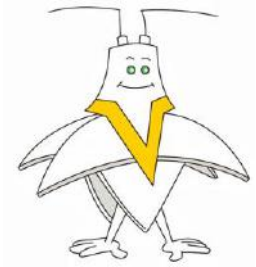
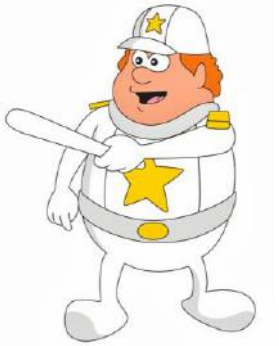
VACUNAS: Bases Inmunológicas

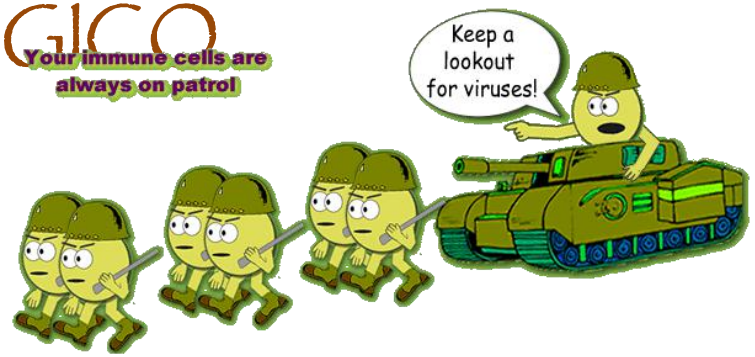


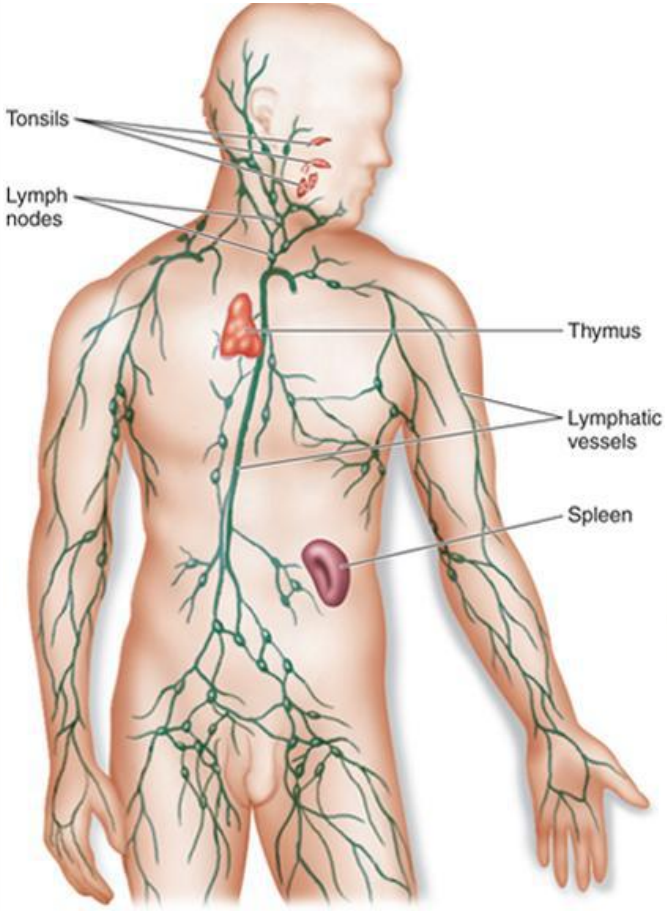


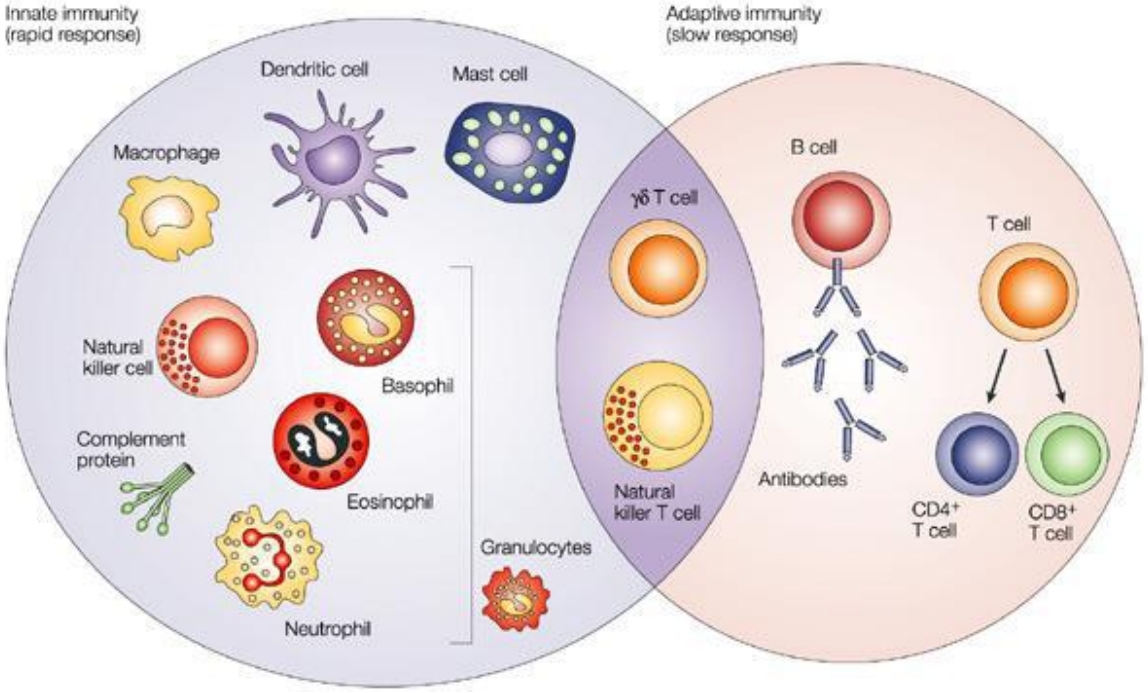
Jose Gómez Rial
F.E.A. Inmunología
Hospital Clínico Universitario de Santiago
Grupo GENVIP/IDIS

EL SISTEMA INMUNOLÓGICO

EL SISTEMA INMUNOLÓGICO

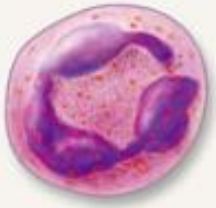


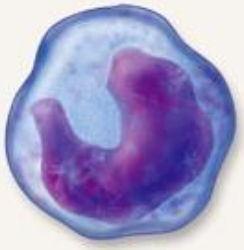
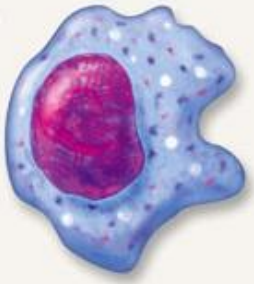




