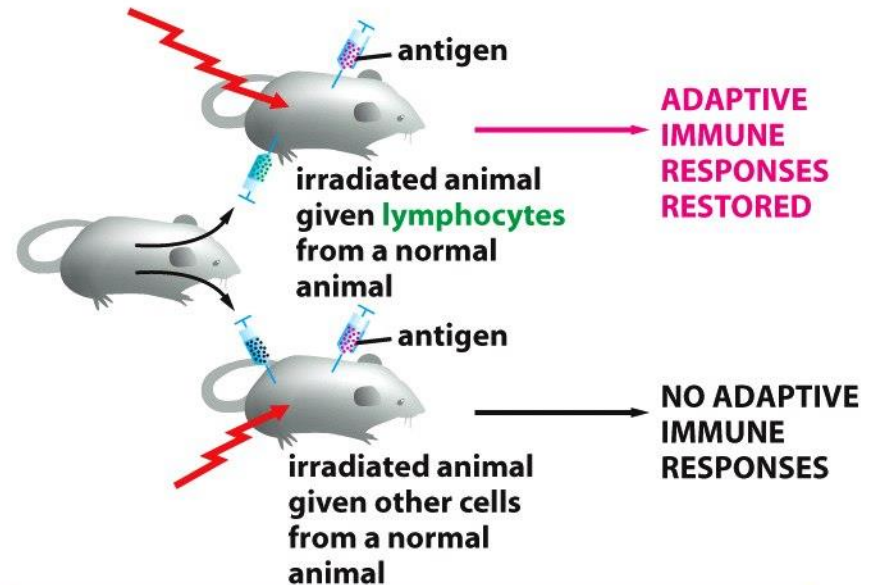


UNIVERSIDAD DE LA REPÚBLICA
URUGUAY

Inmunidad adaptativa

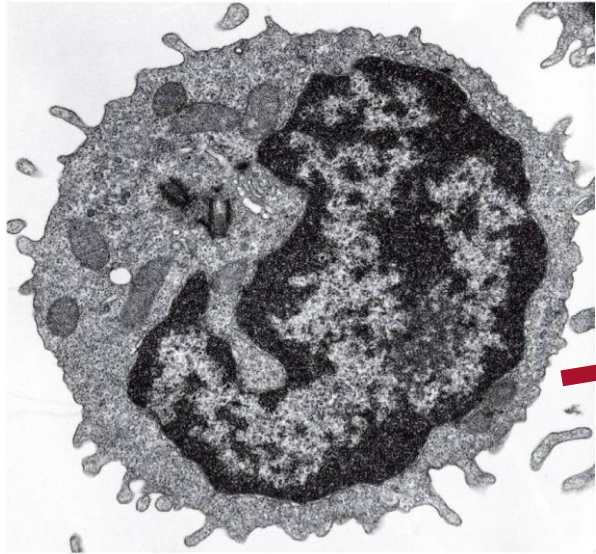


CONTROL

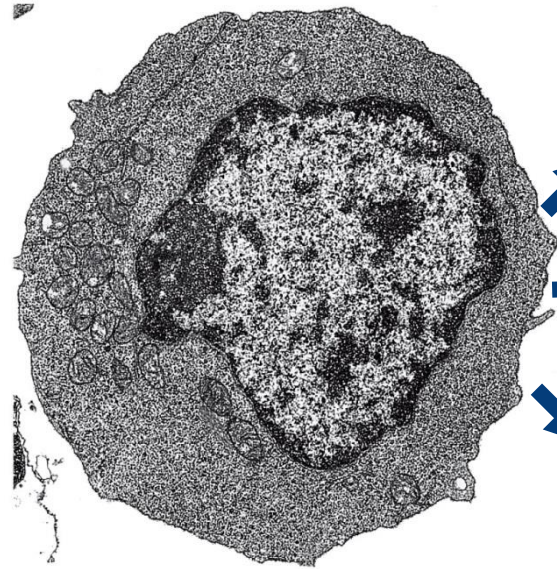
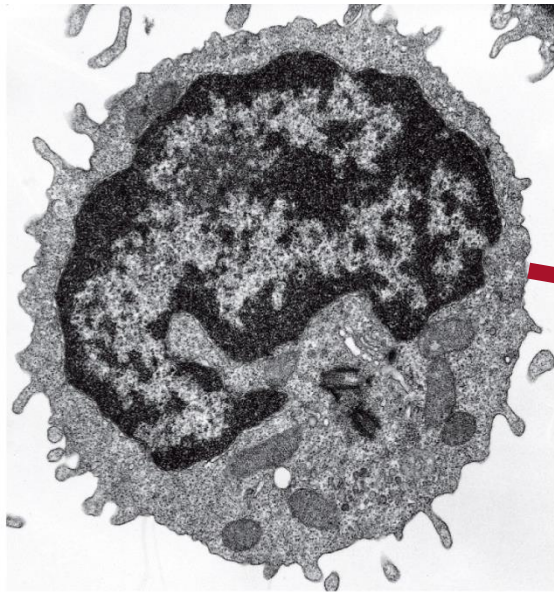


EXPERIMENT

Inmunidad adaptativa: Linfocitos



effector B cell (plasma cell) ┌
└ 1 μm

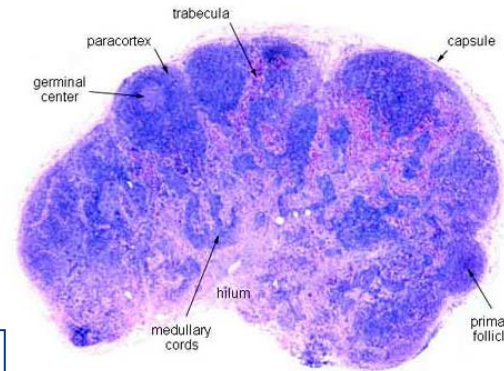
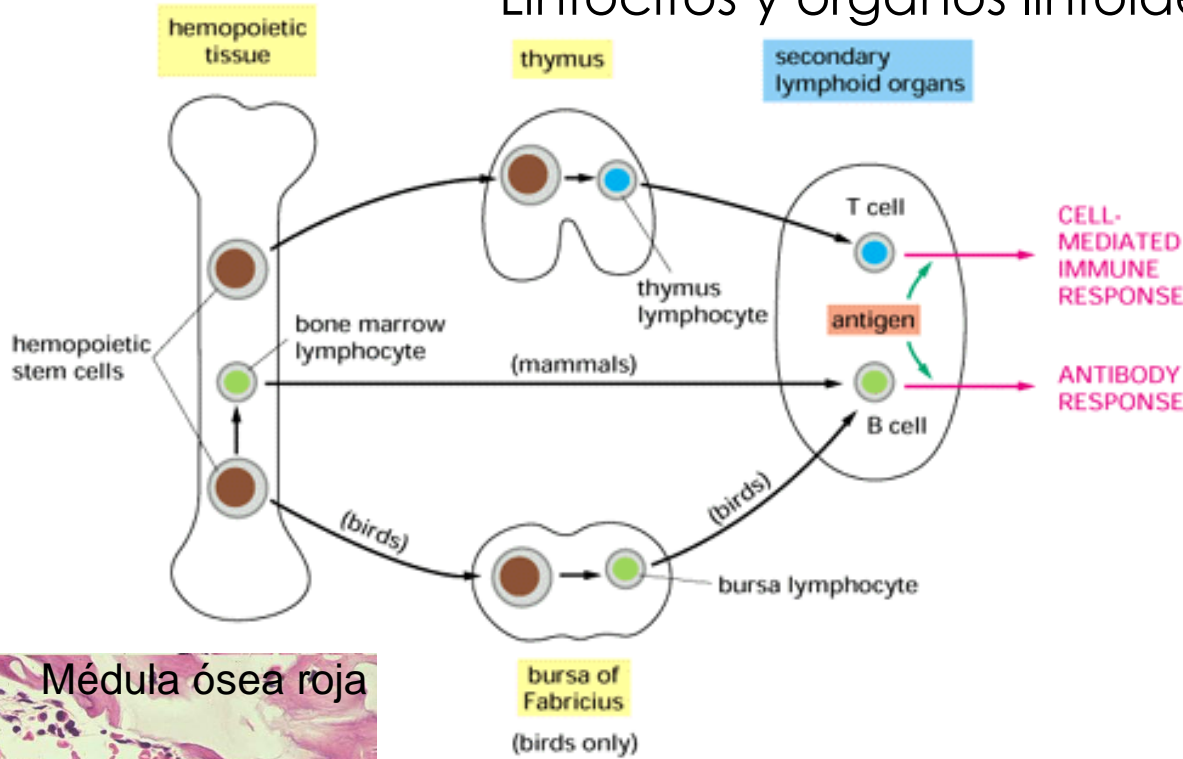


resting T or B cell ┌
└ 1 μm

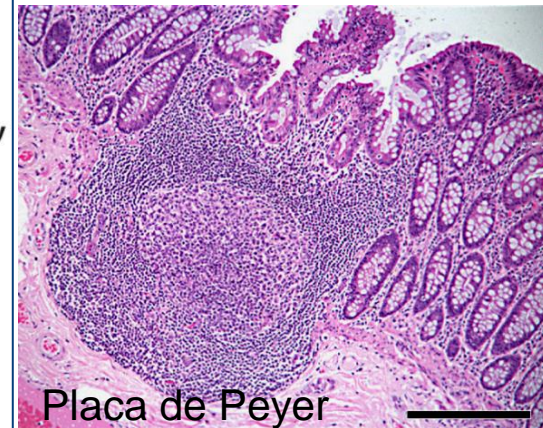
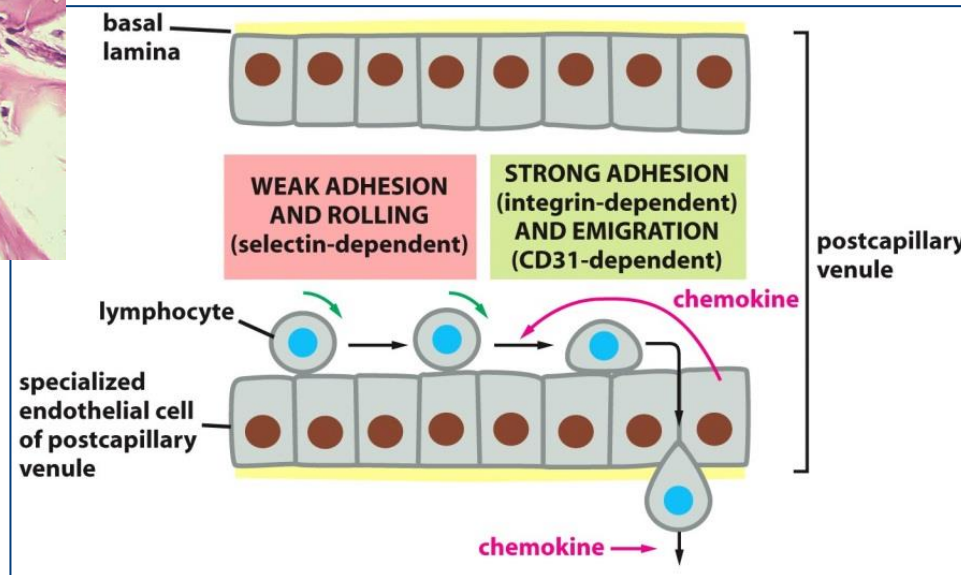
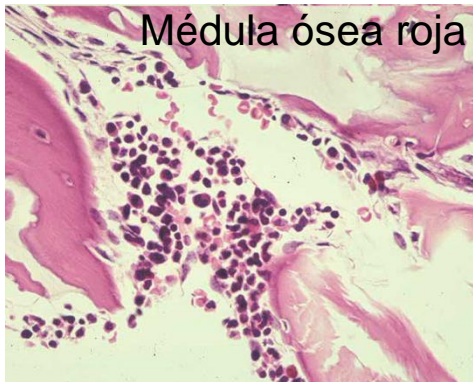
effector T cell ┌
└ 1 μm

- ➡ Citotóxicos
- ➡ Colaboradores
- ➡ Reguladores (supresores)

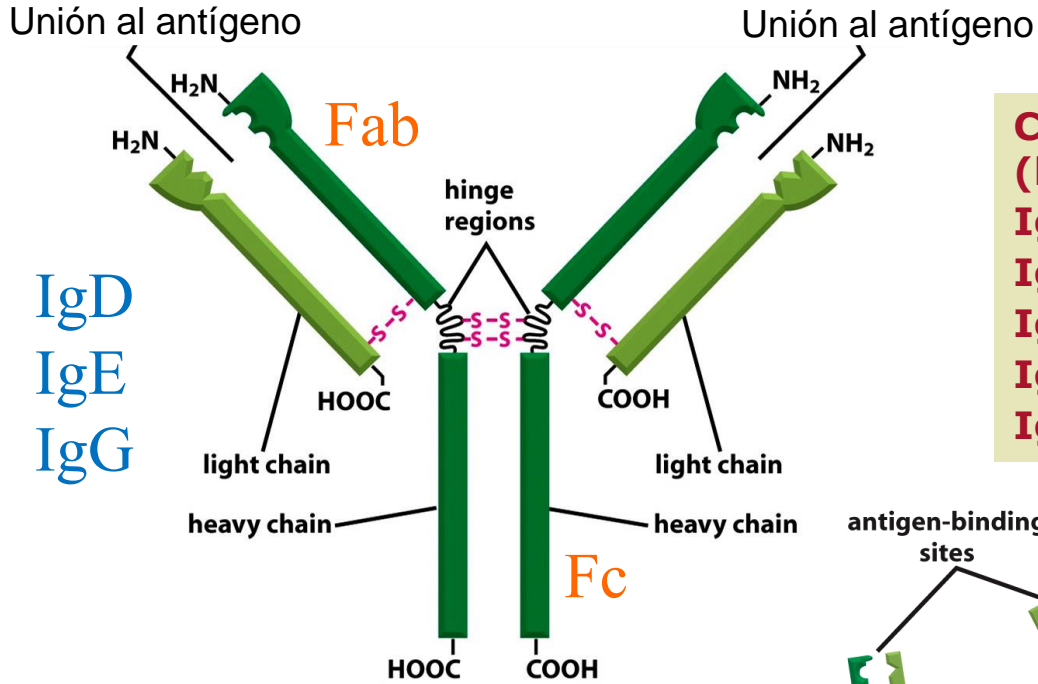
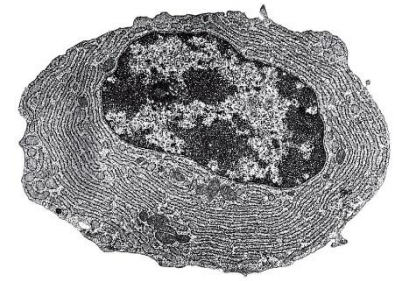
Linfocitos y órganos linfoides



Ganglio linfático



Estructura de los anticuerpos



Cadenas pesadas: (locus único)

IgA--α

IgD--δ

IgE--ε

IgG--γ

IgM--μ

Cadenas livianas: (locus separados)

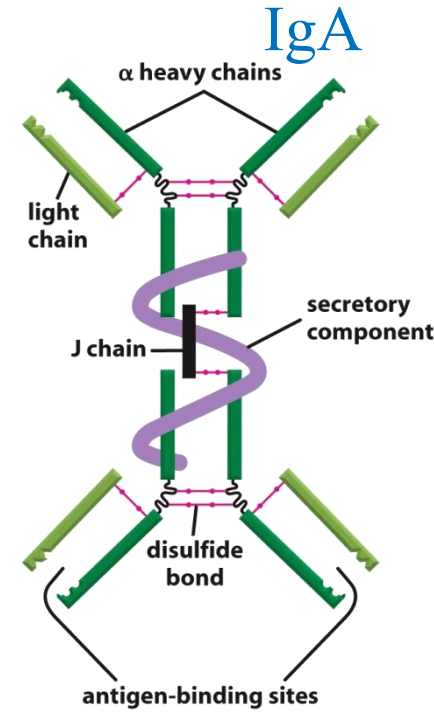
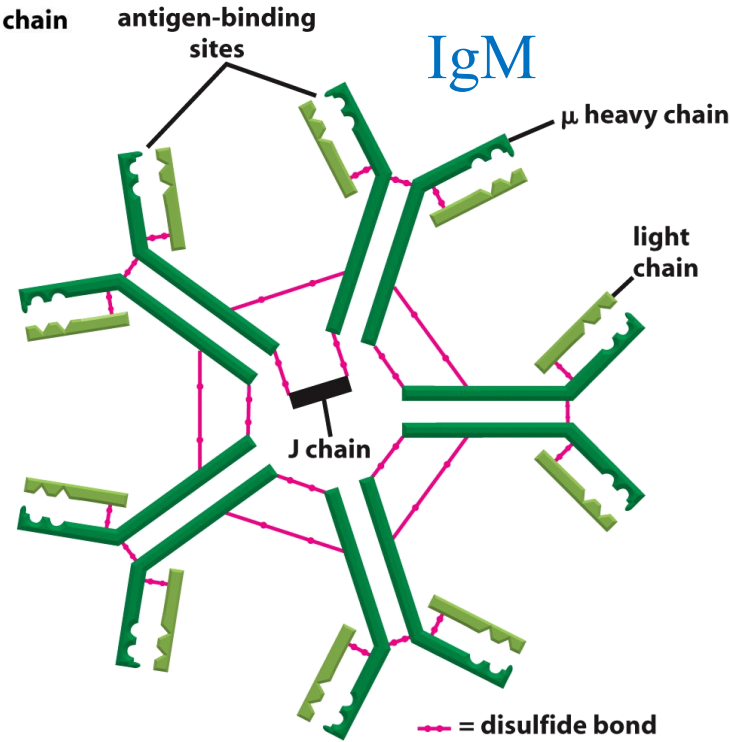
κ

λ

IgD

IgE

IgG



Nobel, 1972



Gerald M. Edelman
(1929 - 2014)



Rodney R. Porter
(1917 - 1985)

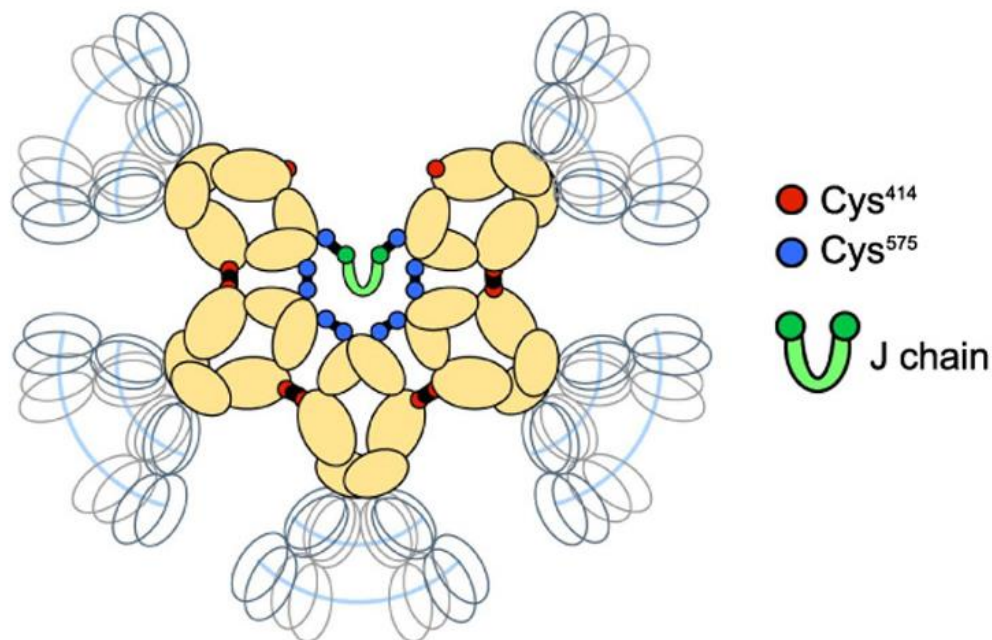
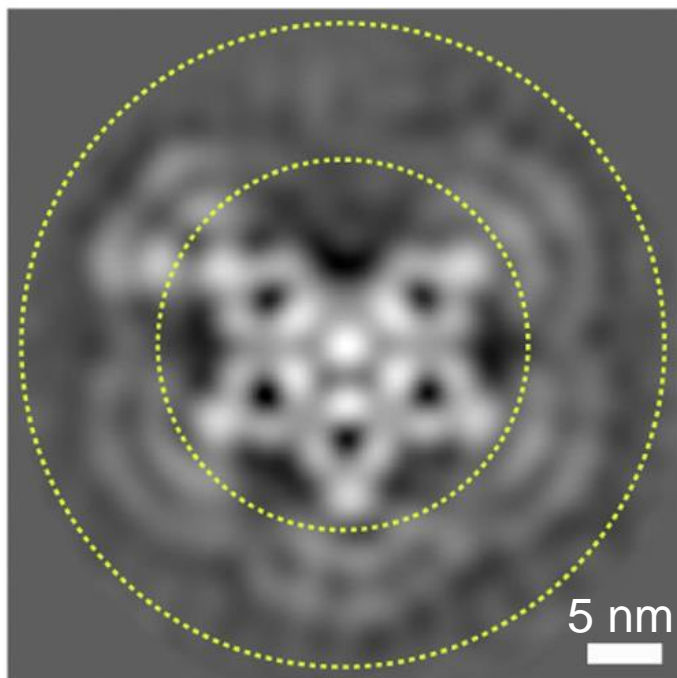
BIOCHEMISTRY

The IgM pentamer is an asymmetric pentagon with an open groove that binds the AIM protein

Emiri Hiramoto¹, Akihisa Tsutsumi², Risa Suzuki¹, Shigeru Matsuoka^{1*}, Satoko Arai^{1†}, Masahide Kikkawa², Toru Miyazaki^{1,3,4†}

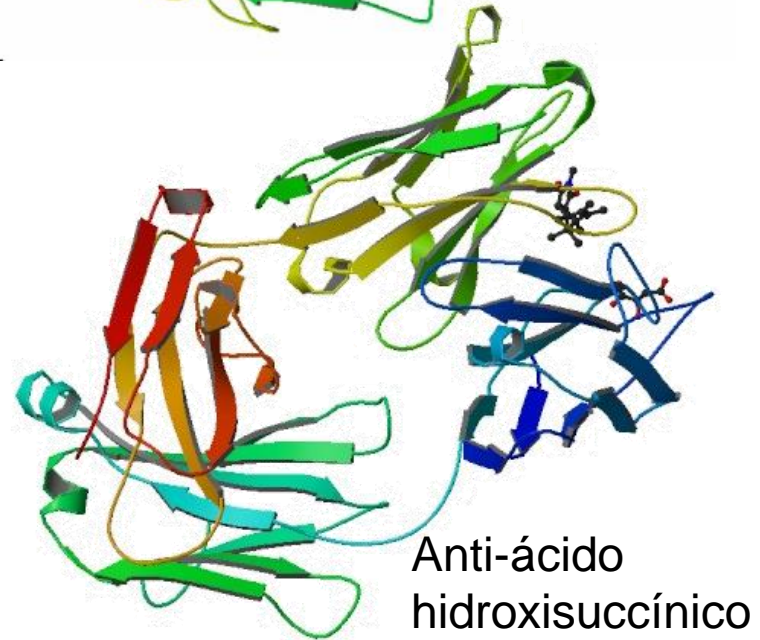
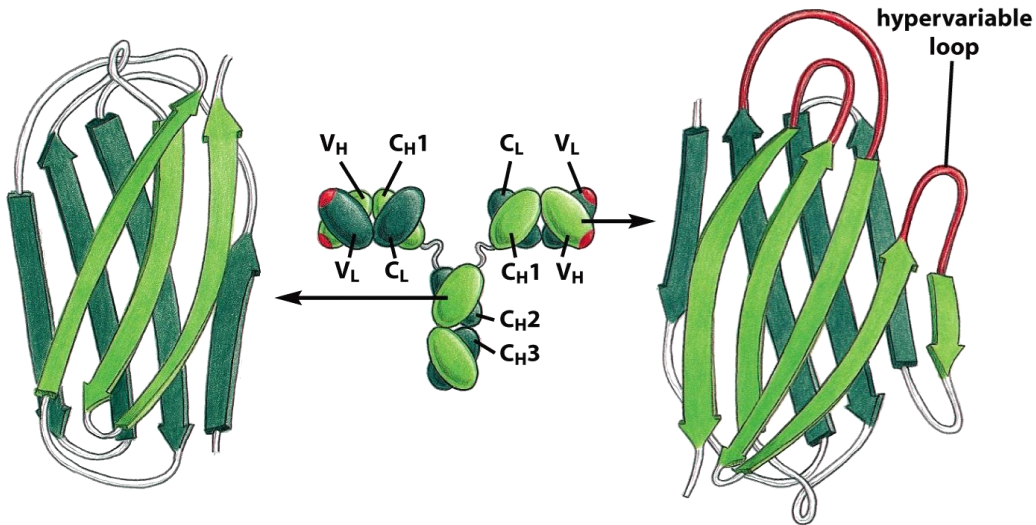
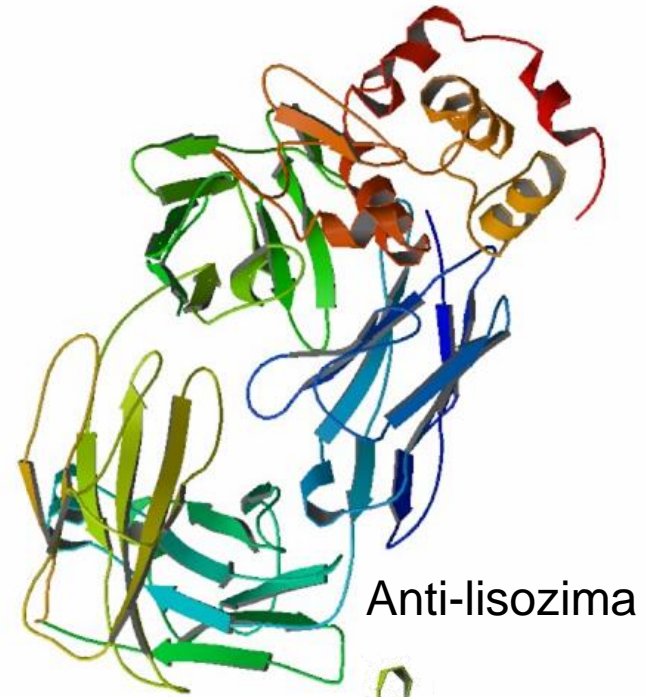
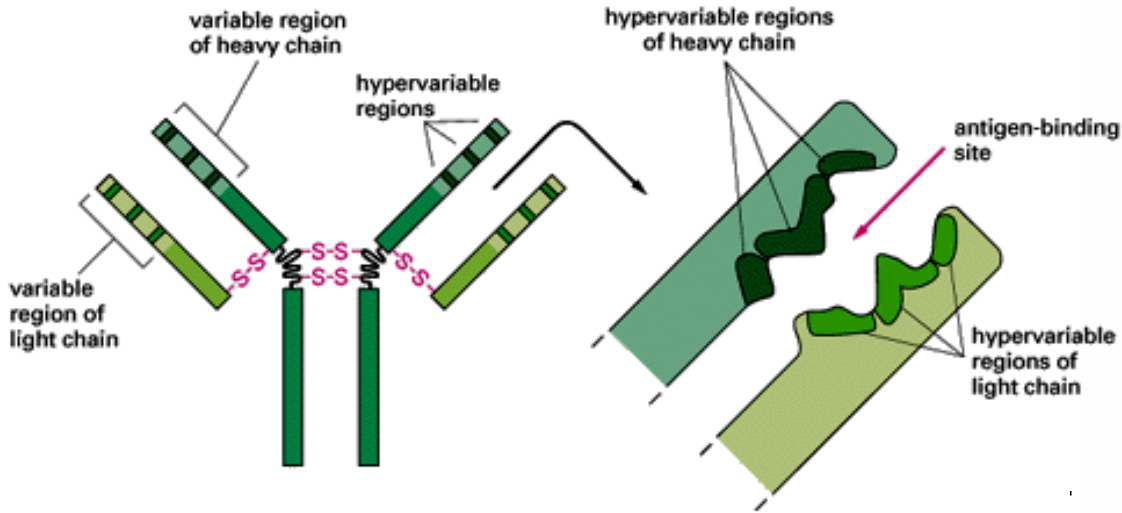
<https://advances.sciencemag.org/content/4/10/eaau1199>

D Mouse IgM (full length)

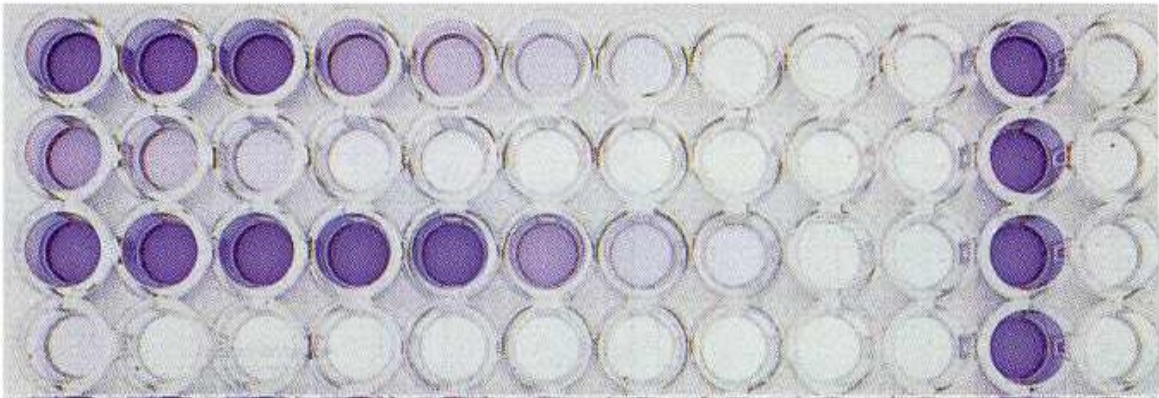
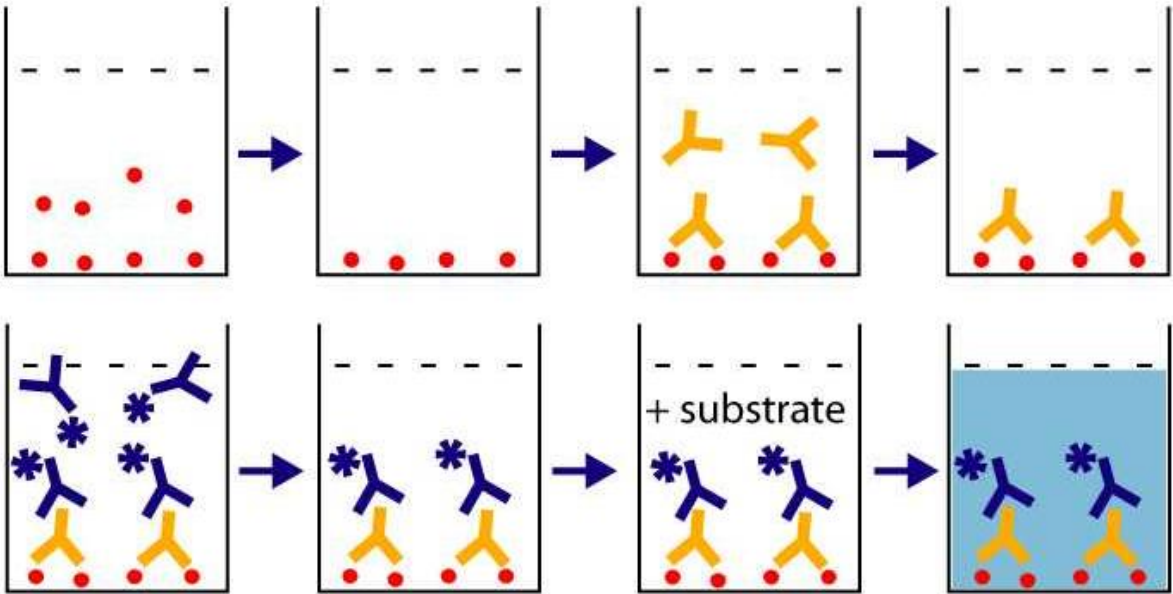