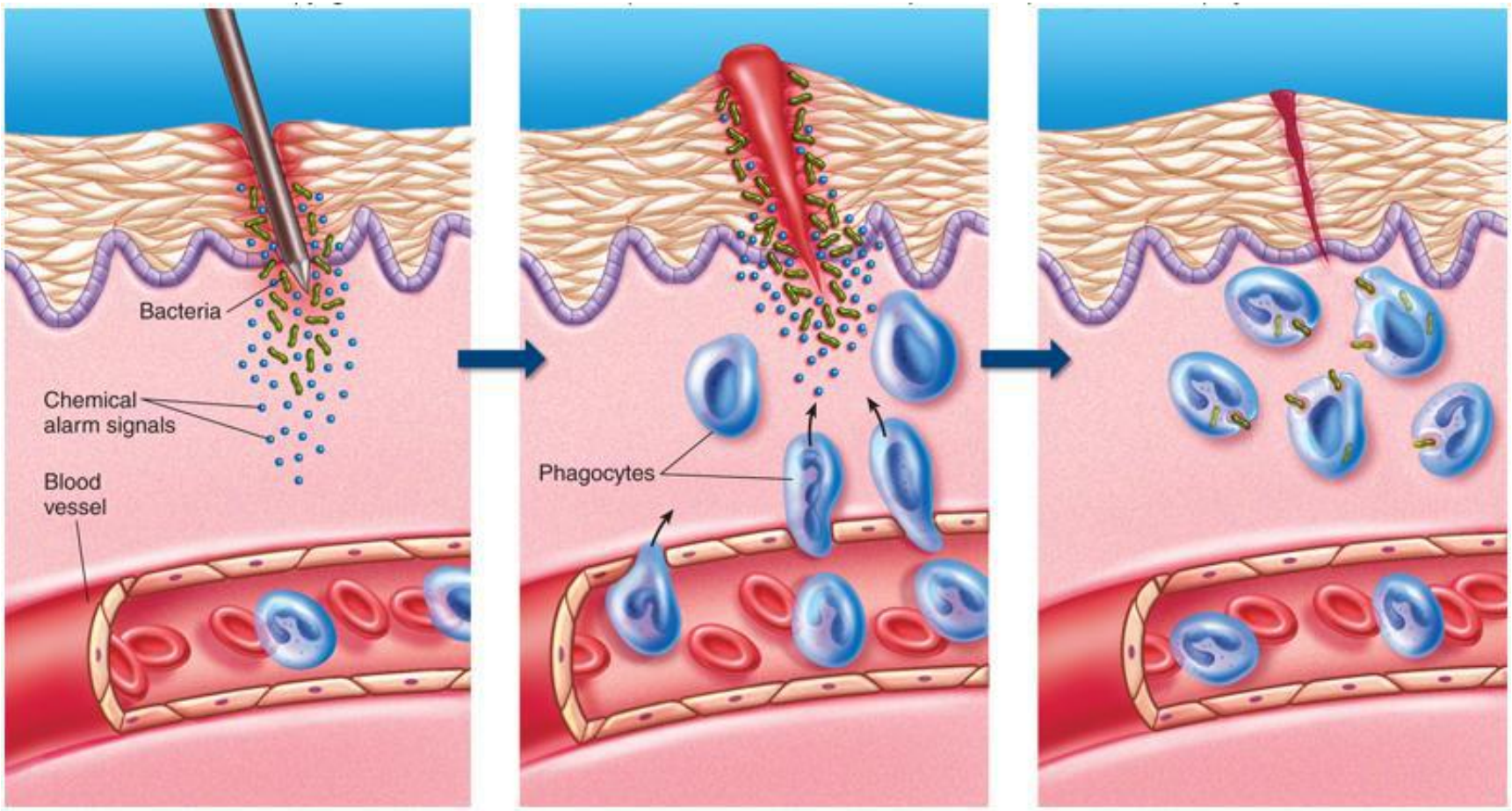
La respuesta inmunitaria se asienta sobre 4 pilares fundamentales.

LOS PROTAGONISTAS

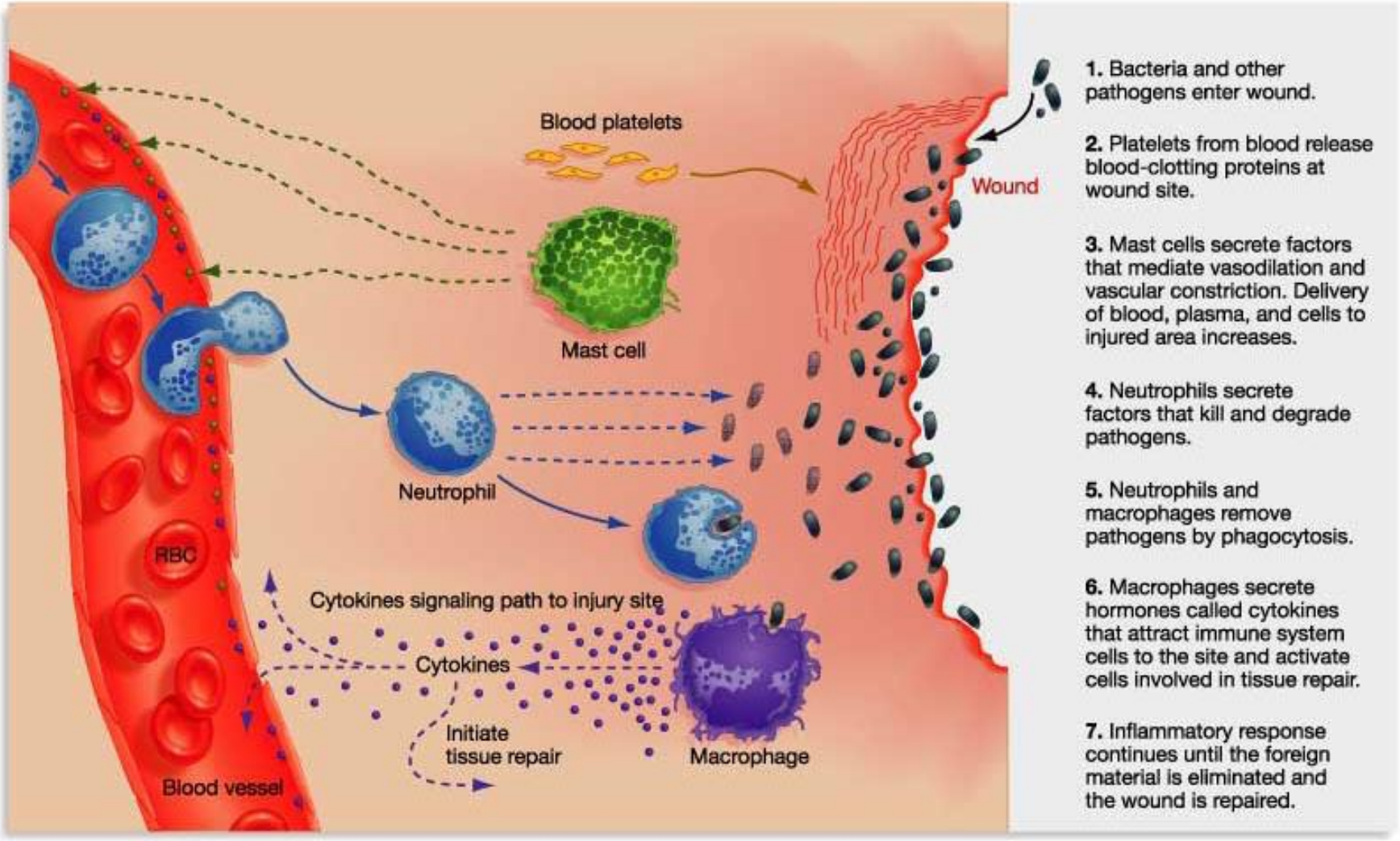
Helper T cell		Commander of the immune response; detects infection and sounds the alarm, initiating both T cell and B cell responses
Memory T cell		Provides a quick and effective response to an antigen previously encountered by the body
Cytotoxic T cell		Detects and kills infected body cells; recruited by helper T cells
Suppressor T cell		Dampens the activity of T and B cells, scaling back the defense after the infection has been checked
B cell		Precursor of plasma cell; specialized to recognize specific foreign antigens
Neutrophil		Engulfs invading bacteria and releases chemicals that kill neighboring bacteria
Plasma cell		Biochemical factory devoted to the production of antibodies directed against specific foreign antigens

Mast cell		Initiator of the inflammatory response, which aids the arrival of leukocytes at a site of infection; secretes histamine and is important in allergic responses
Monocyte		Precursor of macrophage
Macrophage		The body's first cellular line of defense; also serves as antigen-presenting cell to B and T cells and engulfs antibody-covered cells
Natural killer cell		Recognizes and kills infected body cells; natural killer cell detects and kills cells infected by a broad range of invaders

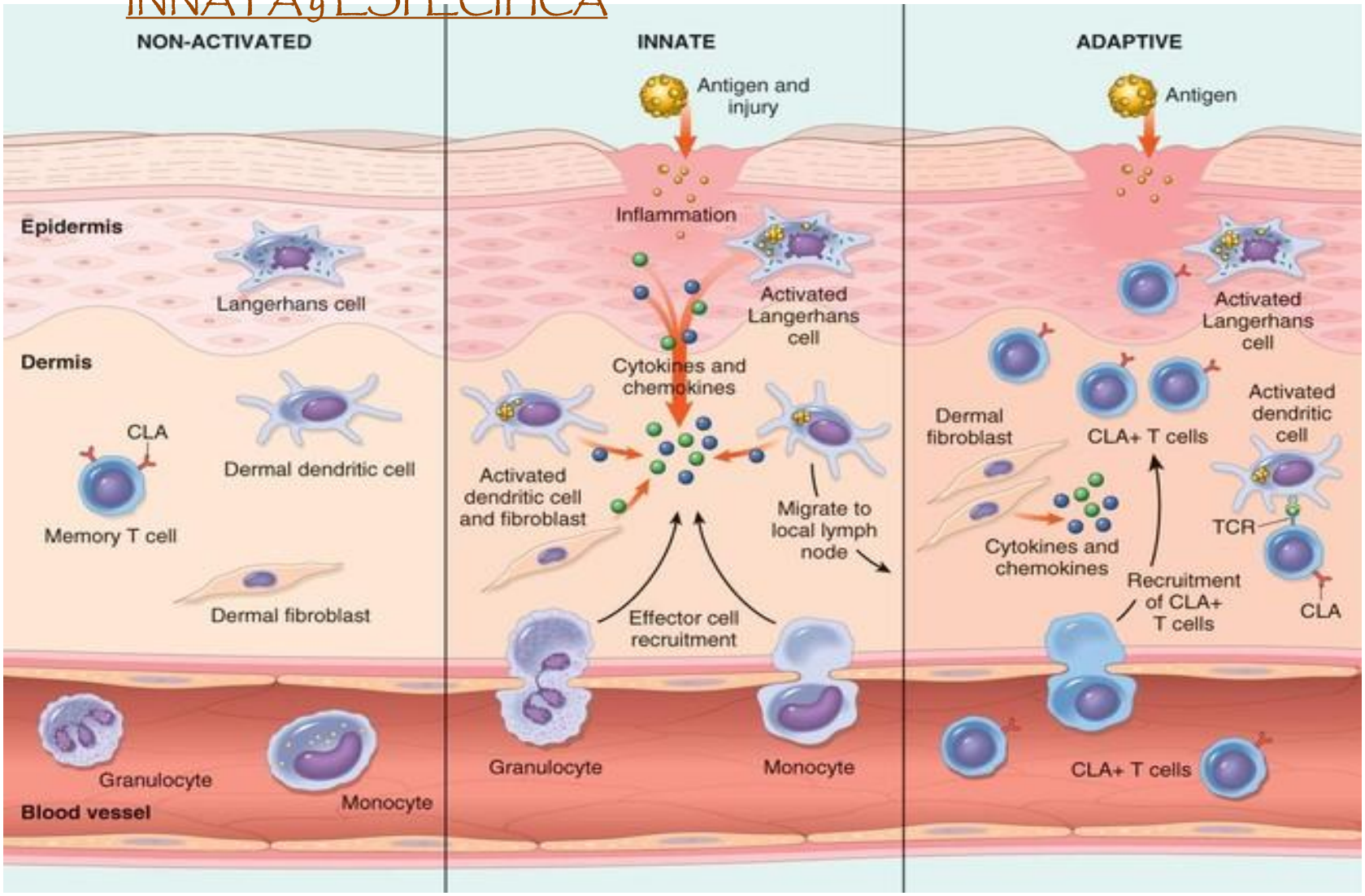
LA RESPUESTA INMUNITARIA: el inicio



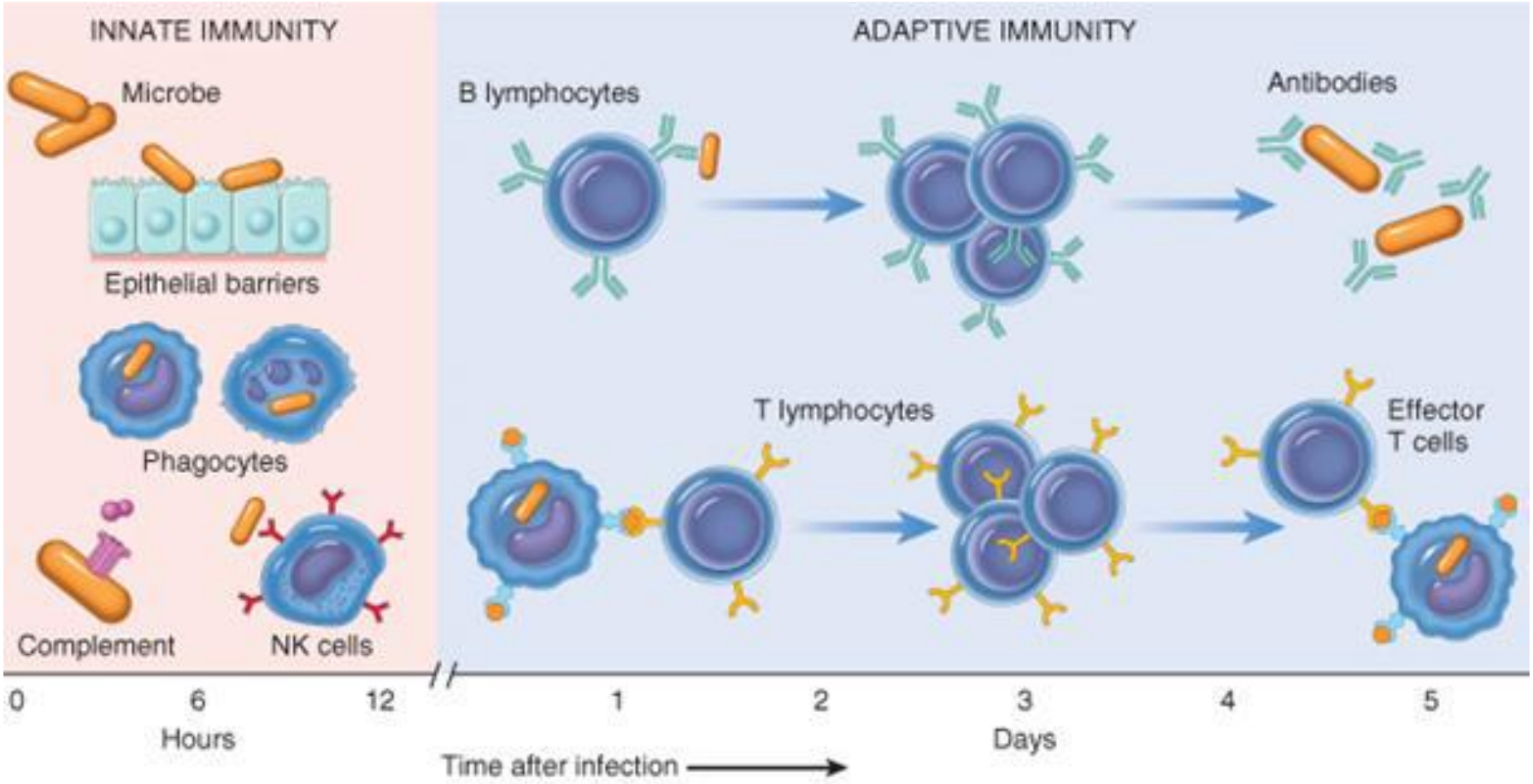
LA RESPUESTA INMUNITARIA: la respuesta inflamatoria (innata)