Tinción negativa - MET

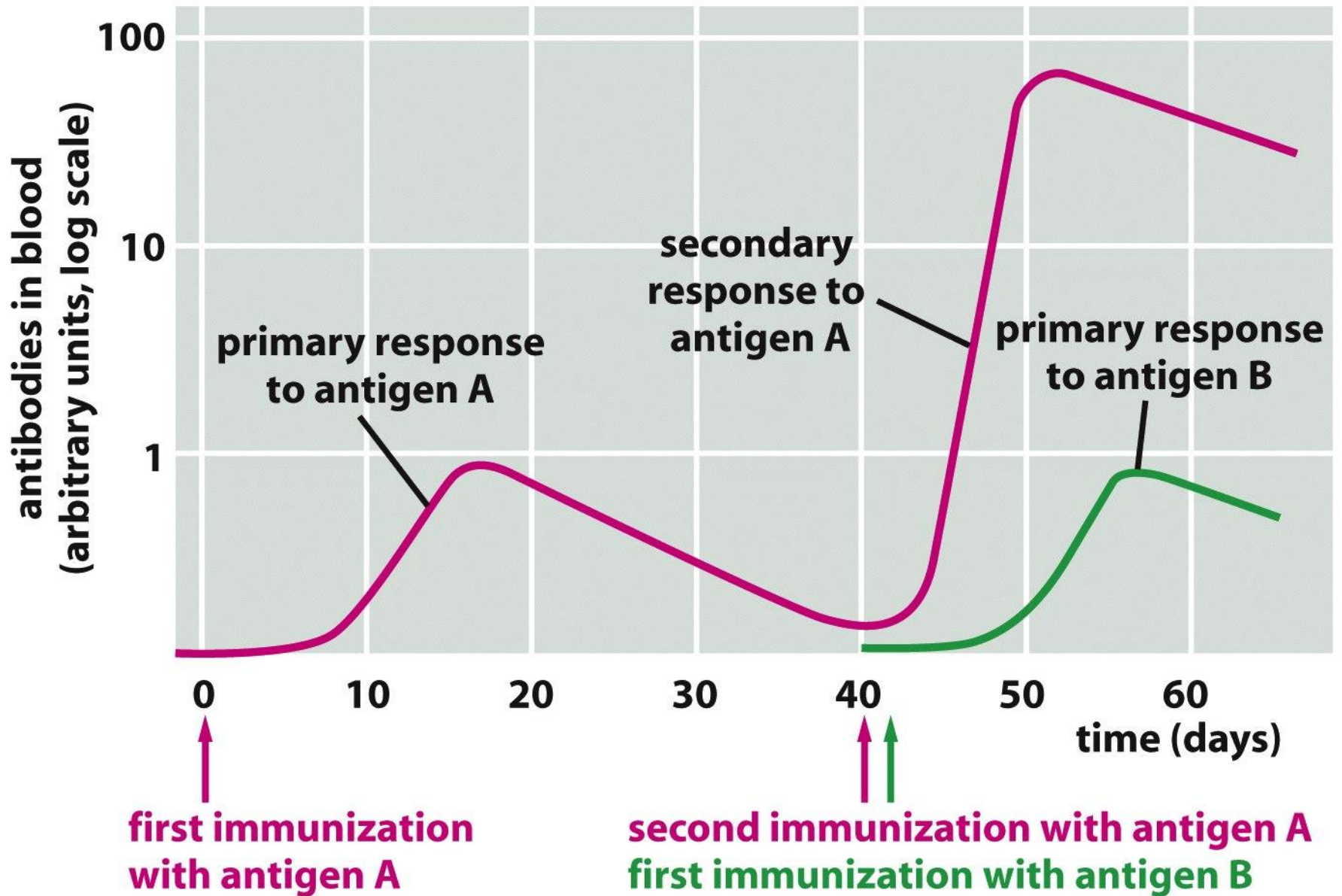
Estructura de los anticuerpos



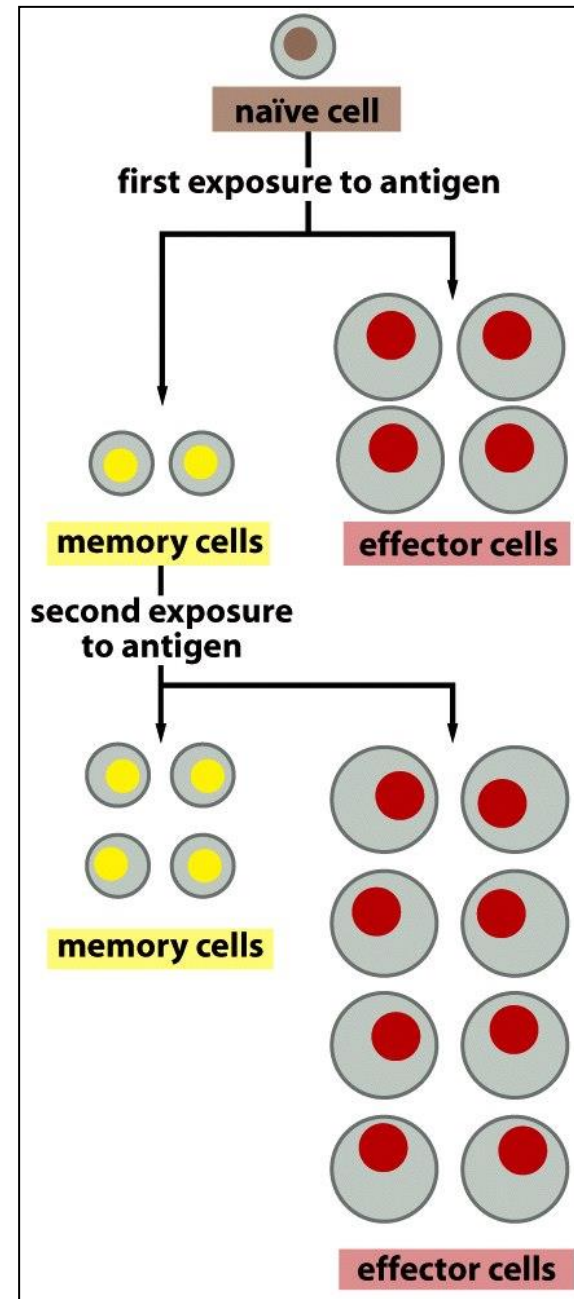
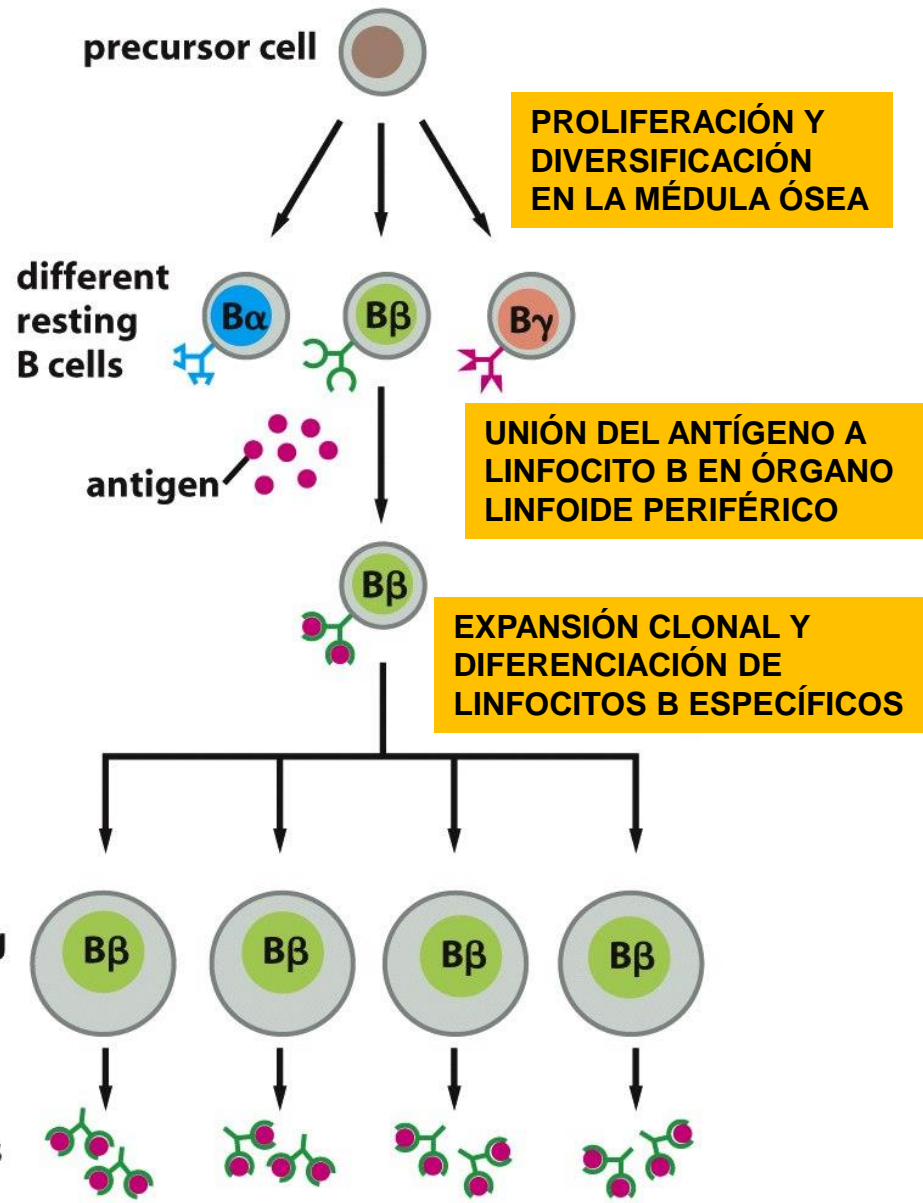
Cuantificación de anticuerpos: ELISA ("Enzyme-Linked ImmunoSorbent Assay")



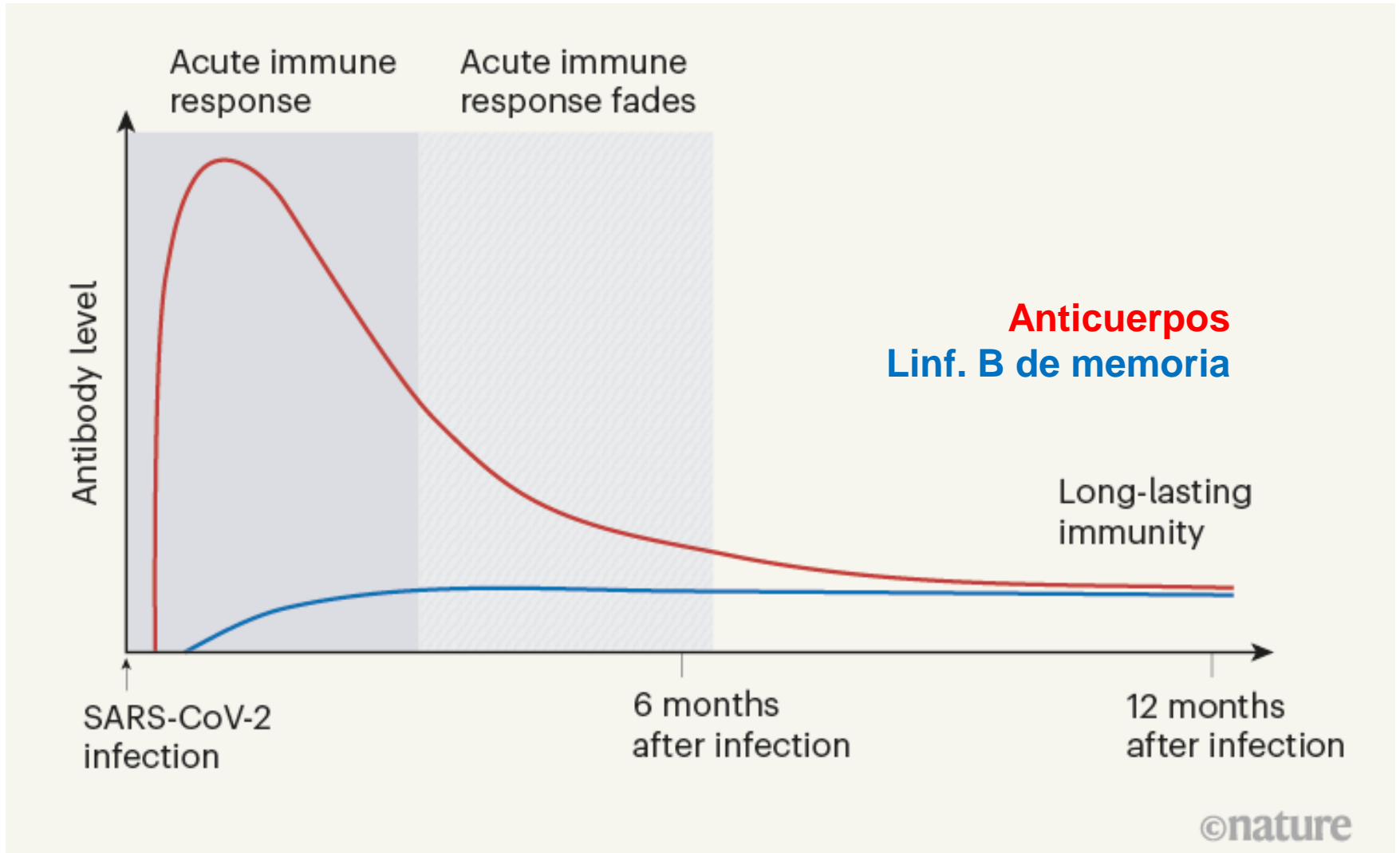
Respuesta de anticuerpos



Teoría de la selección clonal



¿Inmunidad a largo plazo para SARS-CoV-2?



Hadbruch y Chang, 14 de junio de 2021, Nature

doi: <https://doi.org/10.1038/d41586-021-01557-z>

Anticuerpos monoclonales

Nature Vol. 256 August 7 1975

Continuous cultures of fused cells secreting antibody of predefined specificity

*MRC Laboratory of Molecular Biology,
Hills Road, Cambridge CB2 2QH, UK*

G. KÖHLER
C. MILSTEIN

The Nobel Prize in Physiology or Medicine 1984

The Nobel Prize in Physiology or Medicine 1984 was awarded jointly to Niels K. Jerne, Georges J.F. Köhler and César Milstein *"for theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies"*.



Niels K. Jerne
Prize share: 1/3



Georges J.F. Köhler
Prize share: 1/3



César Milstein
Prize share: 1/3

Anticuerpos monoclonales:

1- ¿Qué son y cómo se obtienen?

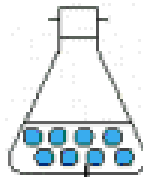
2- ¿Qué aplicaciones tienen hoy en día?

Anticuerpos monoclonales

mouse immunized with antigen X



mutant cell line derived from a tumor of B lymphocytes



cell making anti-X antibody



B lymphocytes (die after a few days in culture)

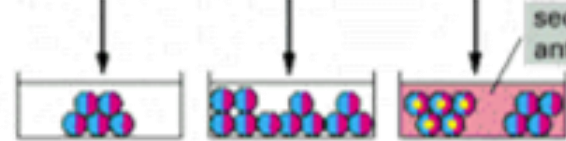
(cells grow indefinitely in normal medium, but die in selective medium)

FUSION

products plated in multiple wells

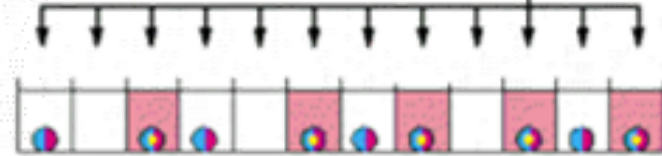


only hybridomas grow on the selective medium



secreted anti-X antibody

test supernatant for anti-X antibody and redistribute cells from positive well at ~1 cell per well

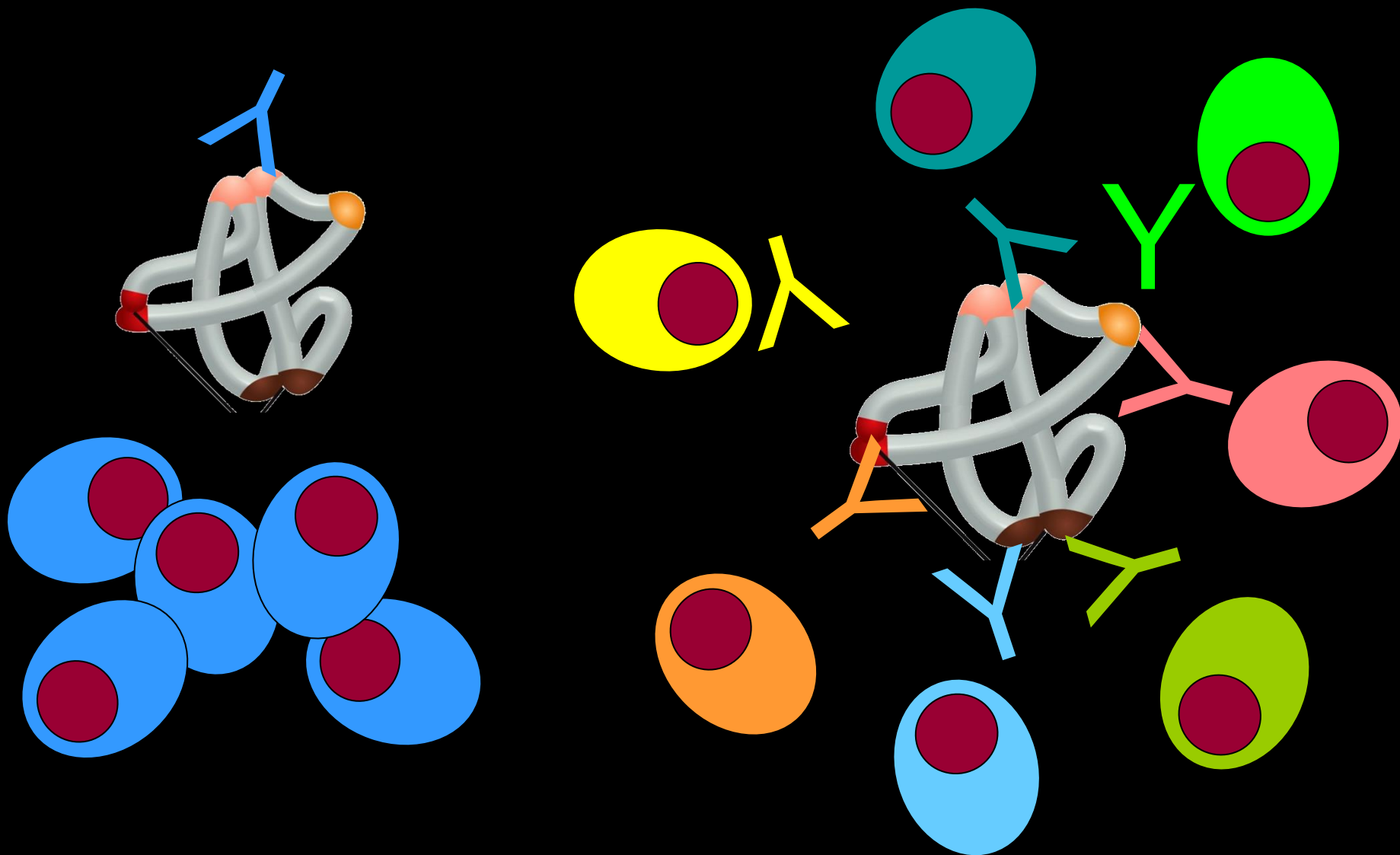


allow cells to multiply, then test supernatant for anti-X antibodies;

positive clones provide a continuing source of anti-X antibody




Epítopes, determinantes antigénicos y respuestas policlonales




Determinantes antigénicos y formación de complejos inmunes

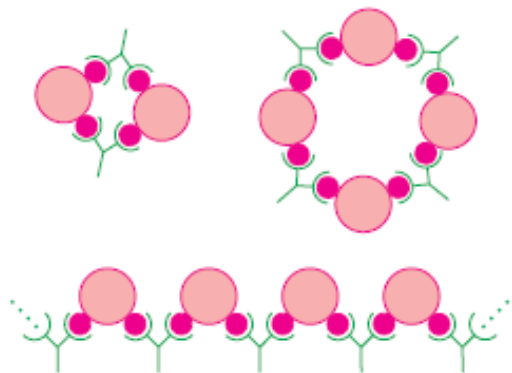
(A)

 one antigenic determinant




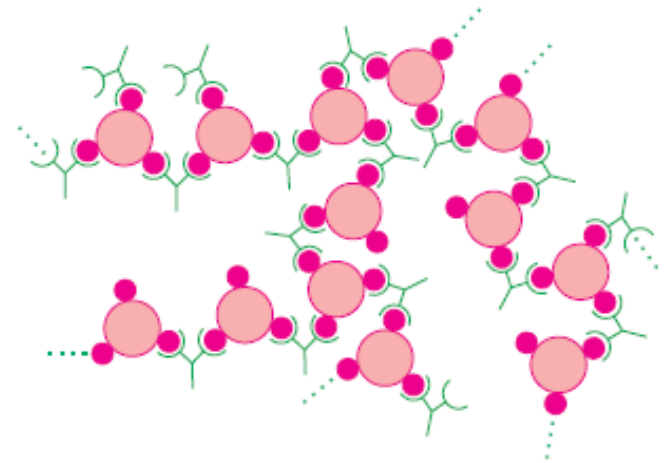
(B)

 two identical antigenic determinants




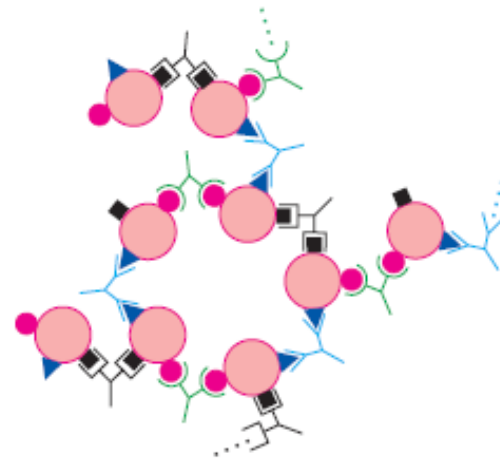
(C)

 three or more identical antigenic determinants



(D)

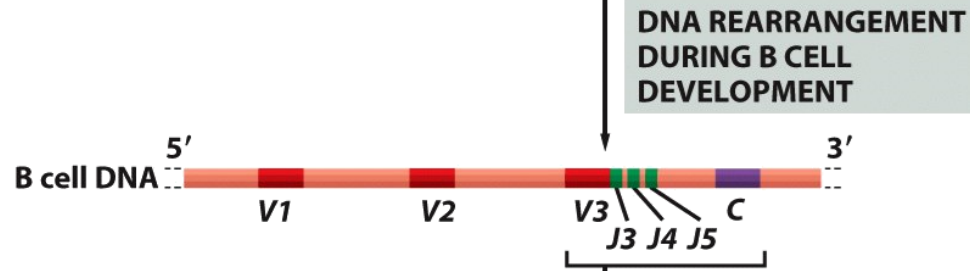
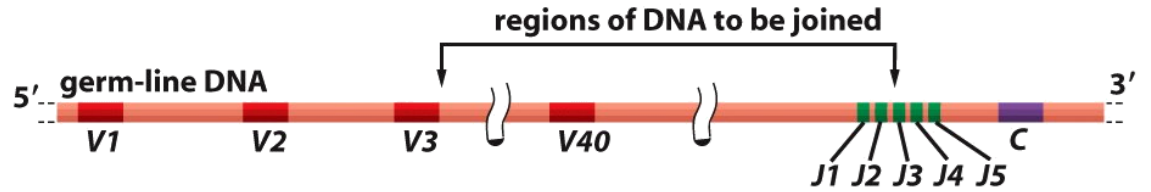
 three or more different antigenic determinants



1.000.000.000.000

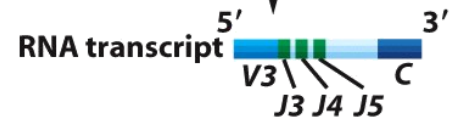
Generación de la diversidad de anticuerpos

Unión combinatoria de segmentos génicos
↓
Diversificación durante la unión de segmentos
↓
Unión combinatoria de cadenas pesadas y livianas
↓
Hipermutación somática
↓
Recombinación en el cambio de clases

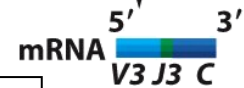


CADENA LIVIANA

TRANSCRIPTION



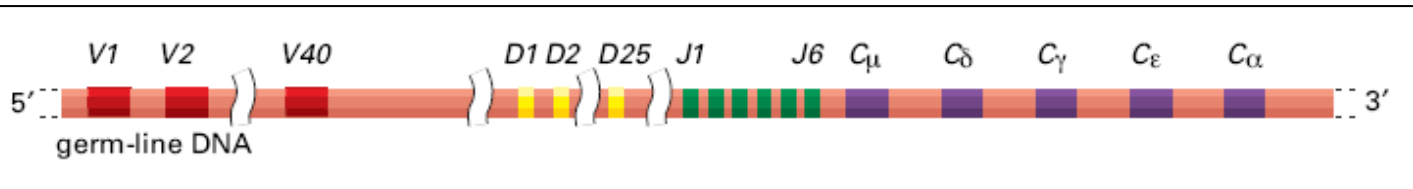
RNA SPLICING



TRANSLATION

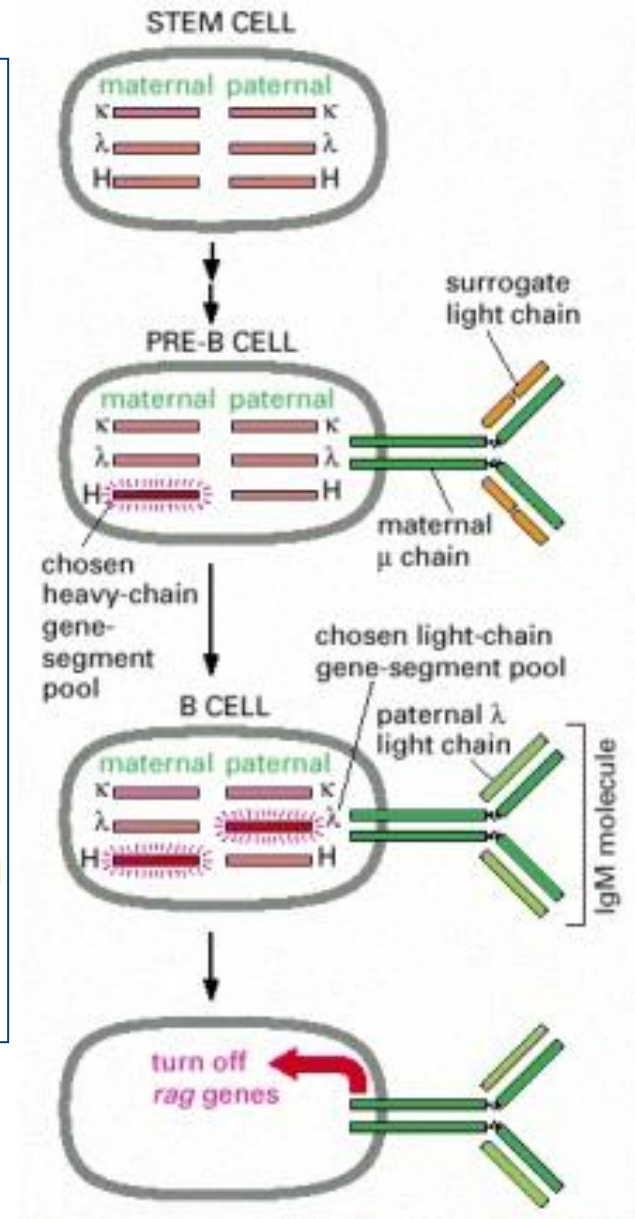
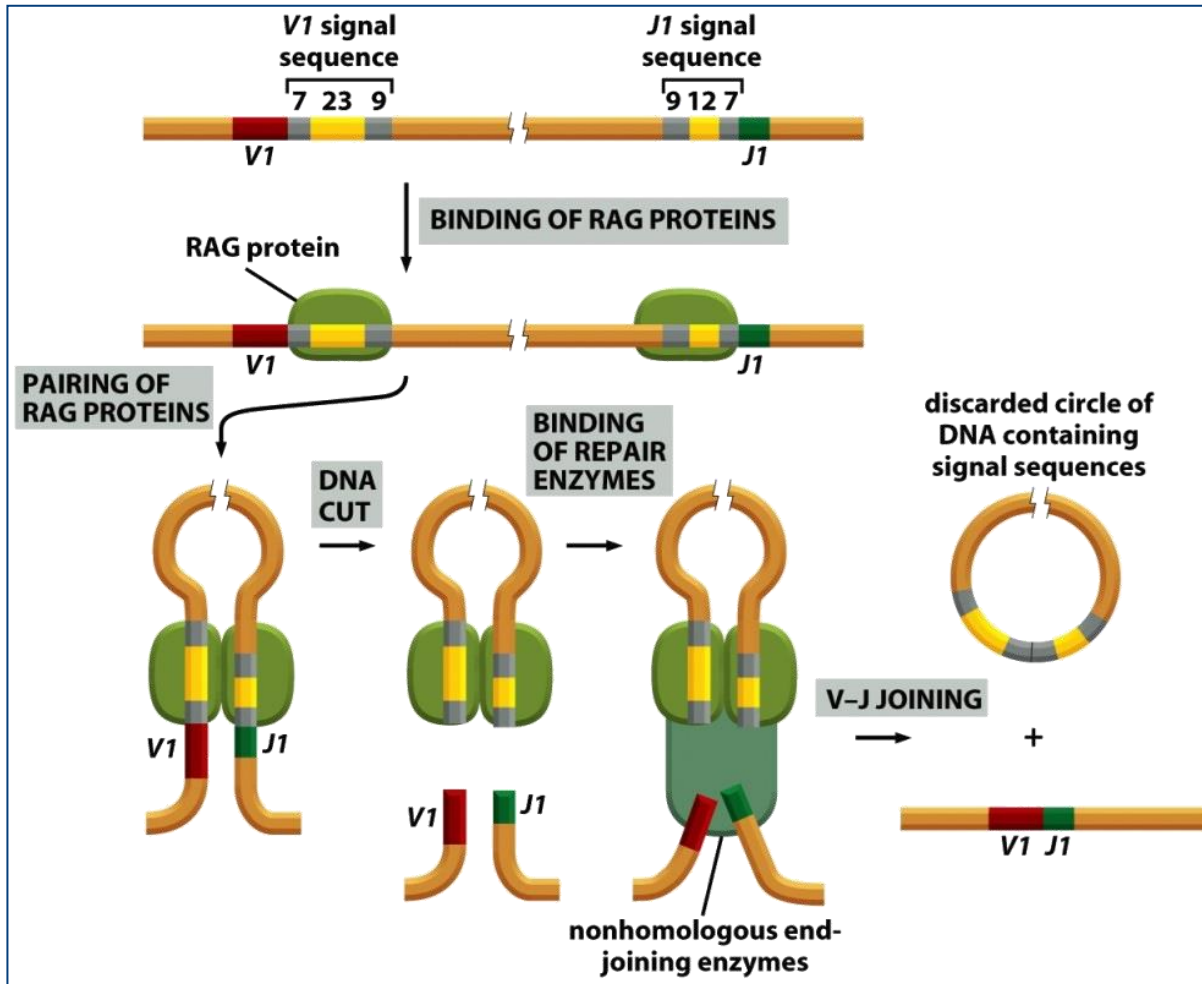


CADENA PESADA

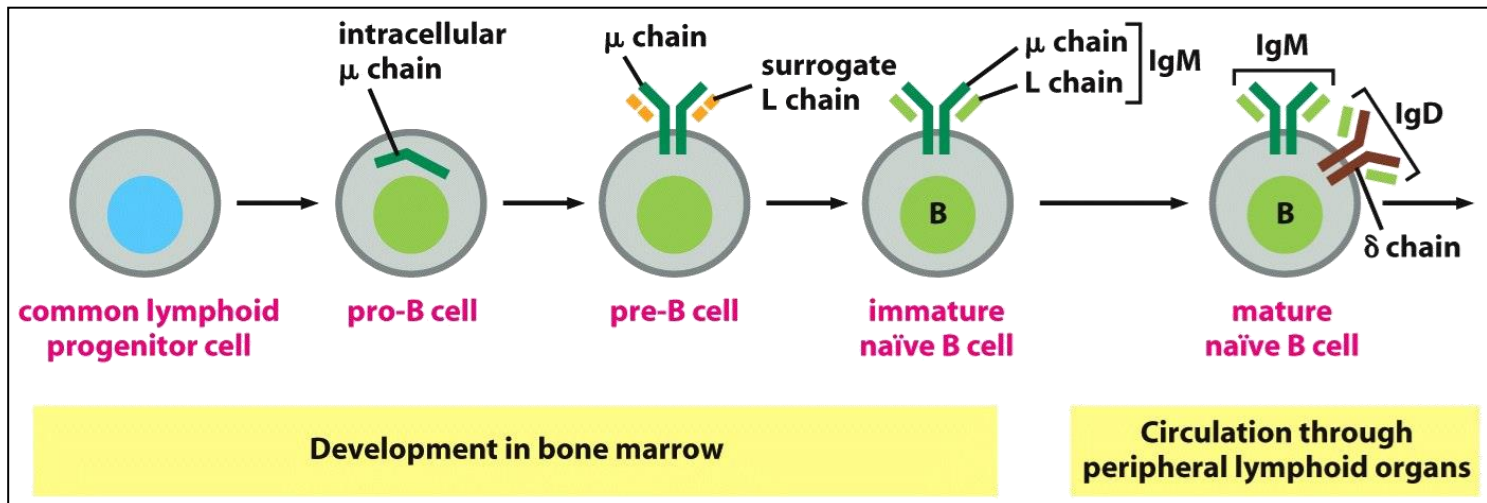
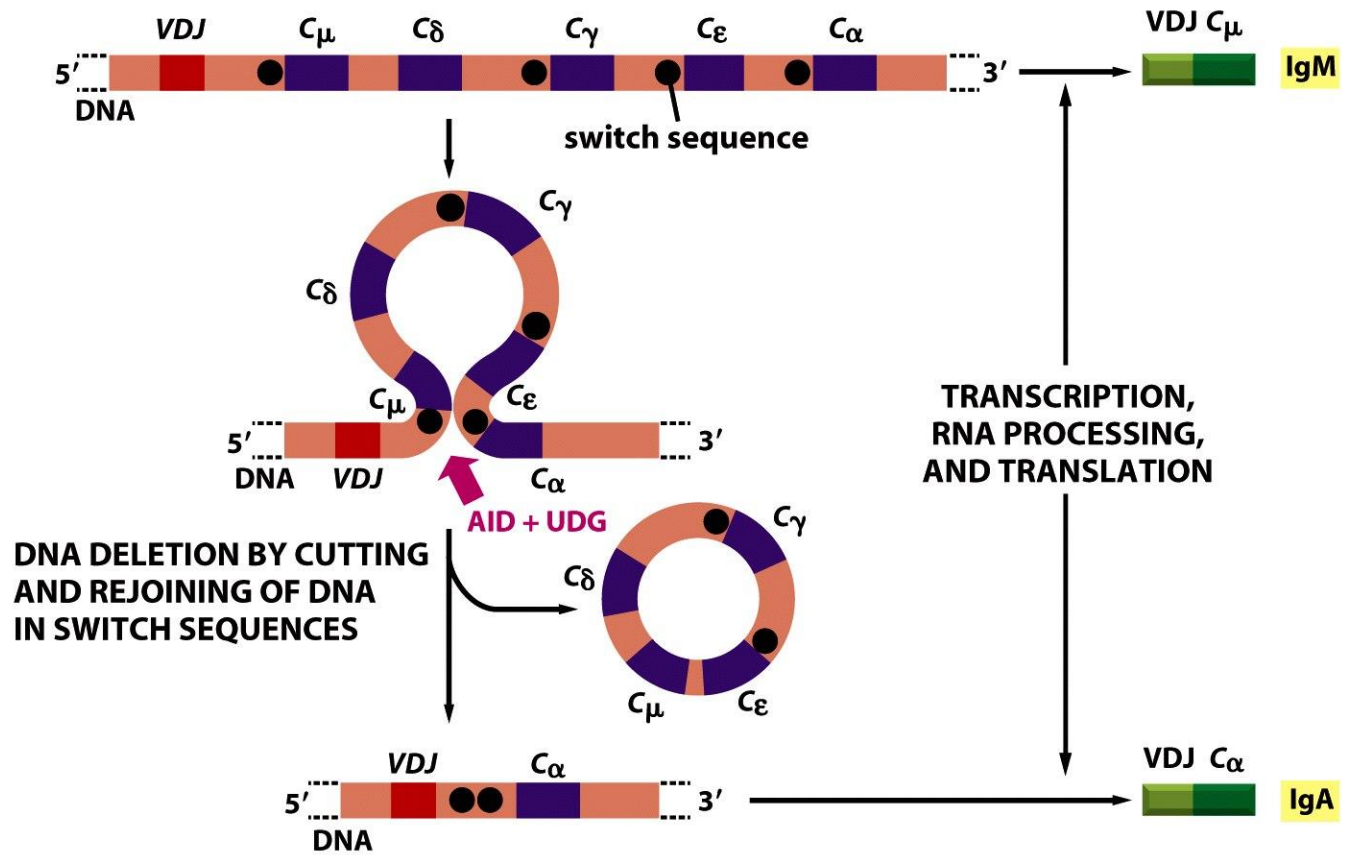


2 Mb

Generación de la diversidad de anticuerpos



Generación de la diversidad de anticuerpos



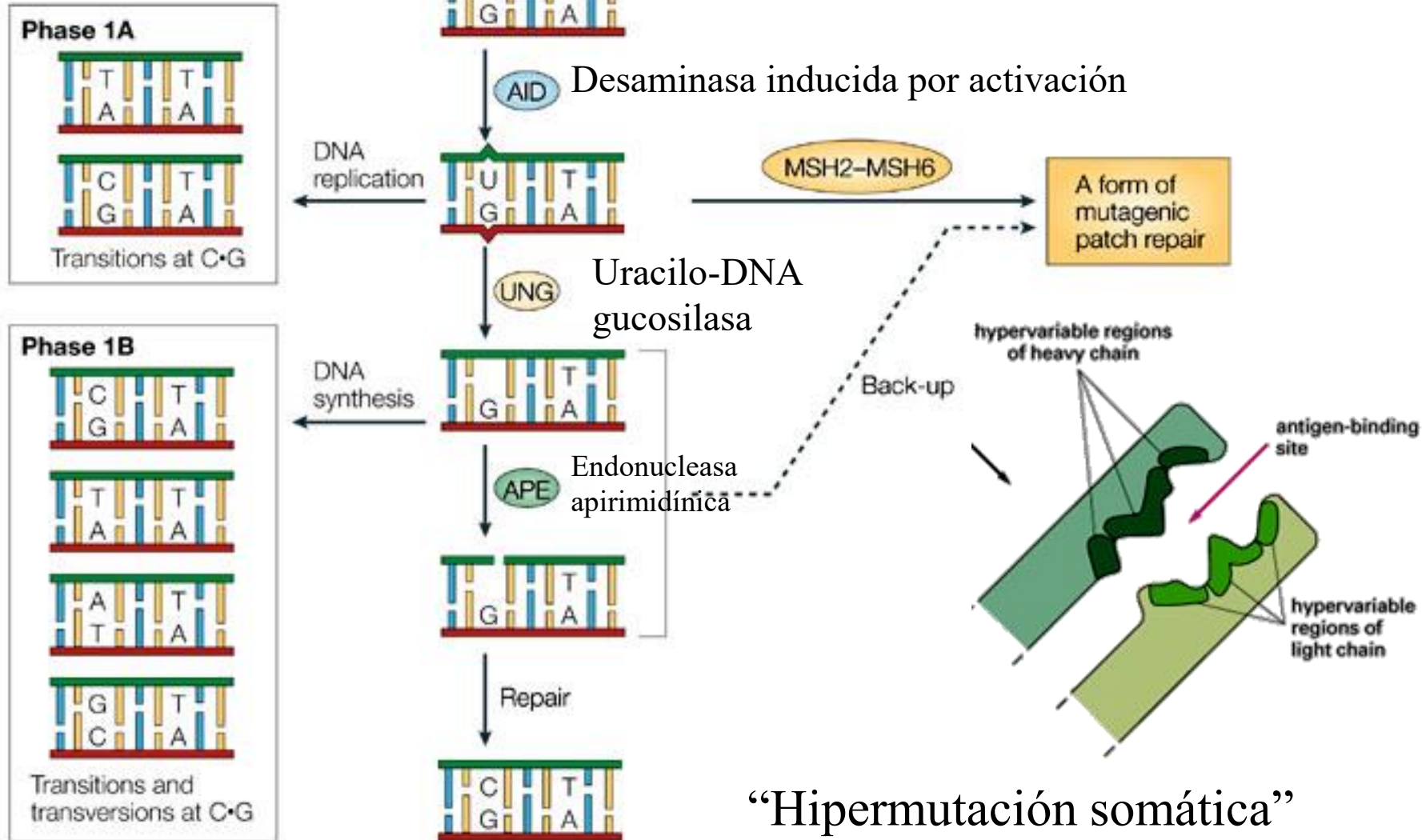
Generación de la diversidad de anticuerpos