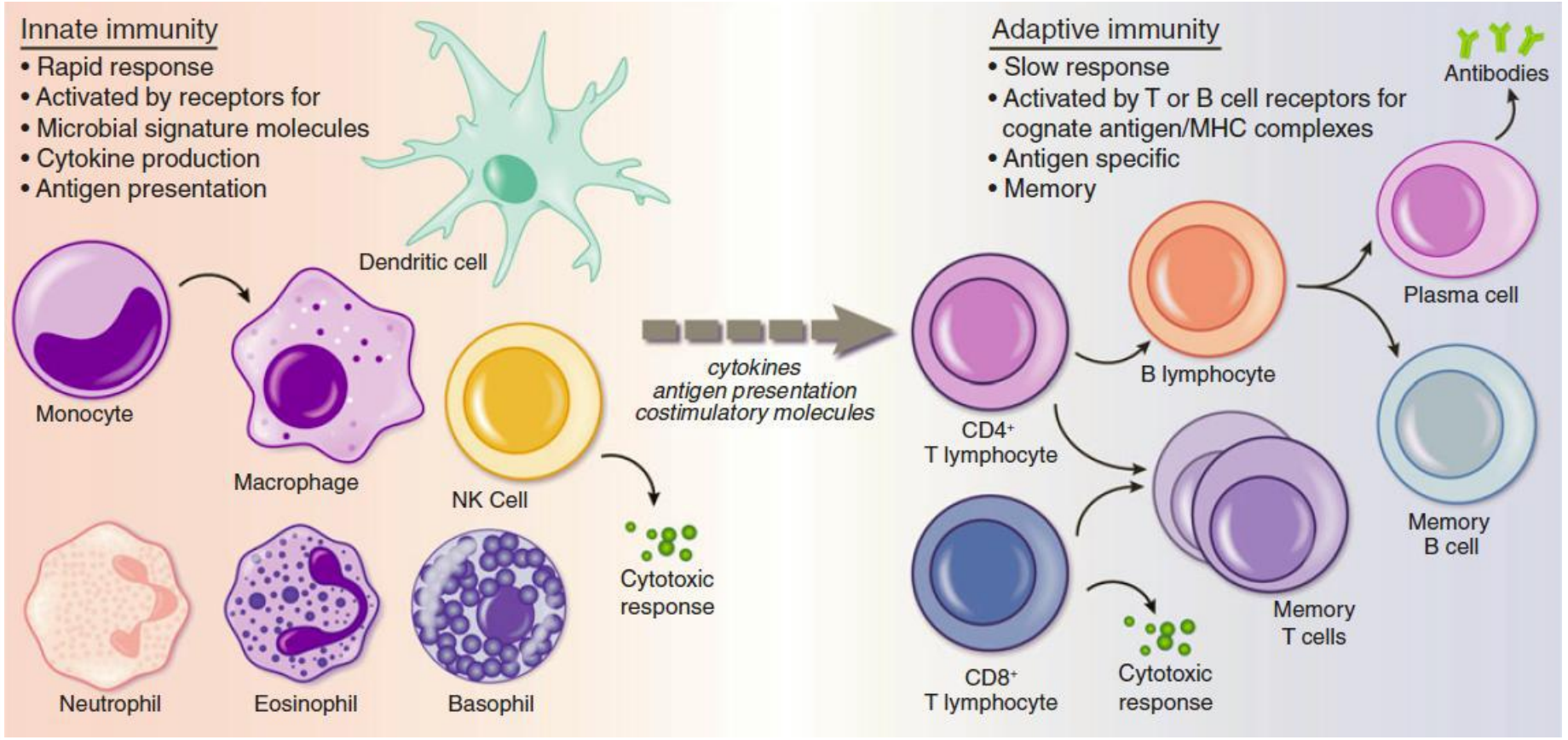
LA RESPUESTA INMUNITARIA: RESPUESTA INNATA y ESPECÍFICA

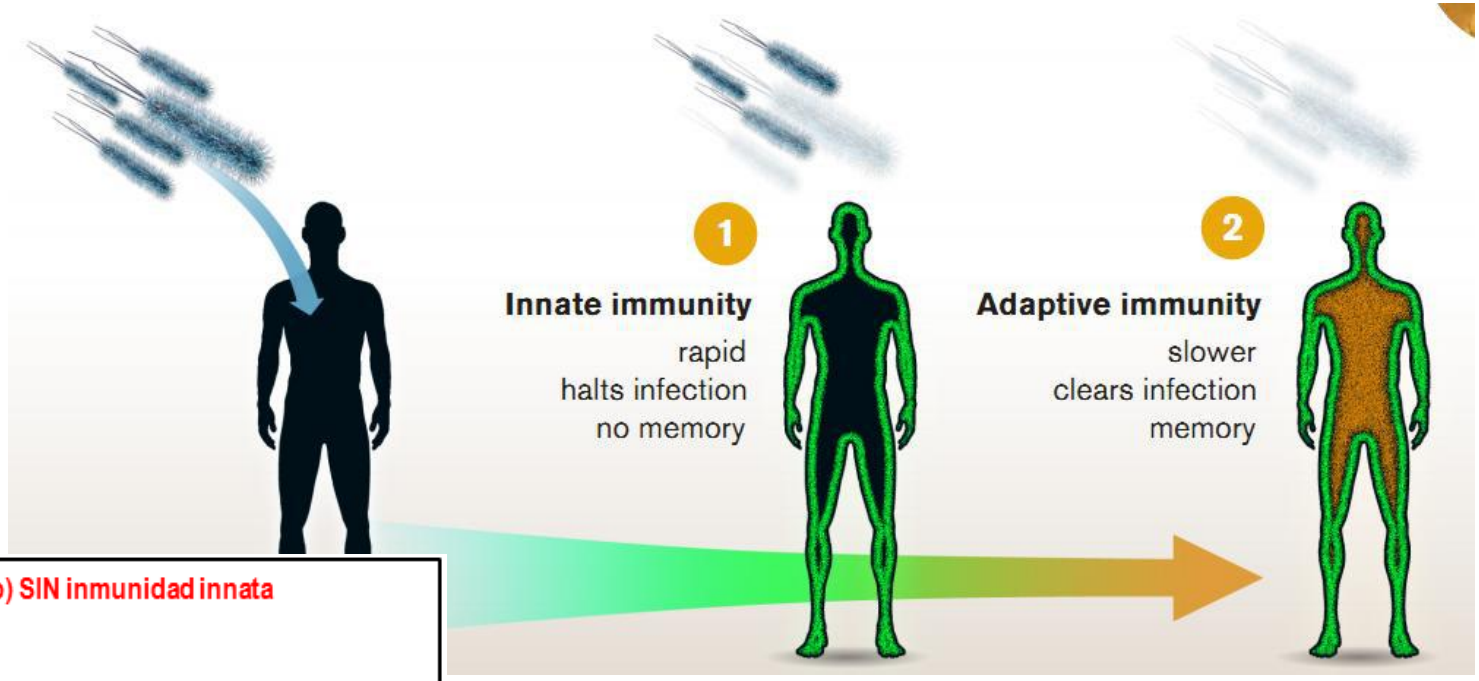


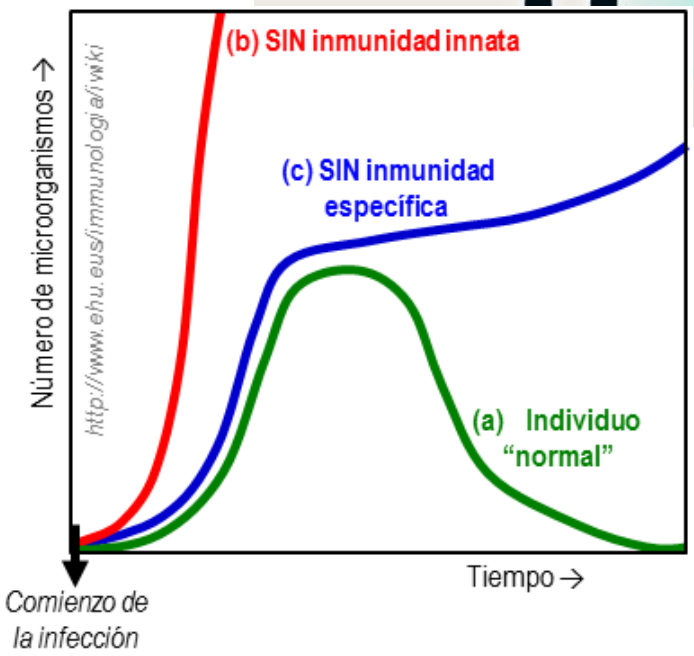
INTEGRACIÓN DE LA RESPUESTA INNATA y ESPECÍFICA



INTEGRACIÓN DE LA RESPUESTA INNATA y ESPECÍFICA