Phase 1

Mutations at C•G pairs by deamination of C to U

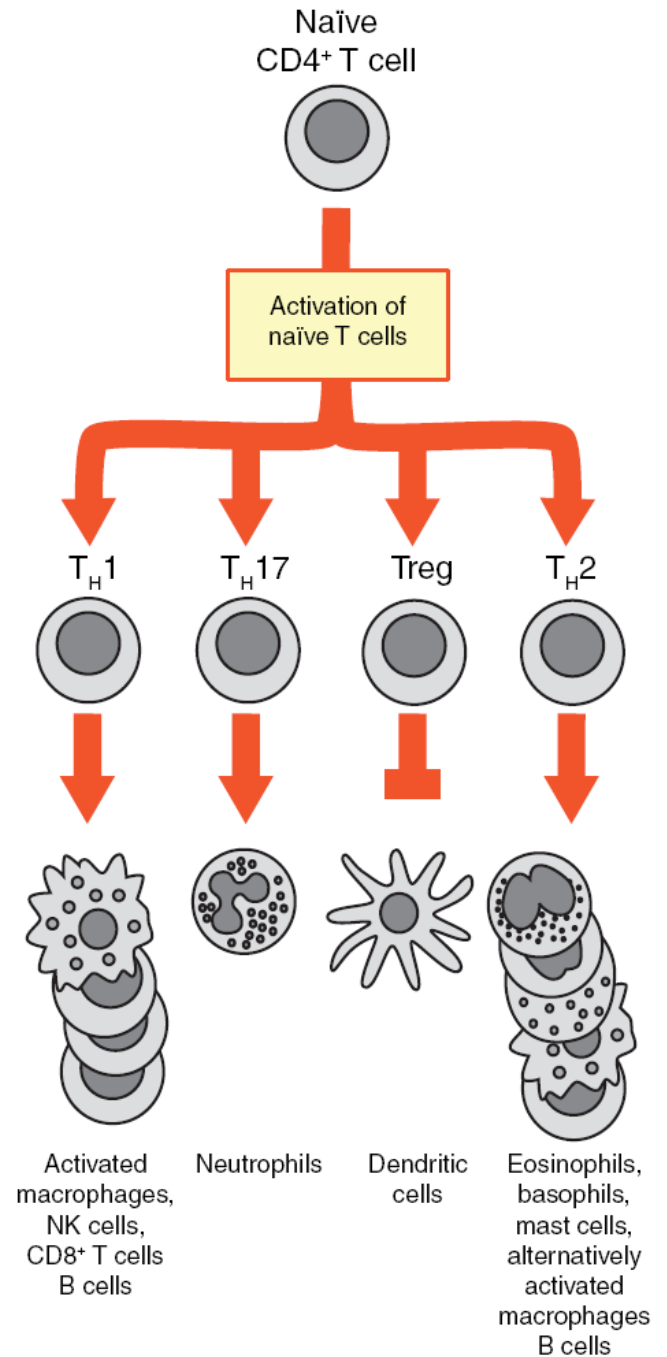
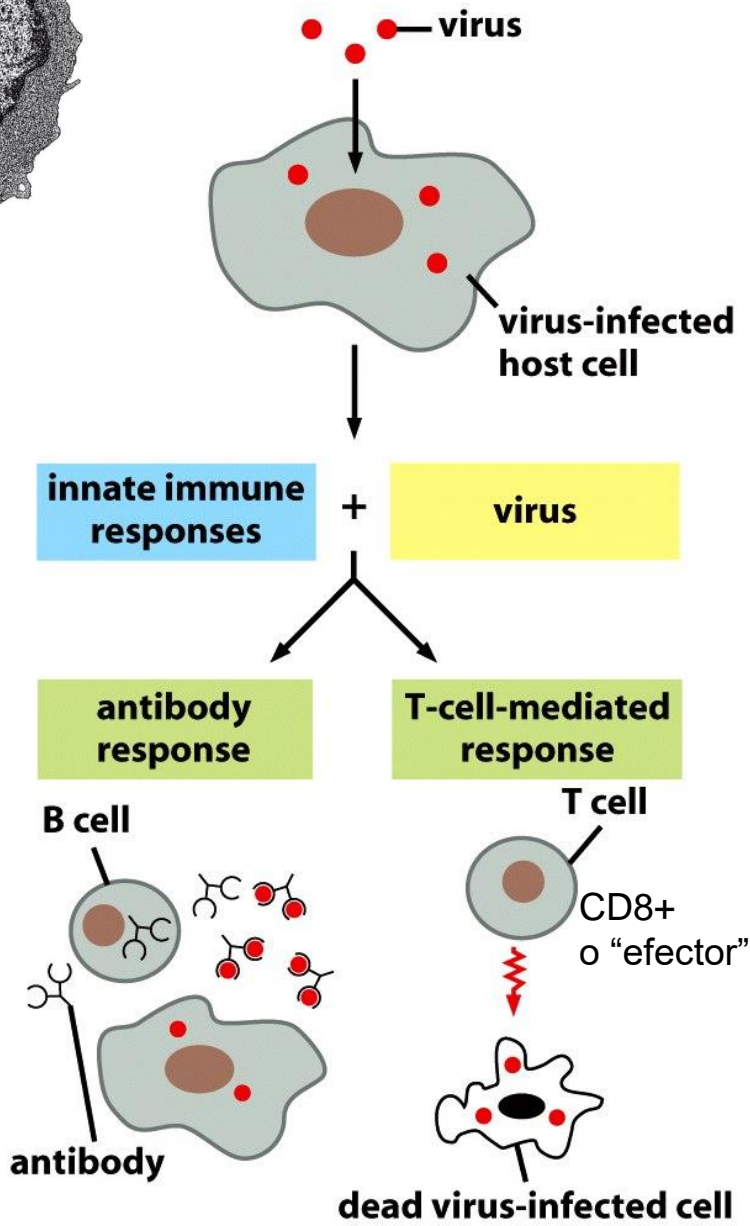
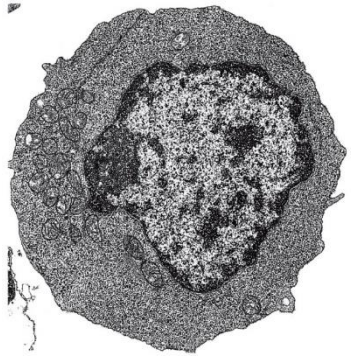
Phase 2

Mutations mainly at A•T pairs (mechanism unknown)

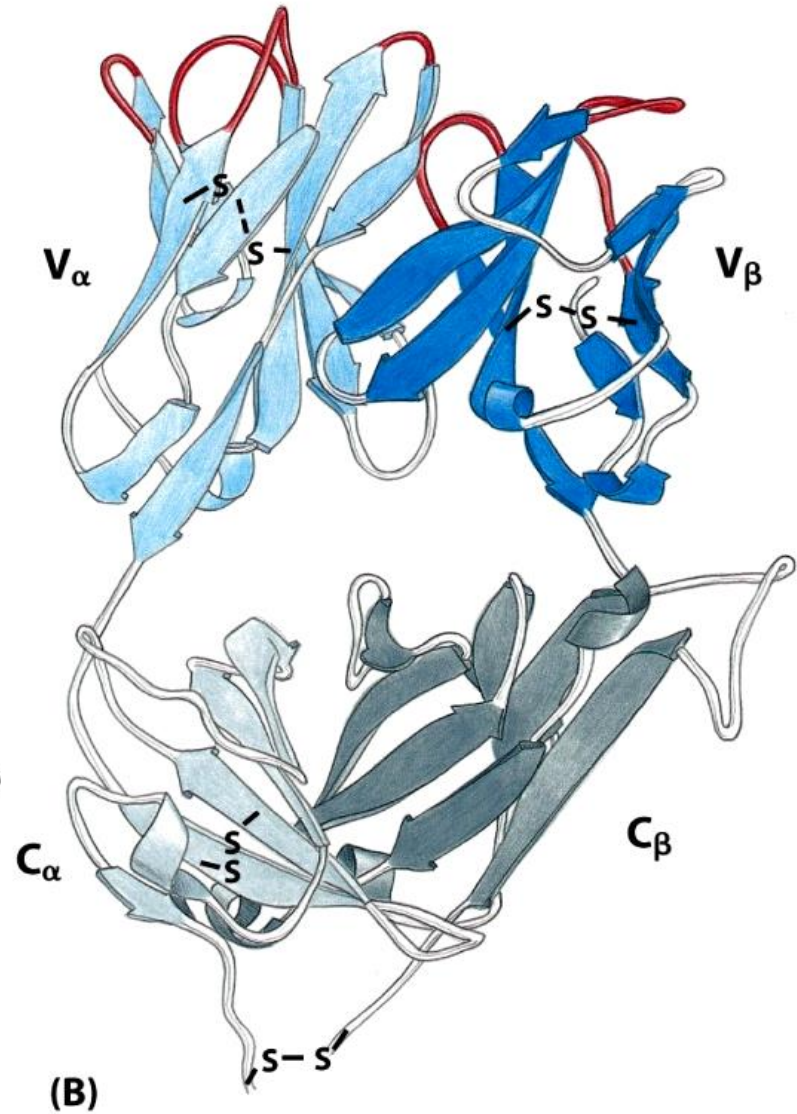
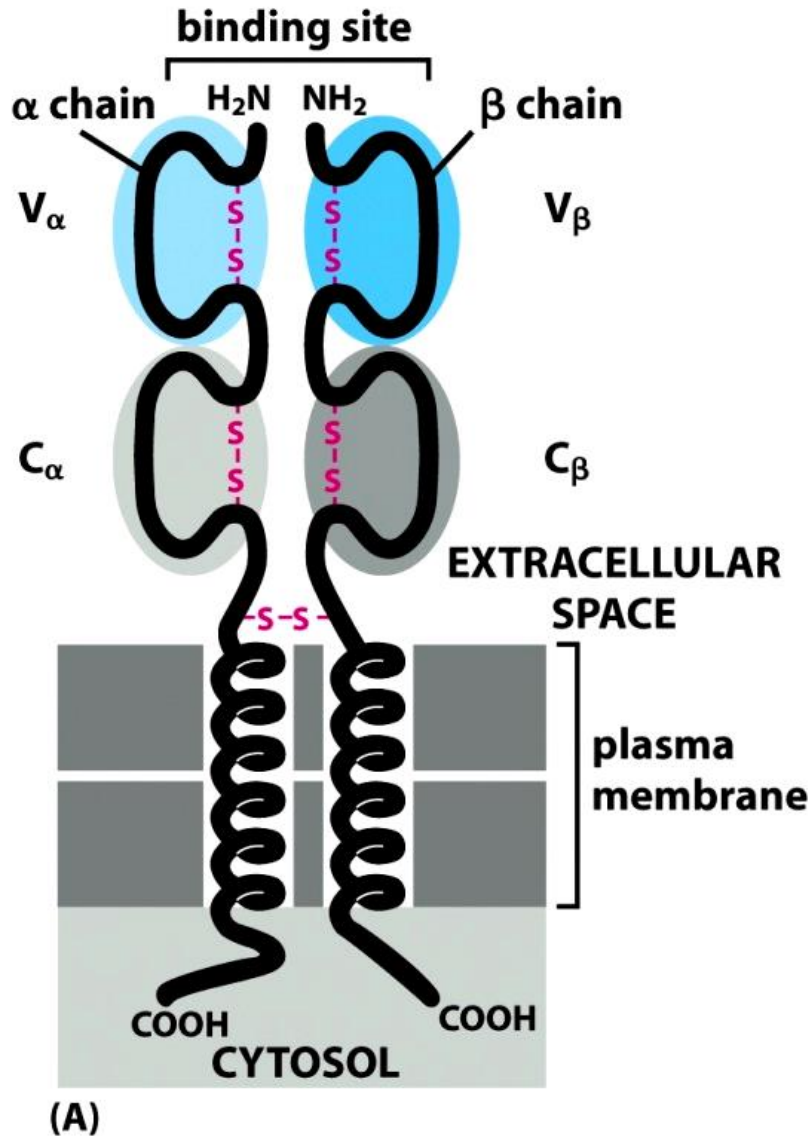


“Hipermutación somática”

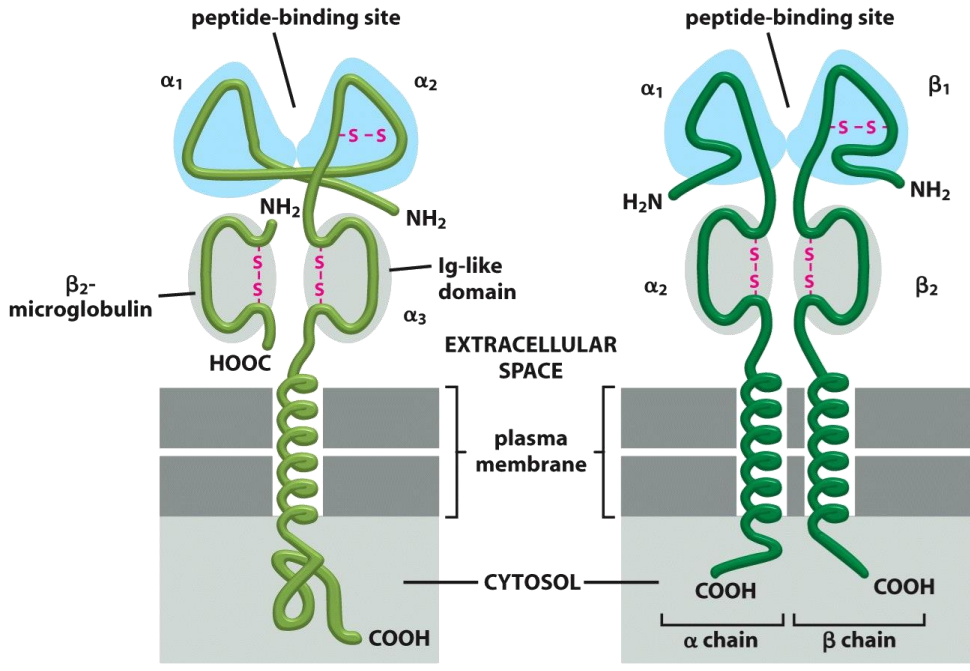
Linfocitos T



El receptor T



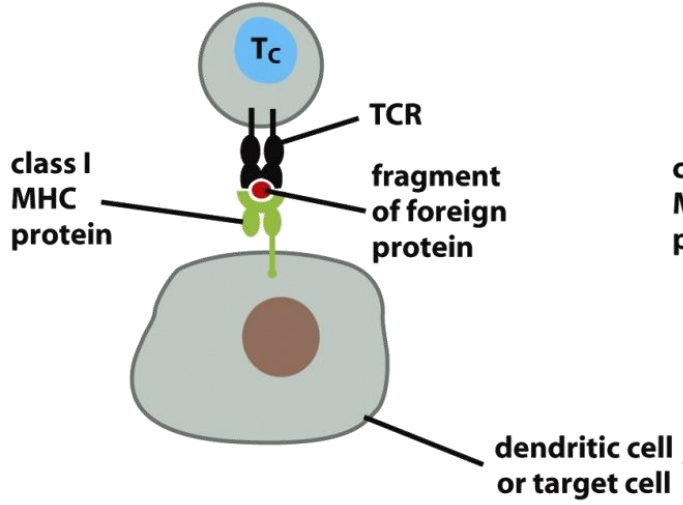
Activación de linfocitos T: Proteínas MHC



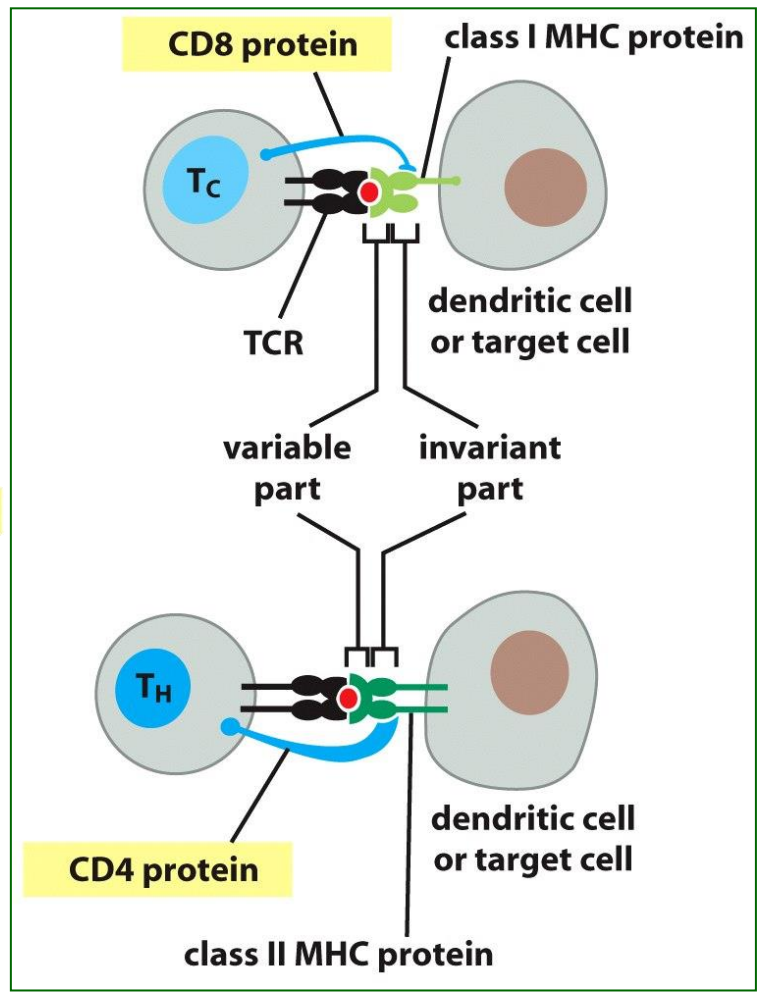
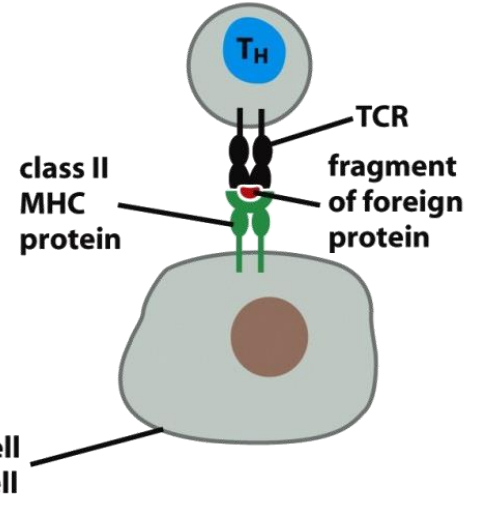
(A) CLASS I MHC PROTEIN

(B) CLASS II MHC PROTEIN

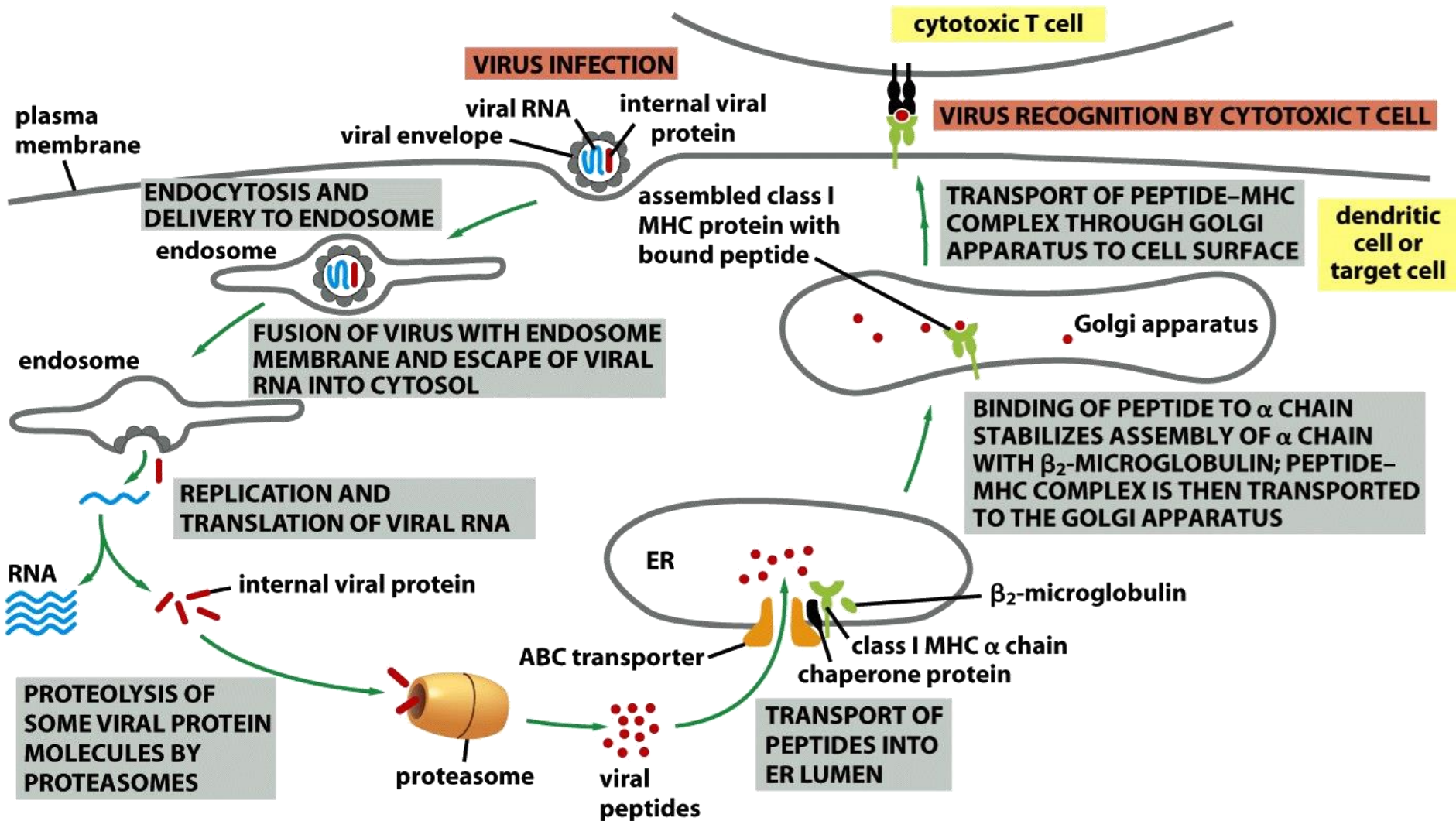
CYTOTOXIC T CELL



HELPER OR REGULATORY T CELL

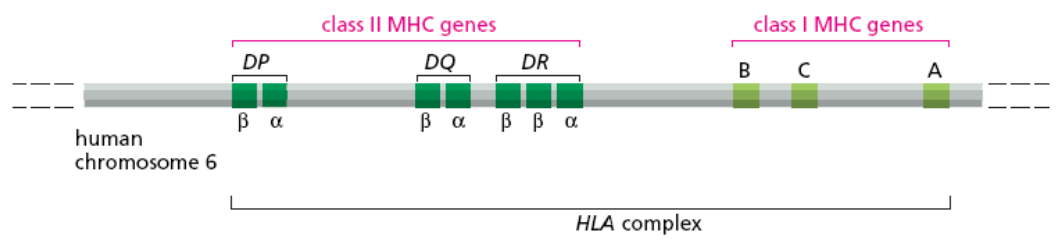
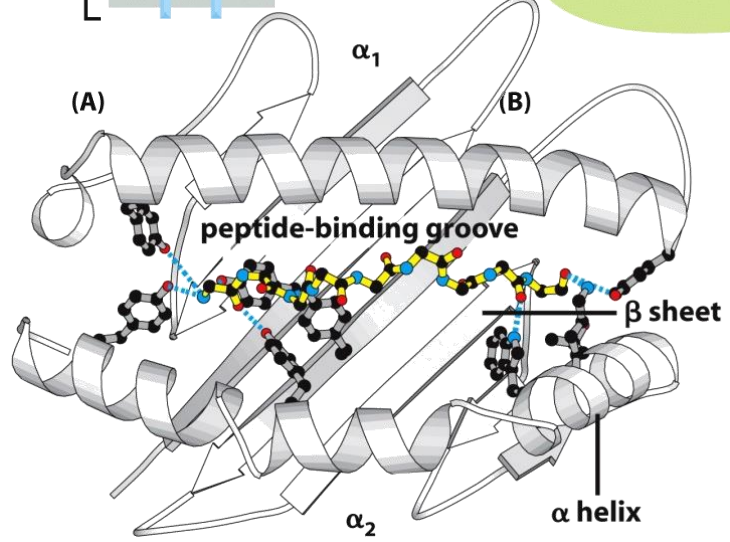
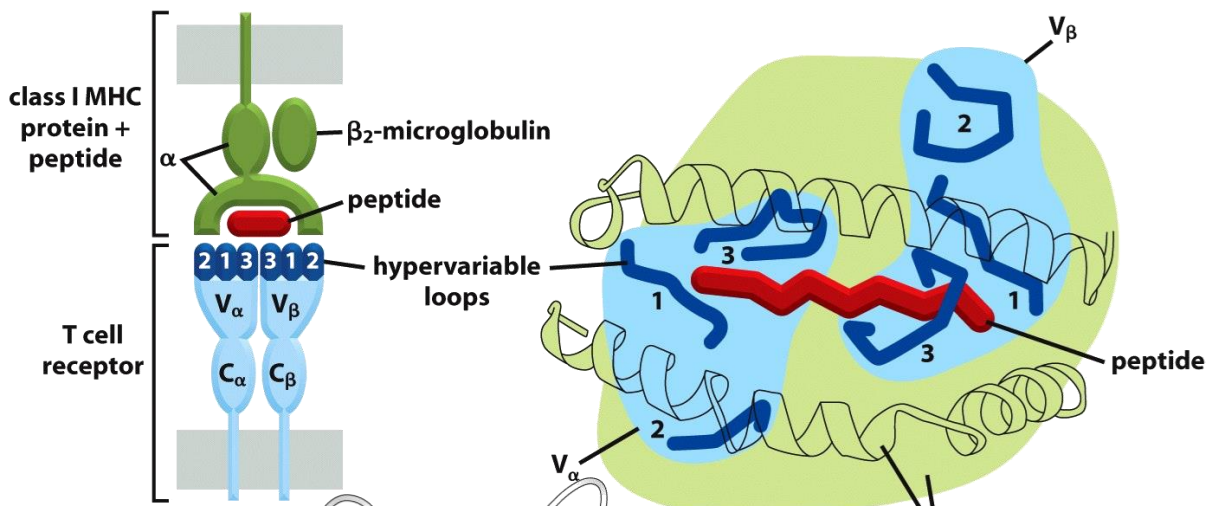
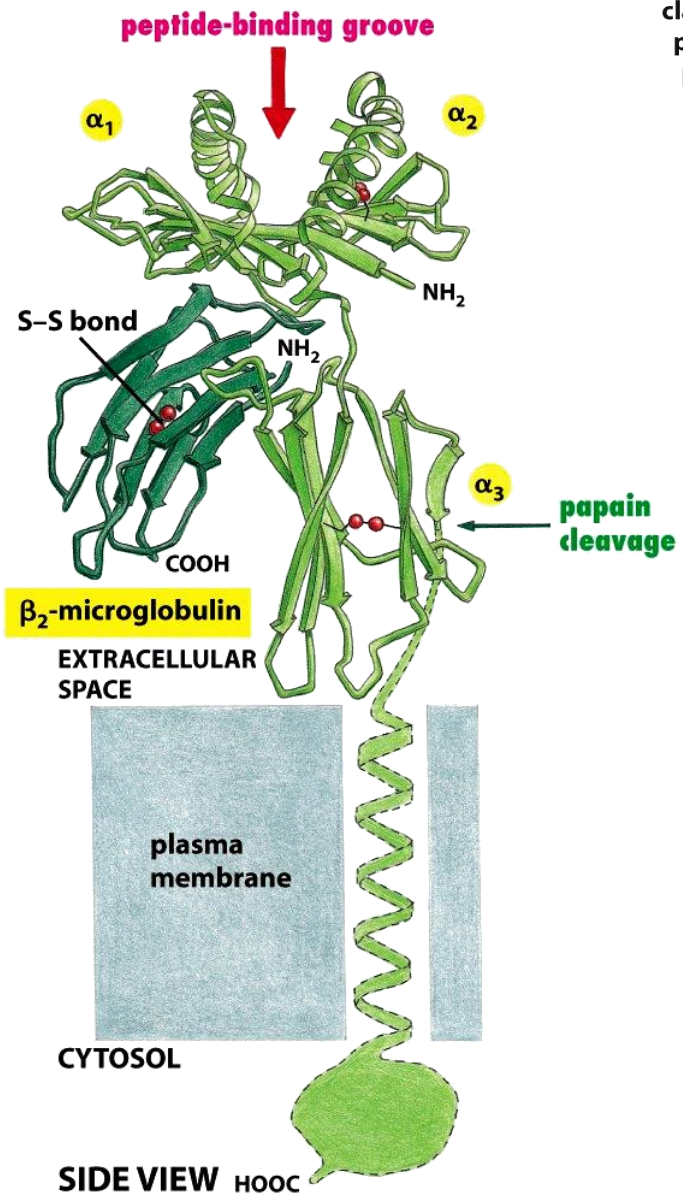


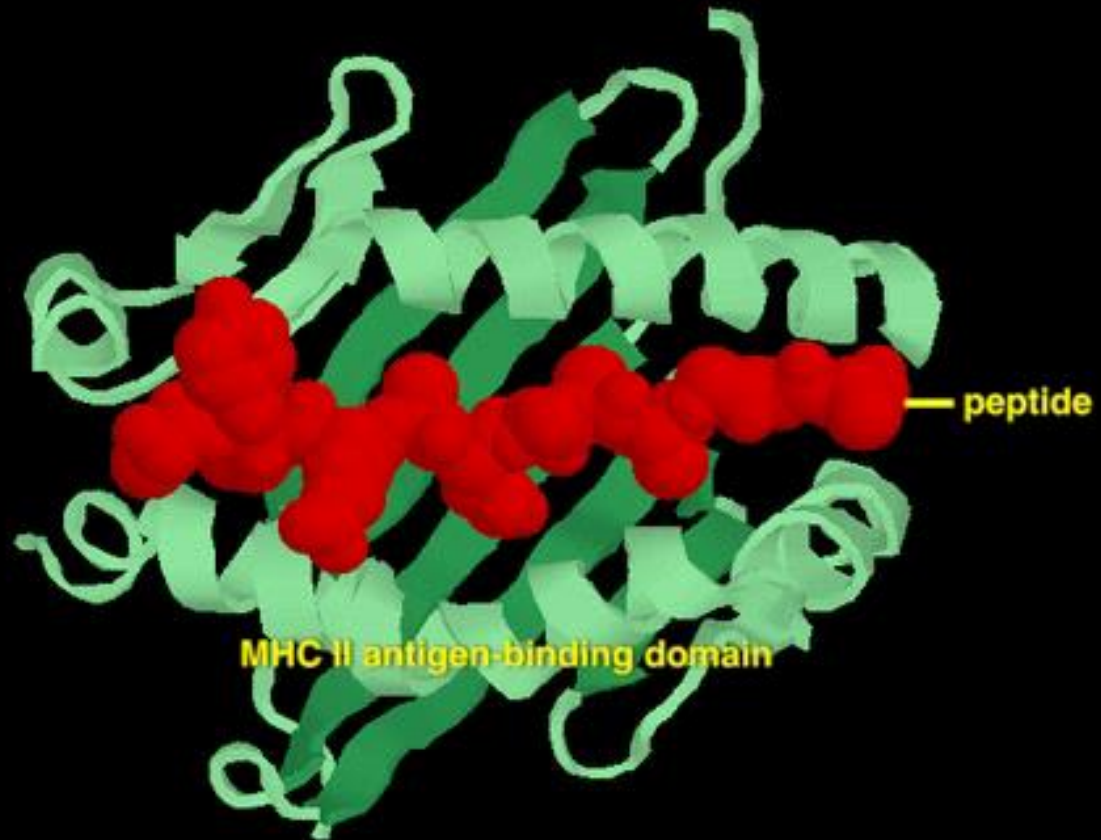
Procesamiento y presentación de antígenos a linfocitos T



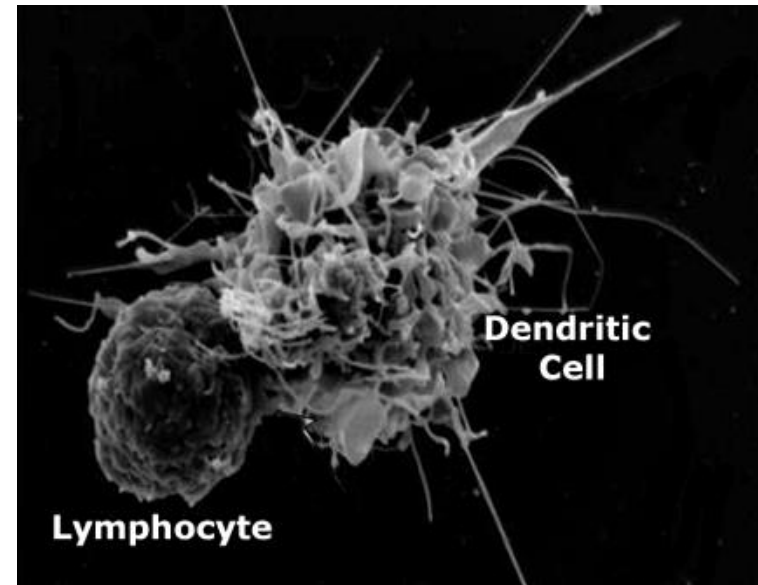
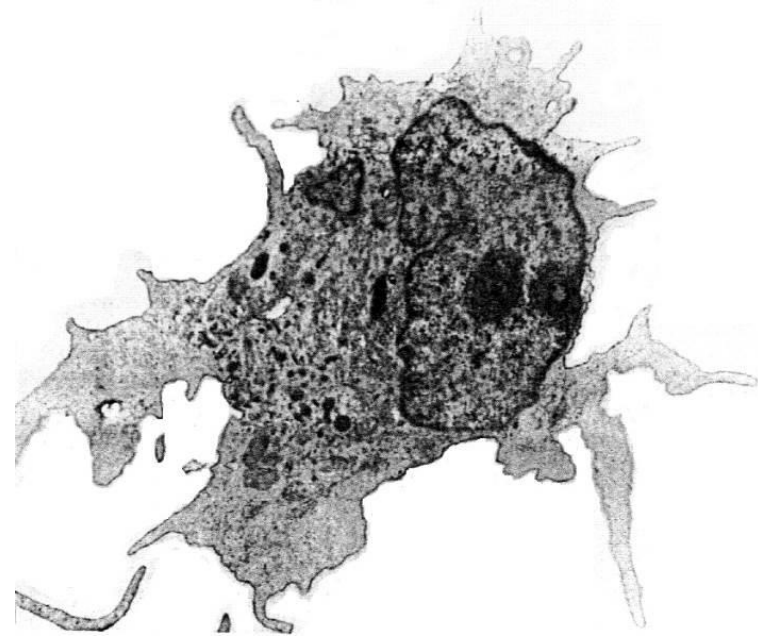
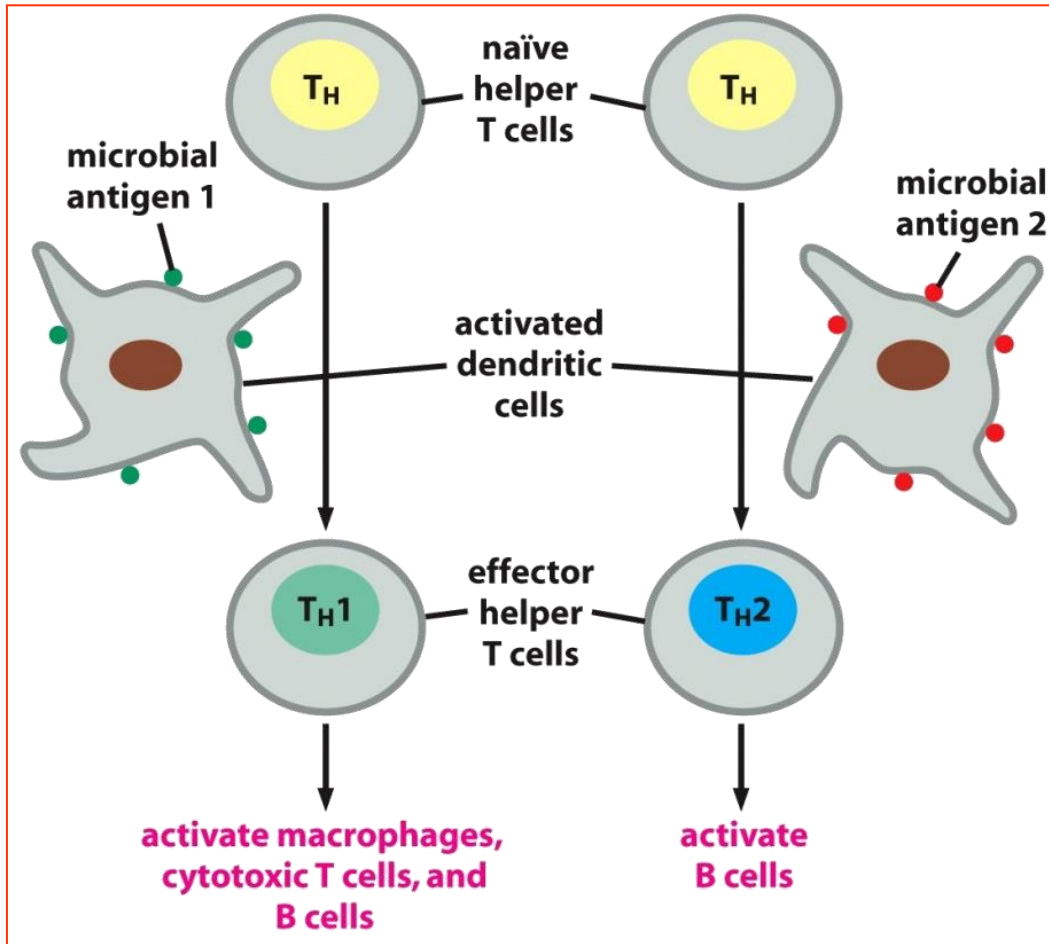
Estructura de los MHC