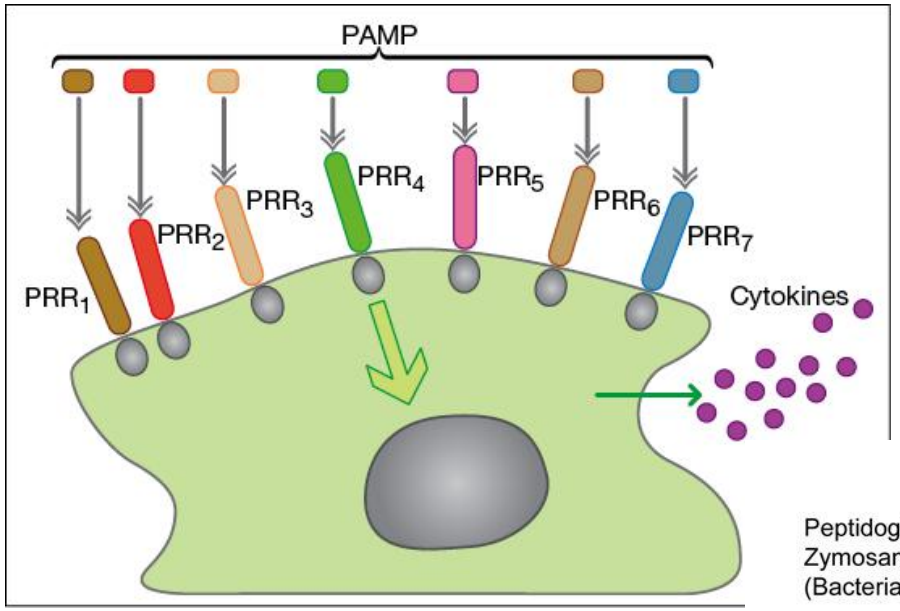


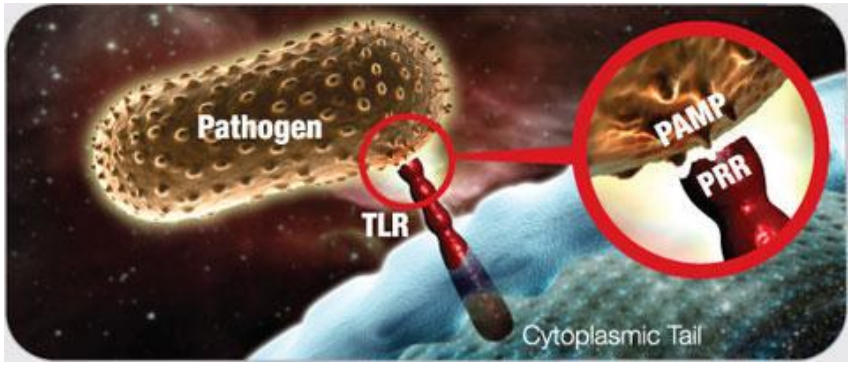


INMUNIDAD INNATA/ INMUNIDAD ESPECÍFICA

RESPUESTA INTEGRADA y COORDINADA

RESPUESTA INNATA



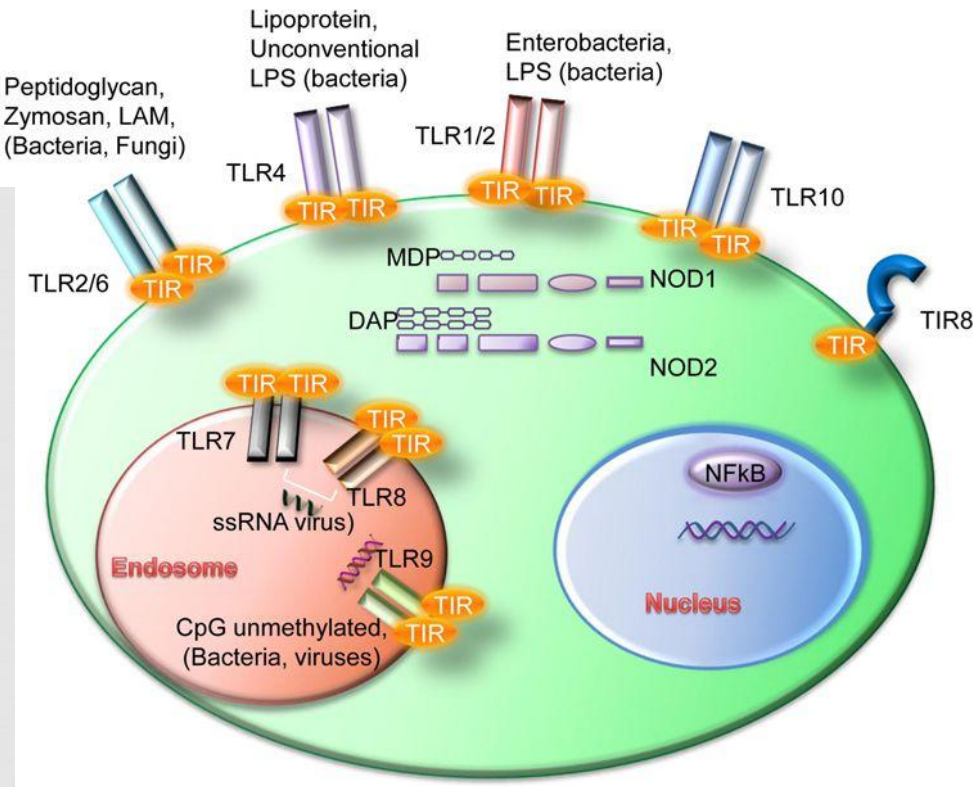


PAMPS

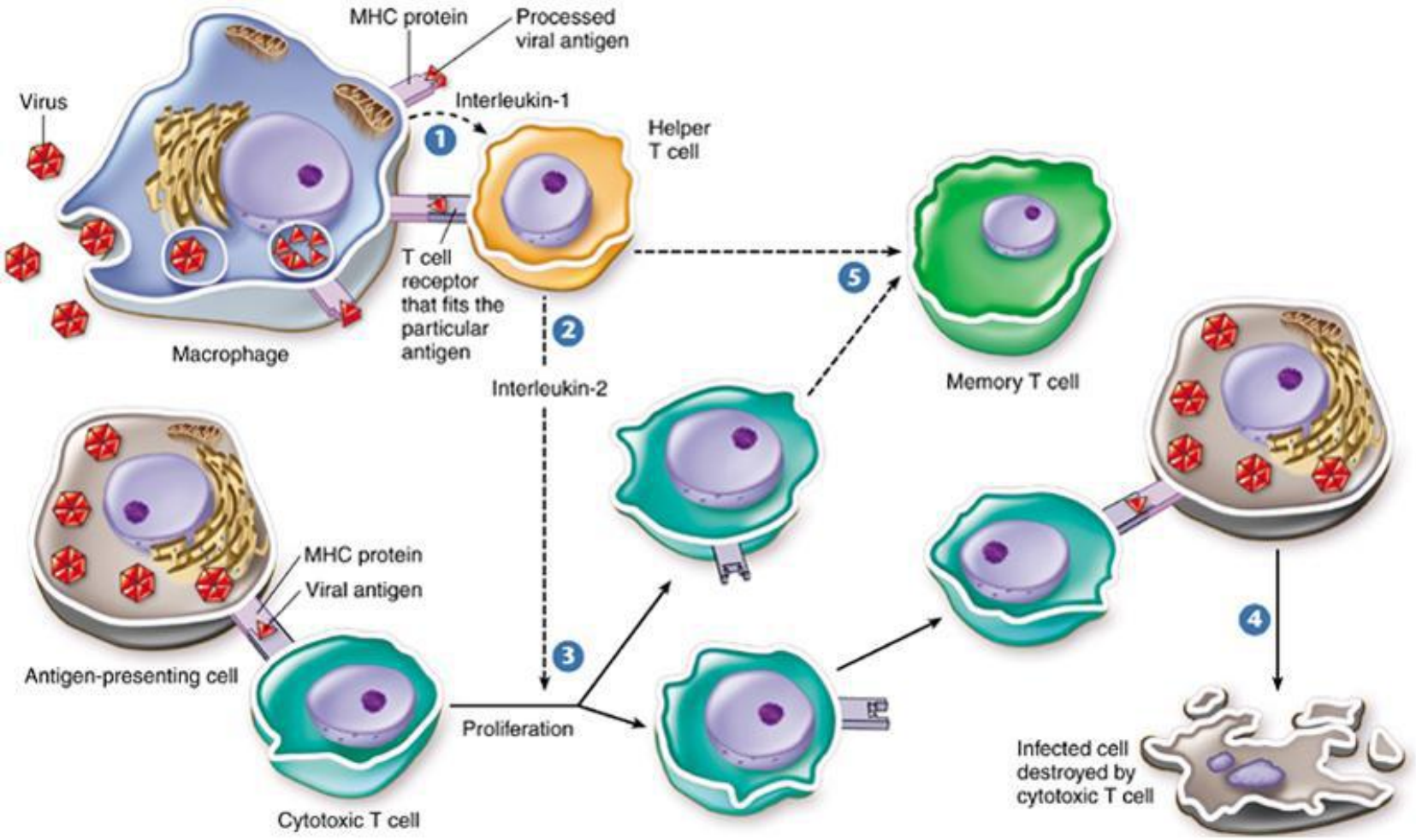
PAMPS recognized by the innate immune system:

Cell wall constituents or microbial nucleic acids

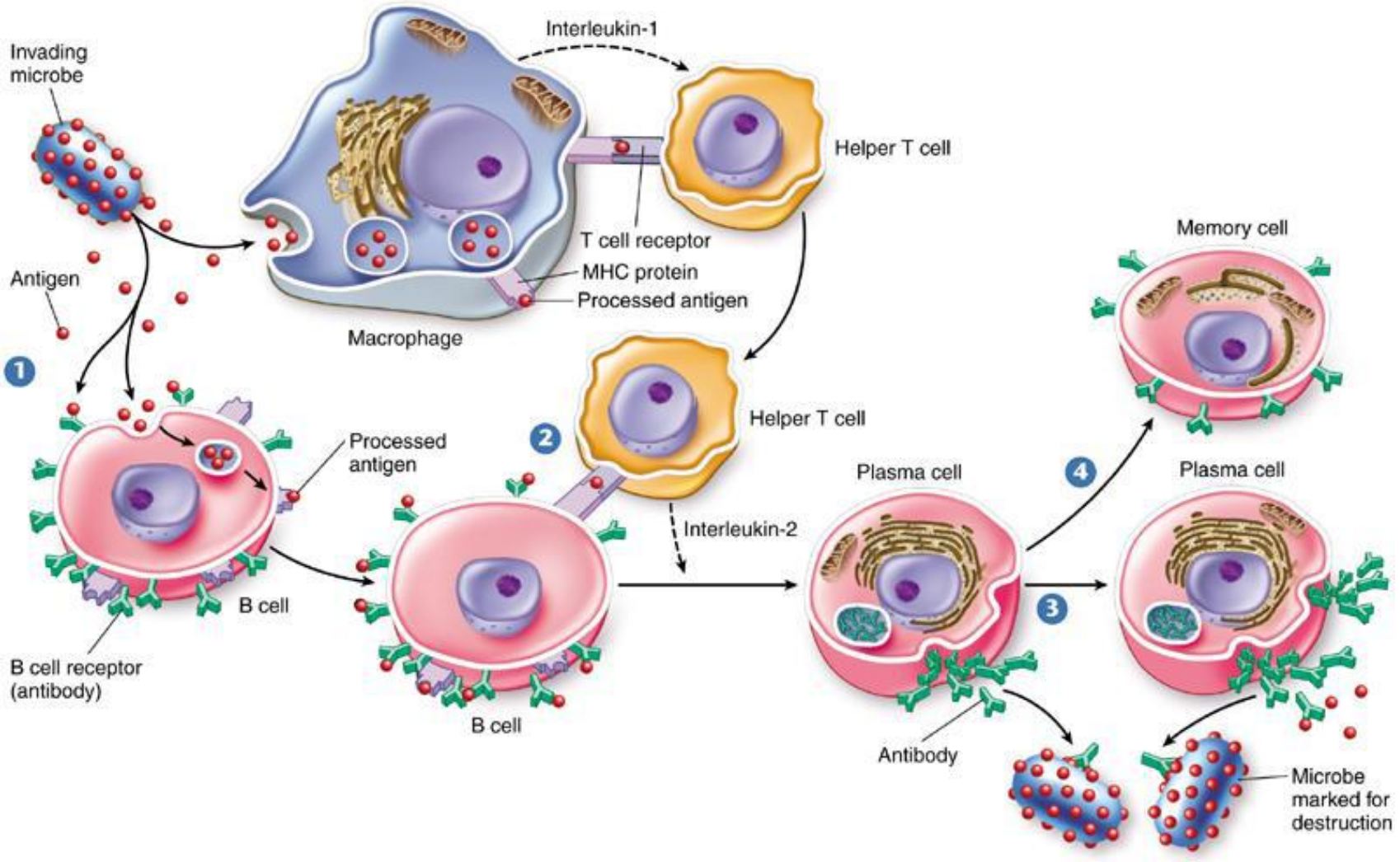
1. **Lipopolysaccharide** (LPS) from the gram -ve cell wall.
2. **Peptidoglycan** found abundantly in the gram-positive cell wall and to a lesser degree in the gram-negative cell wall .
3. **Lipoteichoic acids** in the gram +ve bacterial cell walls
4. **Lipoarabinomannum** (LAM) in mycobacterial wall
5. **Mannose-rich glycans** (common in microbial glycoproteins and glycolipids but rare in those of humans).
6. **Flagellin** found in bacterial flagella.
7. **Pilin** from bacterial pili.
8. **Bacterial and viral nucleic acid**. Bacterial and viral genomes contain a high frequency of unmethylated cytosine-guanine dinucleotide sequences (a cytosine lacking a methyl or CH3 group and located adjacent to a guanine). Mammalian DNA has a low frequency of cytosine-guanine dinucleotides and most are methylated.
9. **Double-stranded RNA** unique to most viruses.
10. **Lipoteichoic acids, glycolipids, and zymosan** from yeast cell walls.



RESPUESTA ESPECÍFICA (CELULAR)



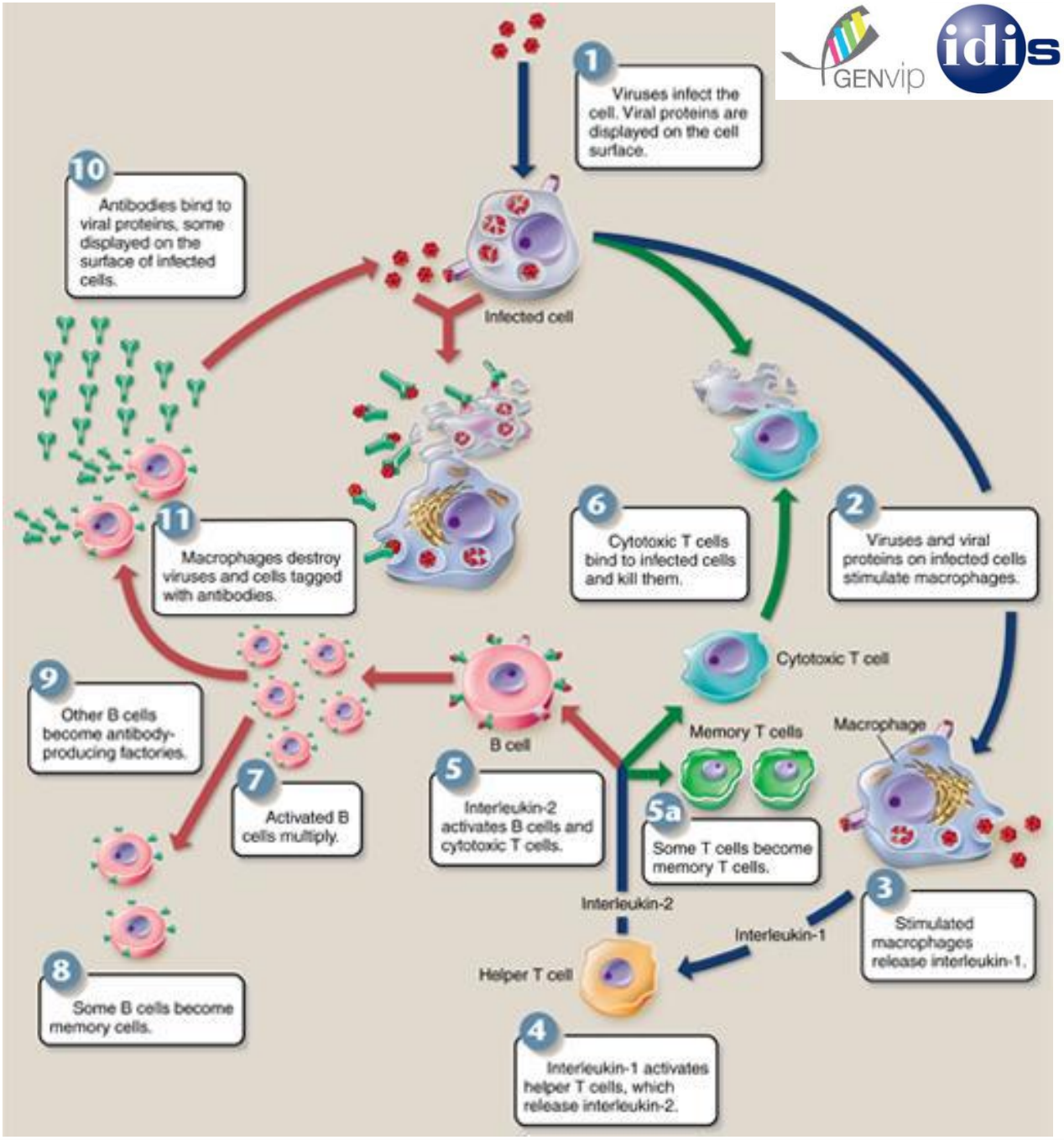
RESPUESTA ESPECÍFICA (HUMORAL)