MHC I

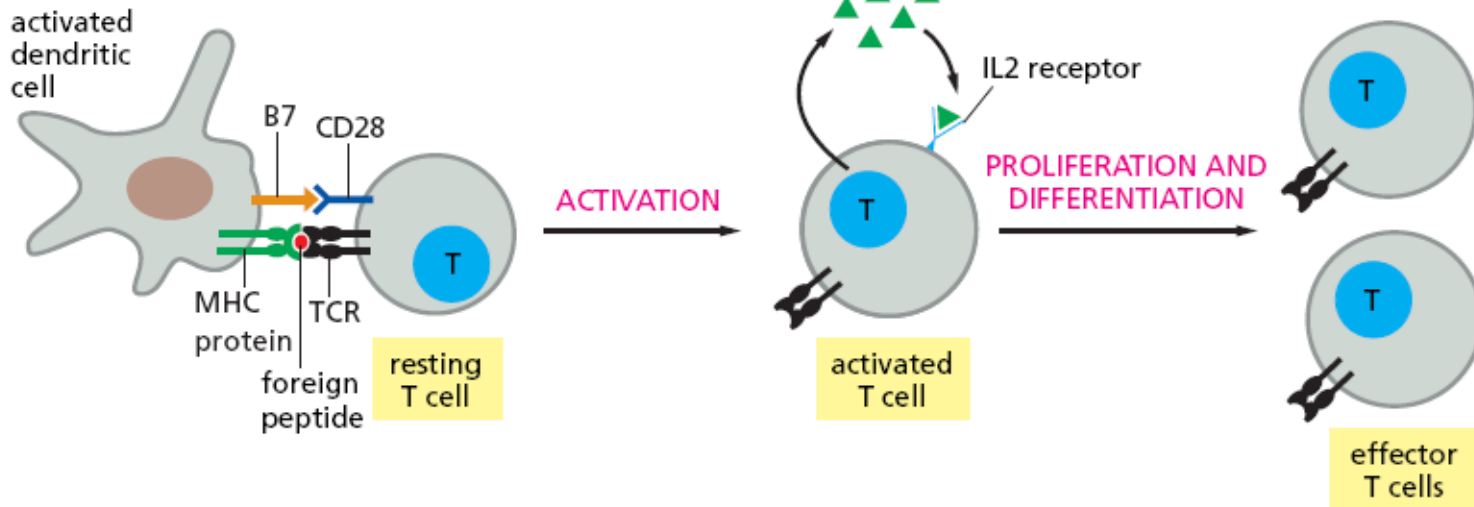
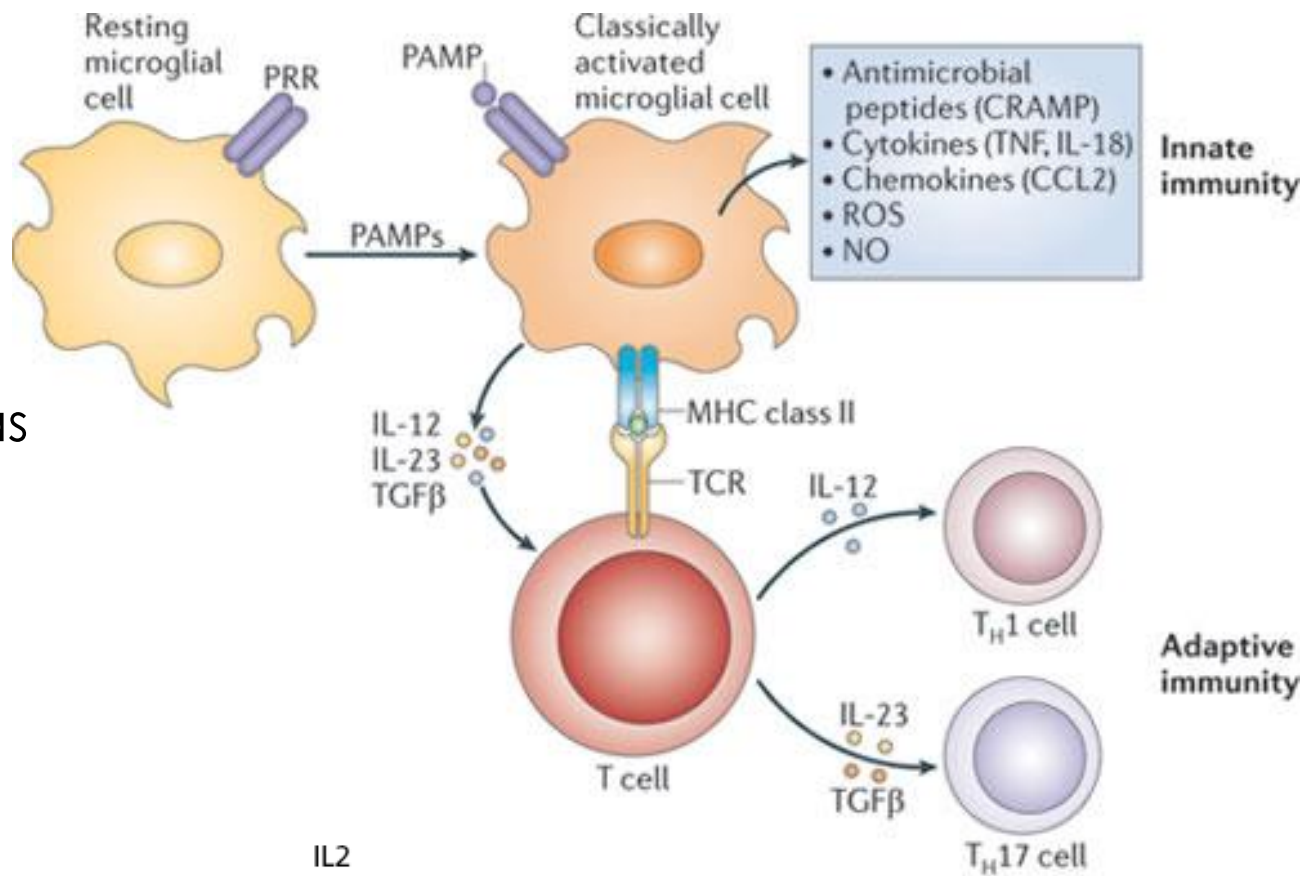




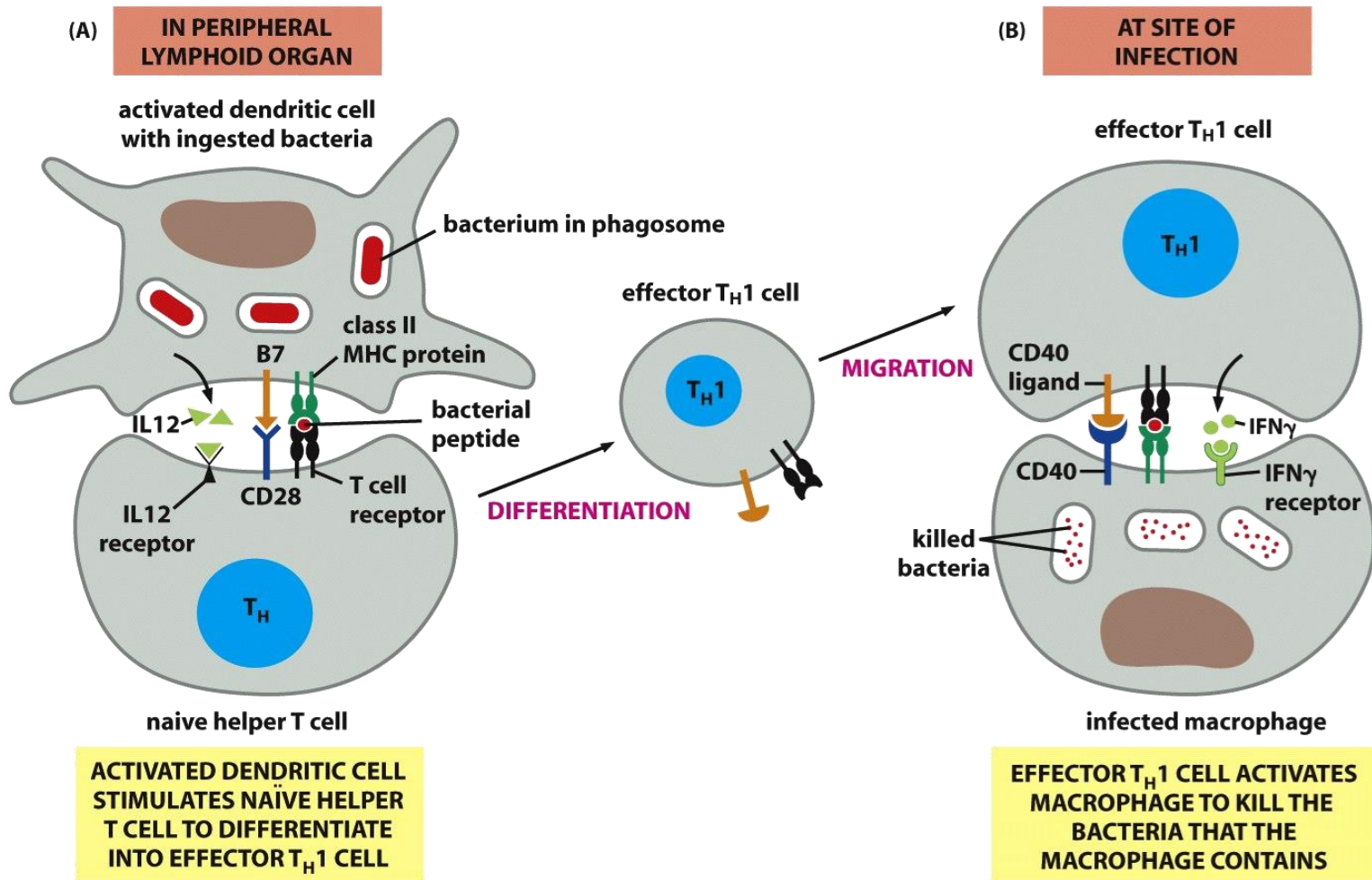
Activación de linfocitos T por células del sistema inmune innato



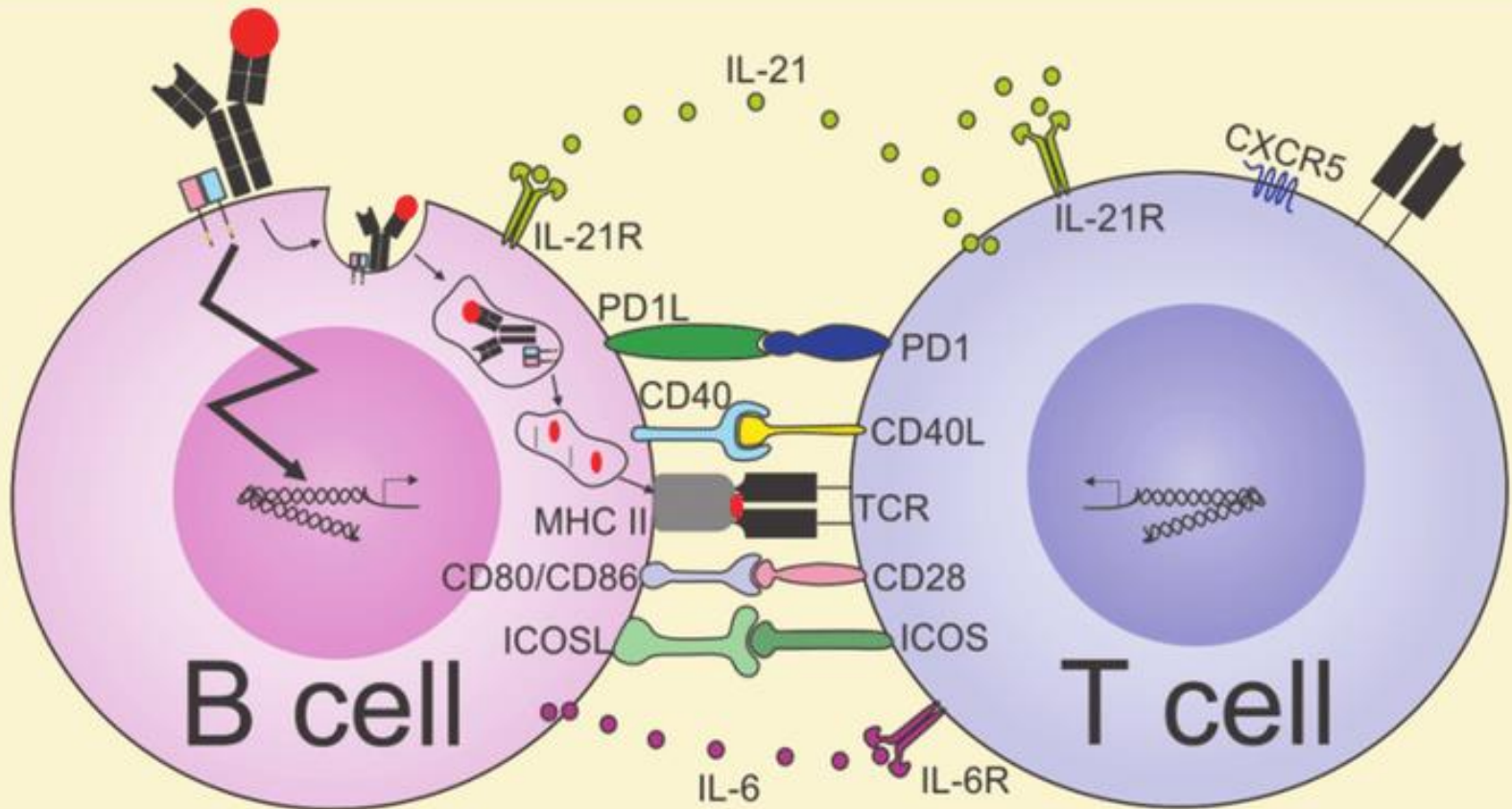
Activación de linfocitos T por células del sistema inmune innato





















Linfocitos T colaboradores (“helper”): Activación de fagocitos



Linfocitos T colaboradores ("helper"): Activación de linfocitos B

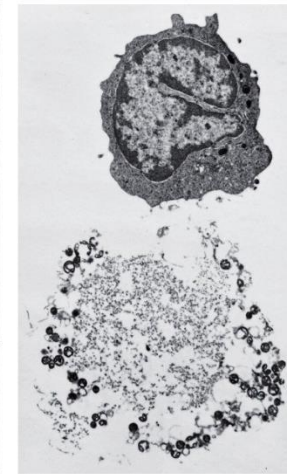


- | | | | |
|---|---|---|--|
|  MHC II |  ICOSL |  CD80/CD86 |  IL-21R |
|  TCR |  ICOS |  CD28 |  IL-21 |
|  Endosomal vesicle |  CD40 |  PD1 |  IL-6 |
|  BCR |  CD40L |  PD1L |  IL-6R |
|  Antigen | |  CXCR5 | |

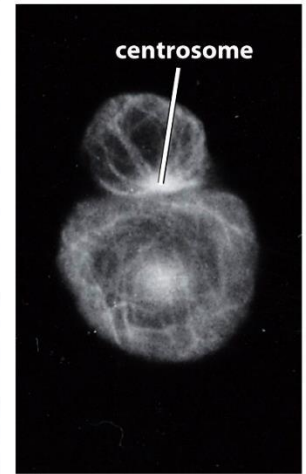
Linfocitos T citotóxicos



(A)



(B)



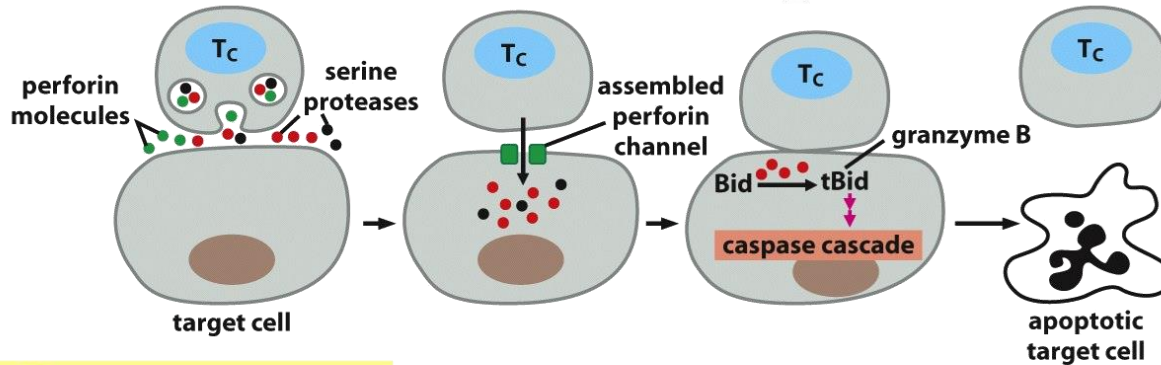
(C)