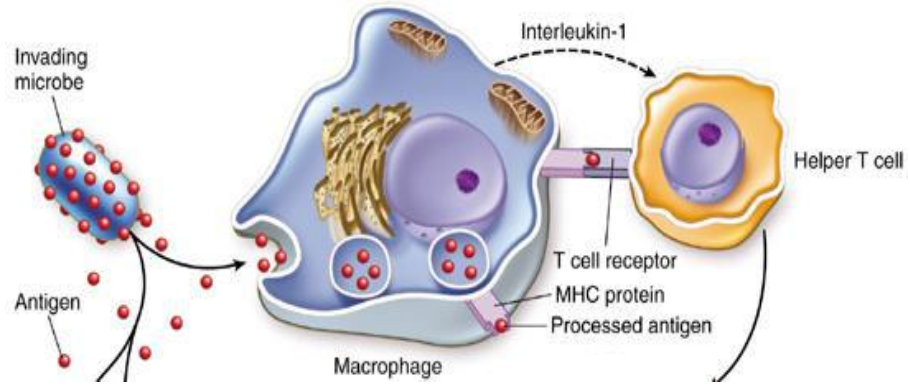


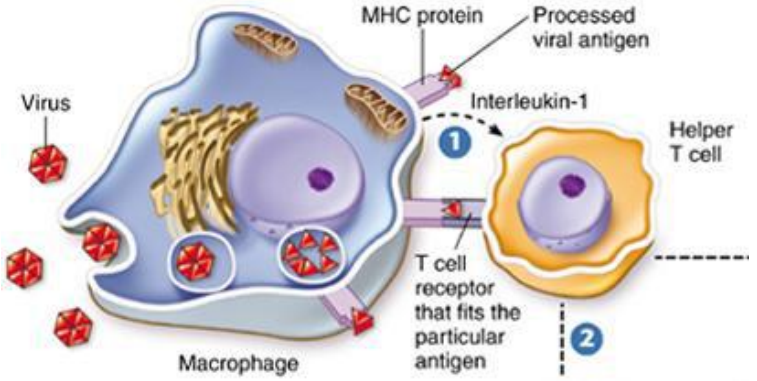
INNATA

ESPECIF CELULAR

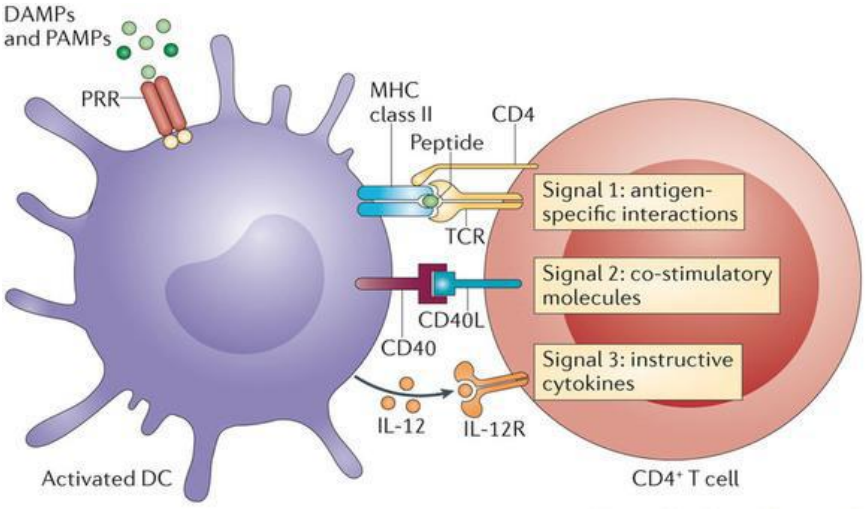
ESPECIF HUMORAL

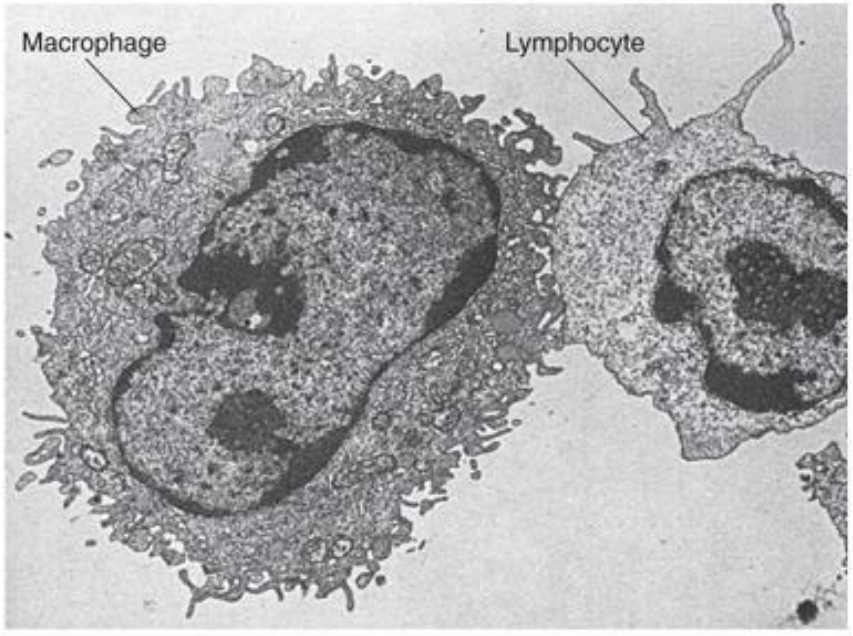




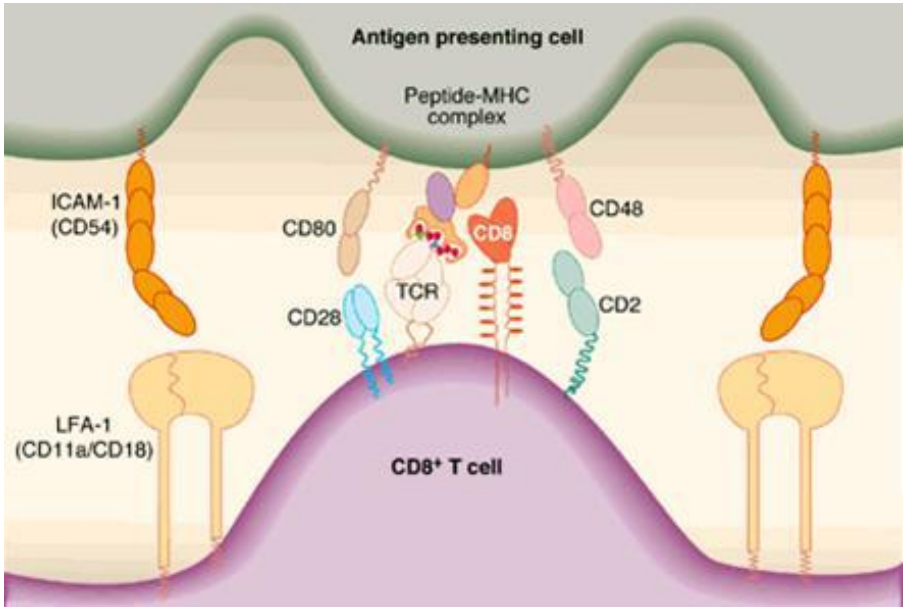