5 μ m

10 μ m

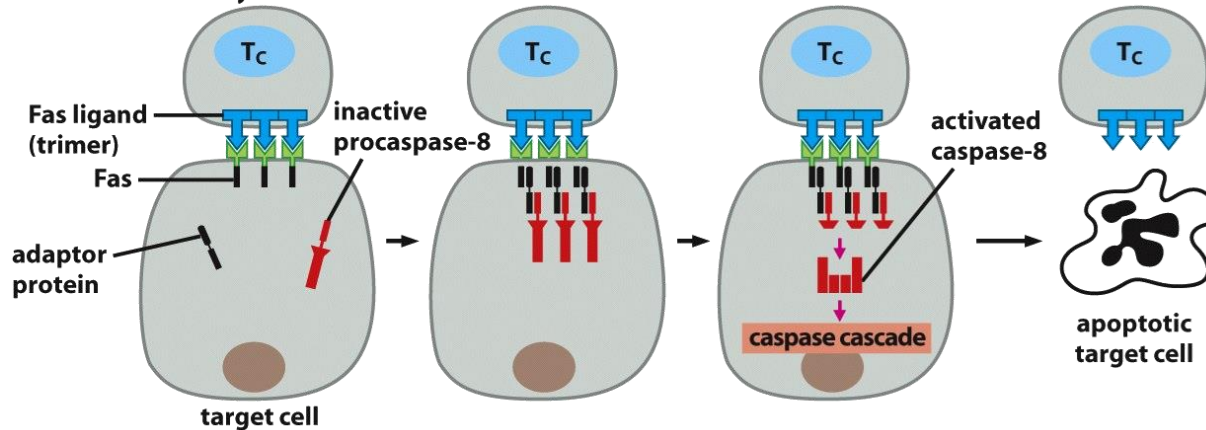
A Perforin-dependent killing

effector cytotoxic T cell



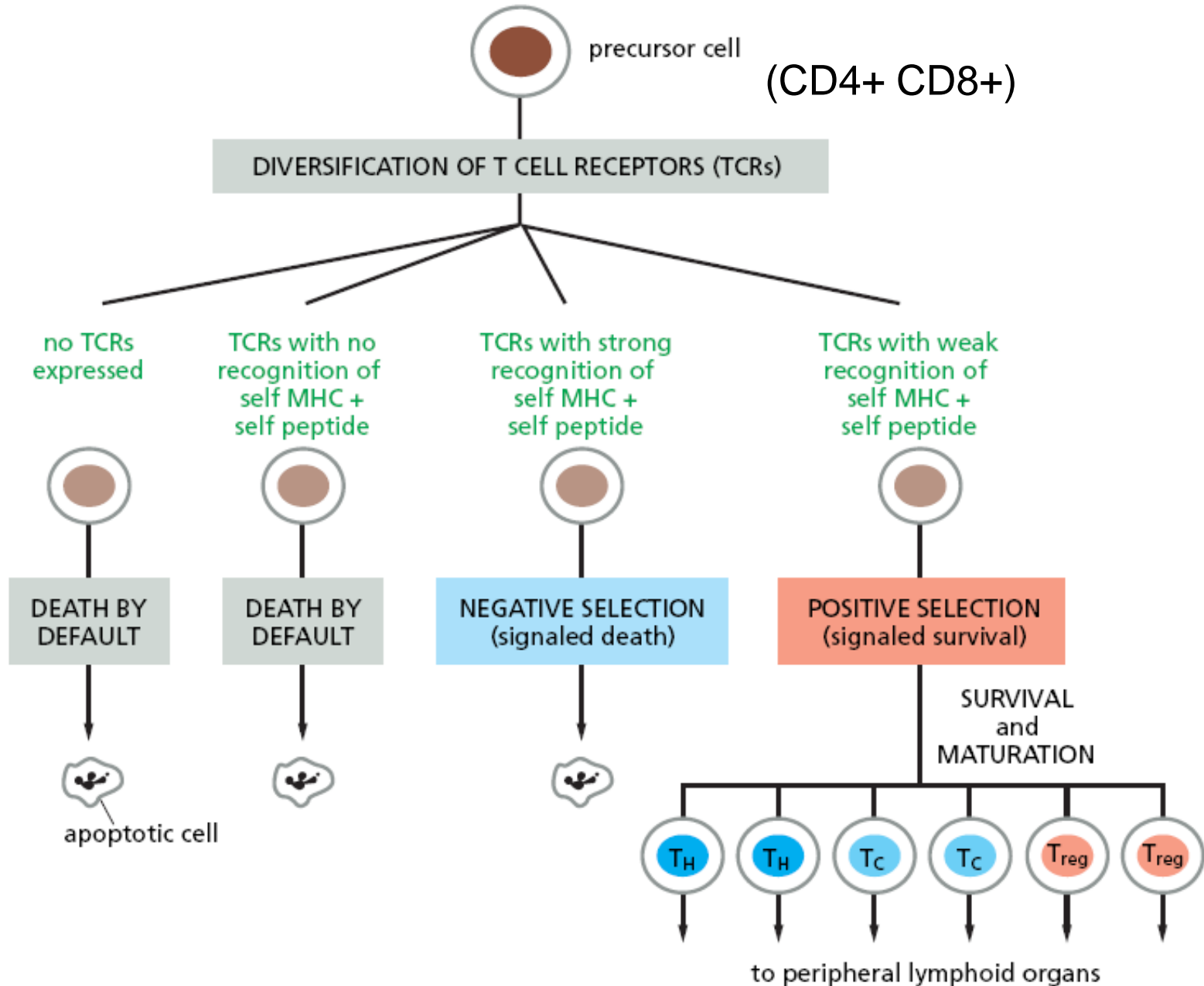
B Fas-dependent killing

effector cytotoxic T cell

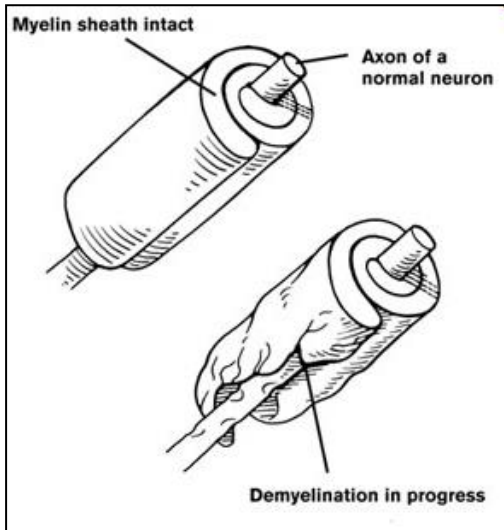
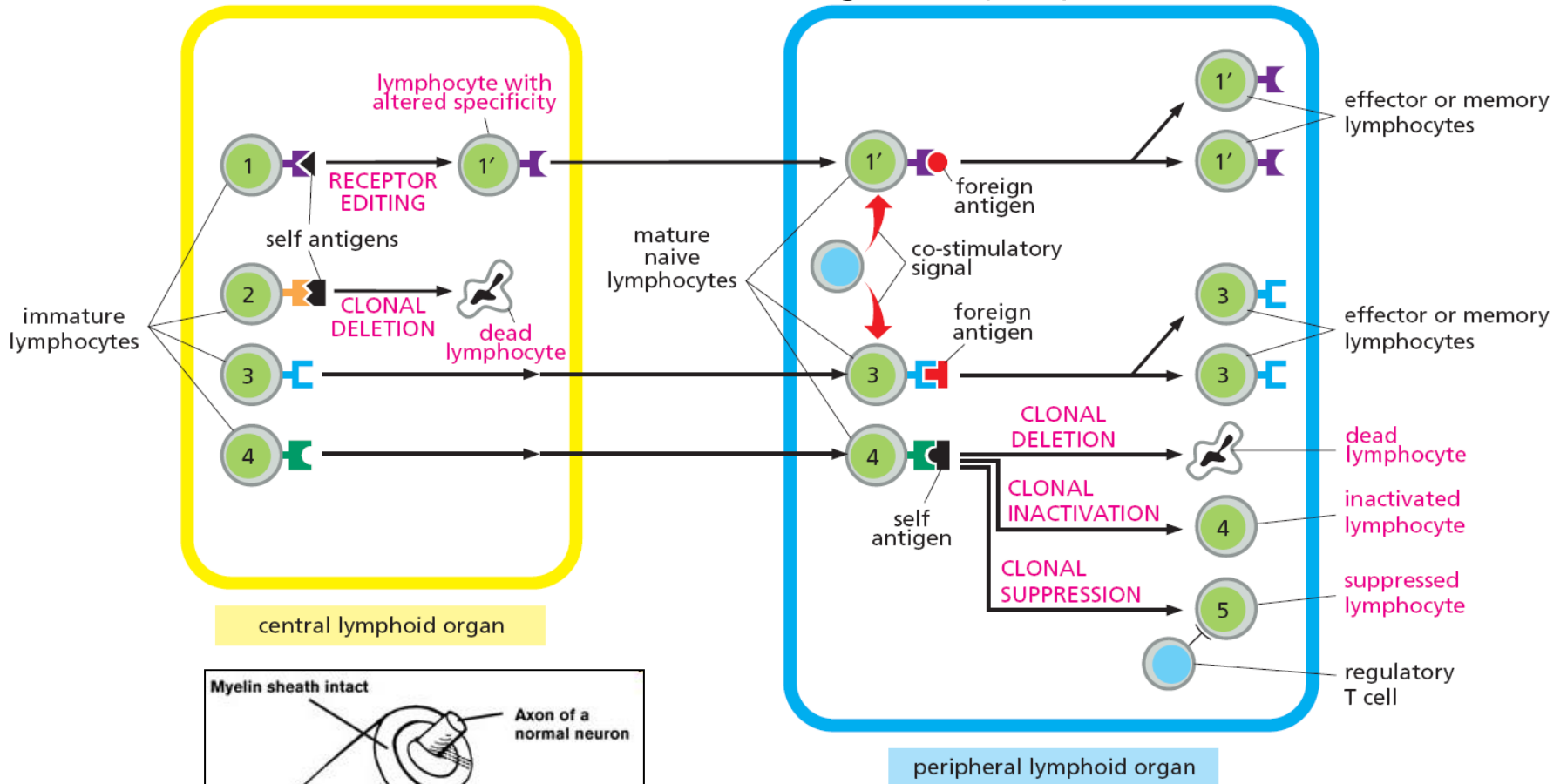


Jaume Barba, 1930
Cementerio Poblenou, Barcelona

Diferenciación de linfocitos T: selección positiva y negativa en el timo

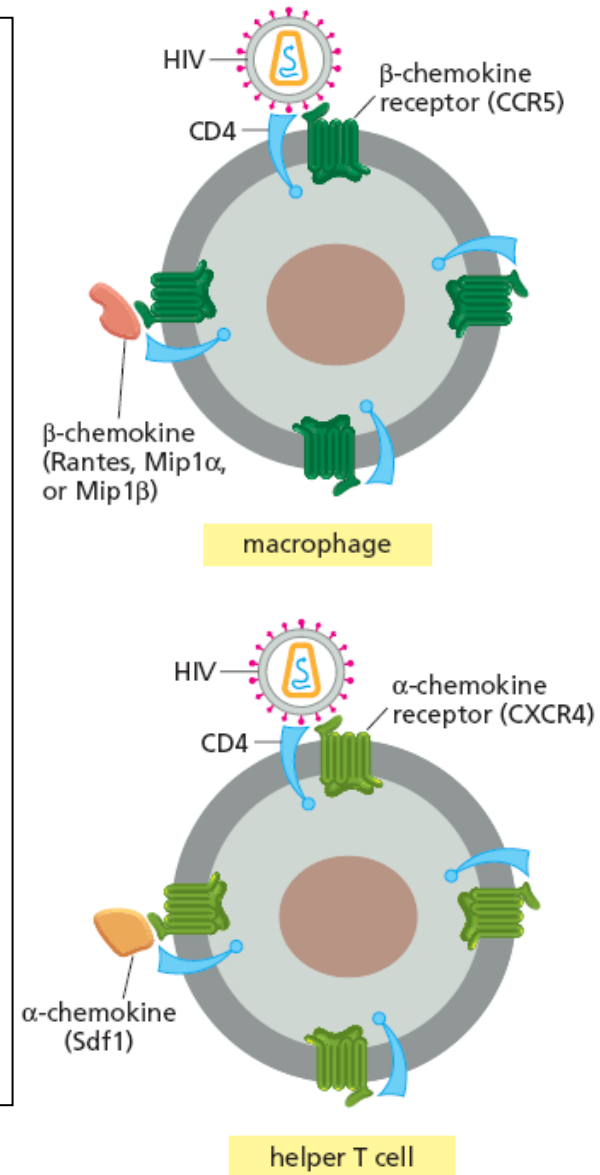
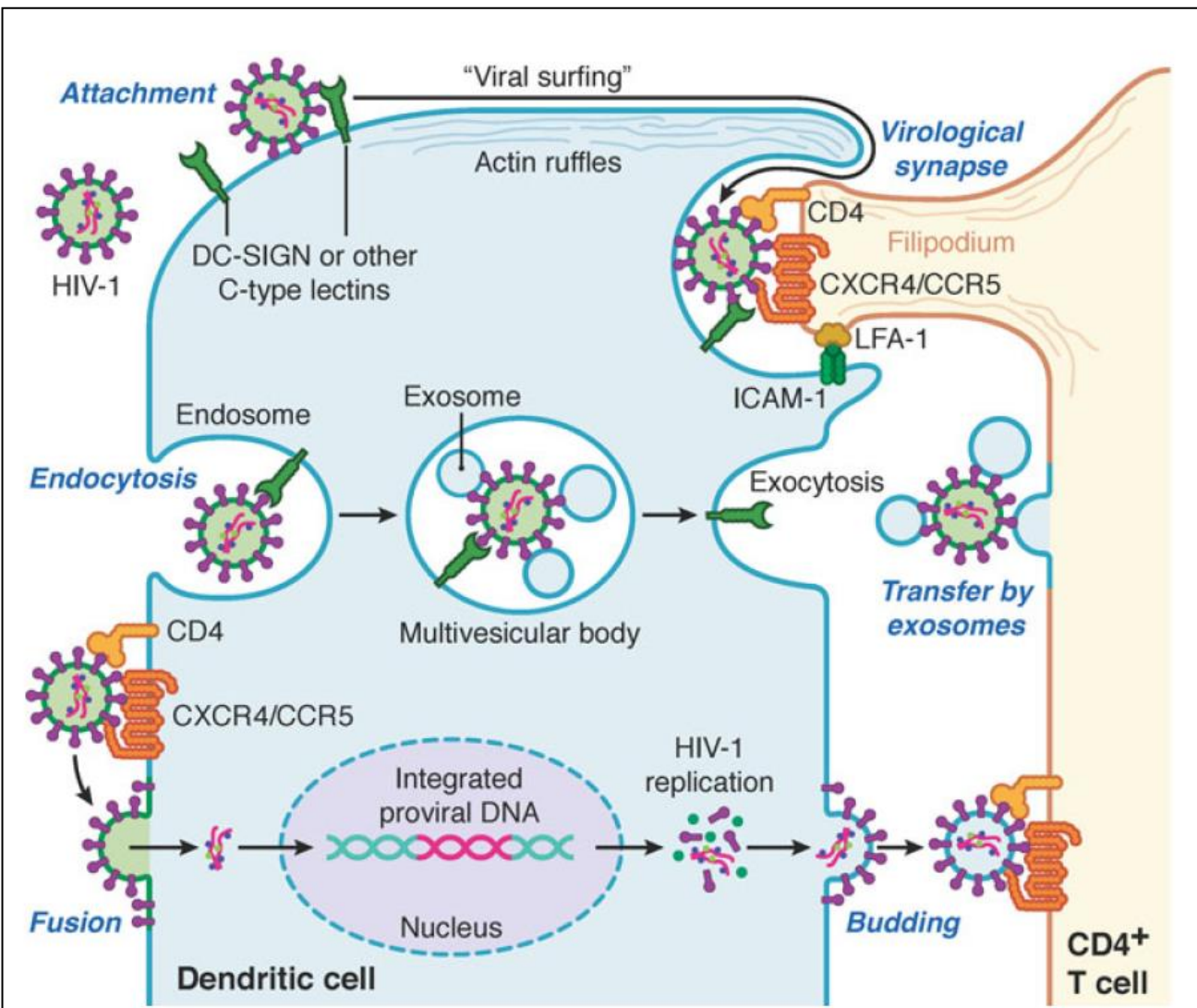


Tolerancia a antígenos propios



Esclerosis múltiple

Infección de linfocitos T CD4+ por HIV

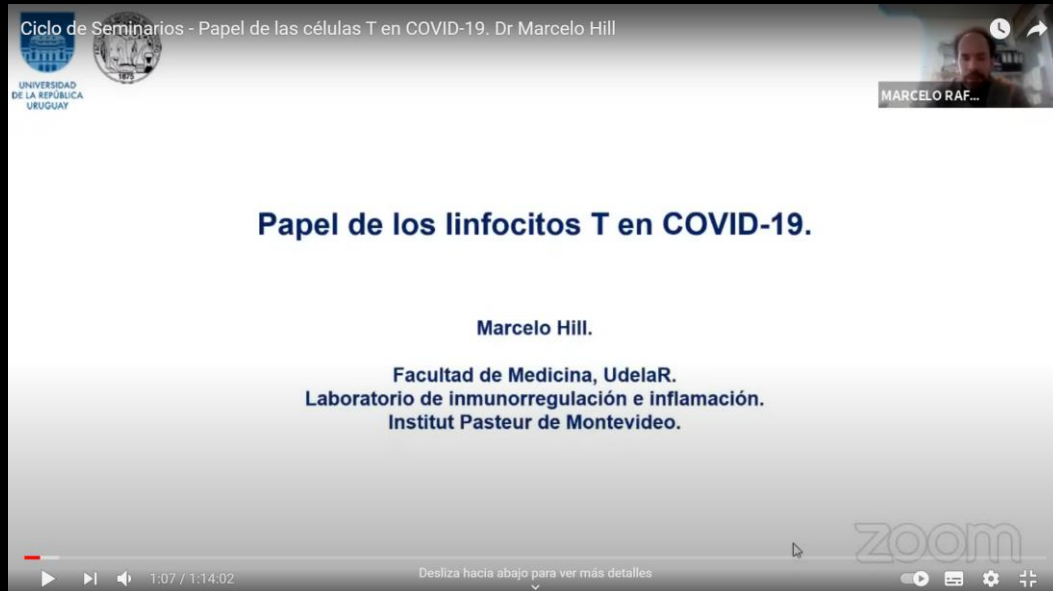


Preguntas pendientes a responder:

1- ¿En qué consisten los tres tipos principales de vacunas para SARS-CoV-2 usadas actualmente?

2- ¿Hay alguna base teórica para que las desarrolladas más recientemente sean más eficientes?

Charla recomendada:



Ciclo de Seminarios - Papel de las células T en COVID-19. Dr Marcelo Hill

UNIVERSIDAD DE LA REPÚBLICA URUGUAY

Papel de los linfocitos T en COVID-19.

Marcelo Hill.

Facultad de Medicina, UdelaR.
Laboratorio de inmunorregulación e inflamación.
Institut Pasteur de Montevideo.

zoom

1:07 / 1:14:02

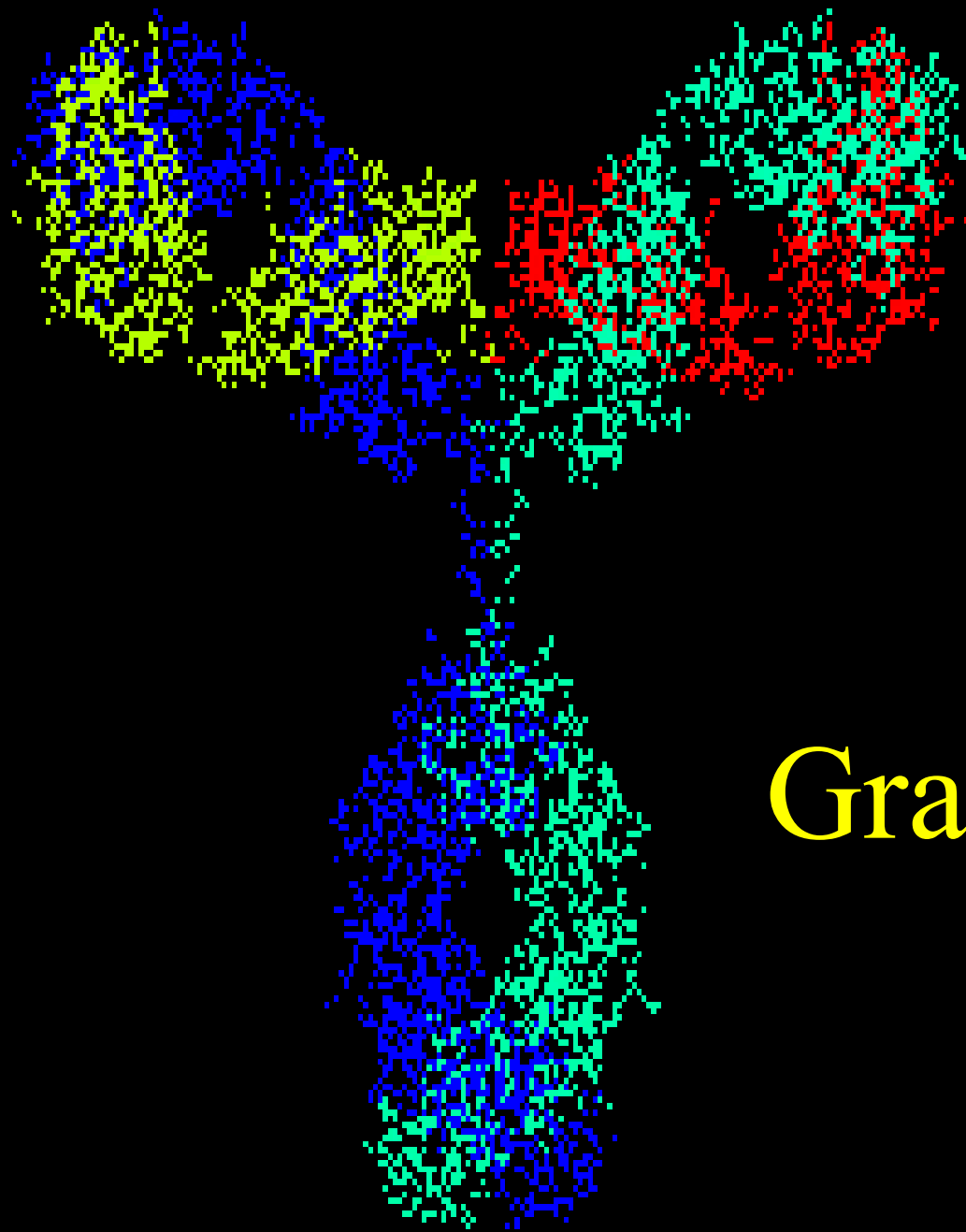
Desliza hacia abajo para ver más detalles

<https://youtu.be/q4RPDm6GR68>



The Cow-Pock — or — the Wonderful Effects of the New Inoculation! — vide. the Publications of the Anti-Vaccine Society.

Pub. June 10, 1858. by H. Murphy, 5, James Street.



Gracias