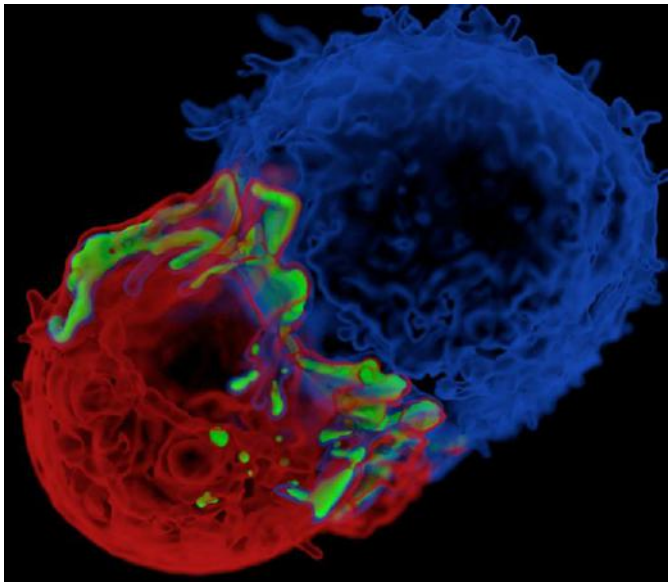
UNIÓN MACRÓFAGO - LINFOCITO T *helper*

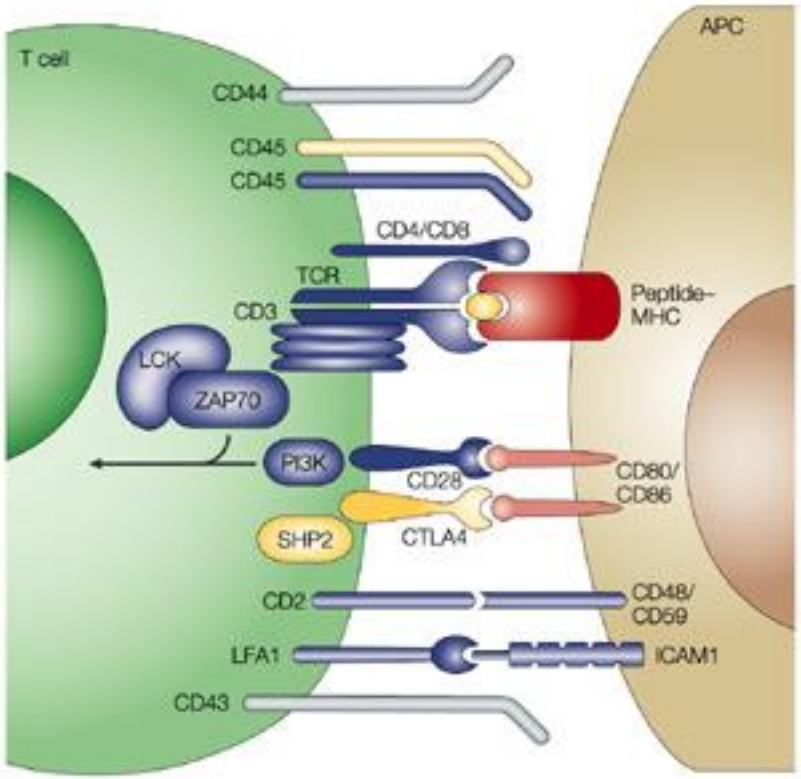




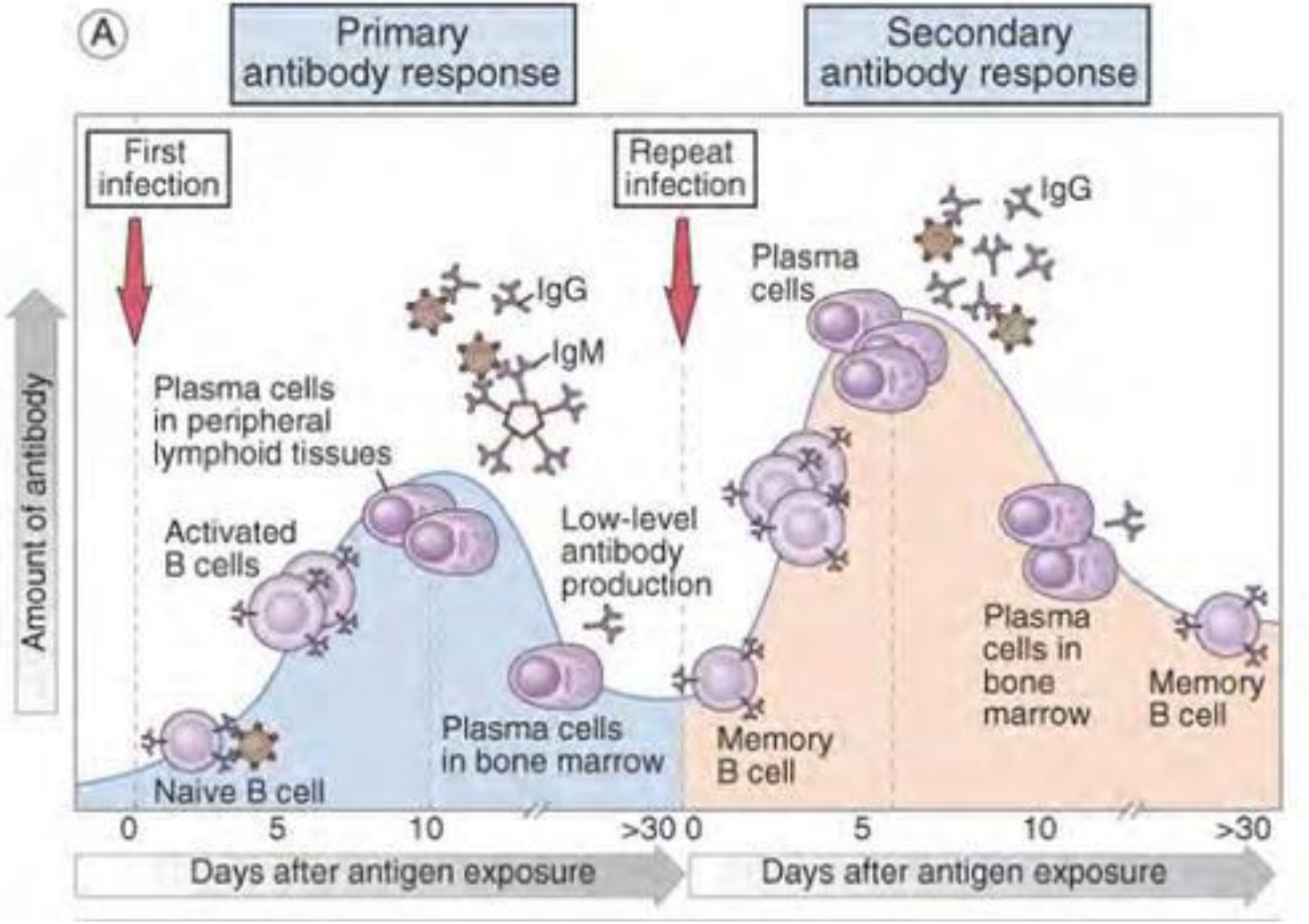
SINAPSIS INMUNOLÓGICA



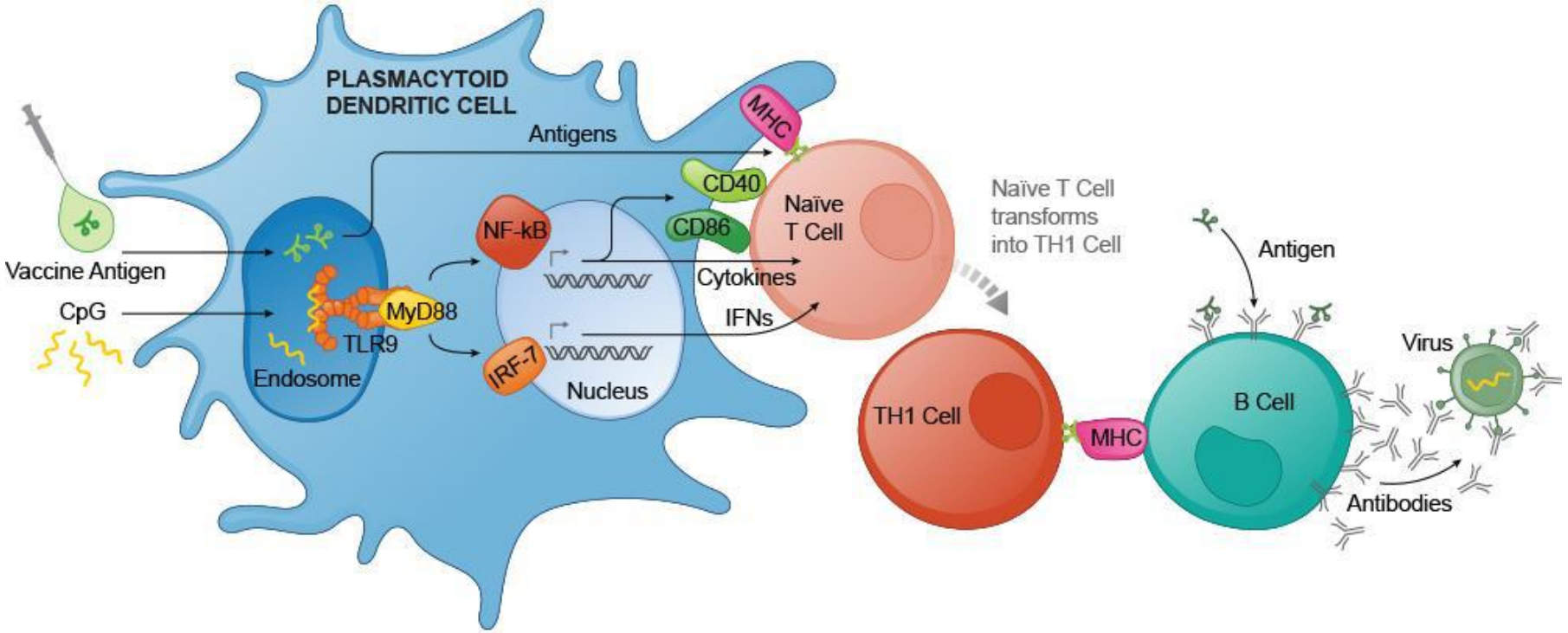




MEMORIA INMUNOLÓGICA



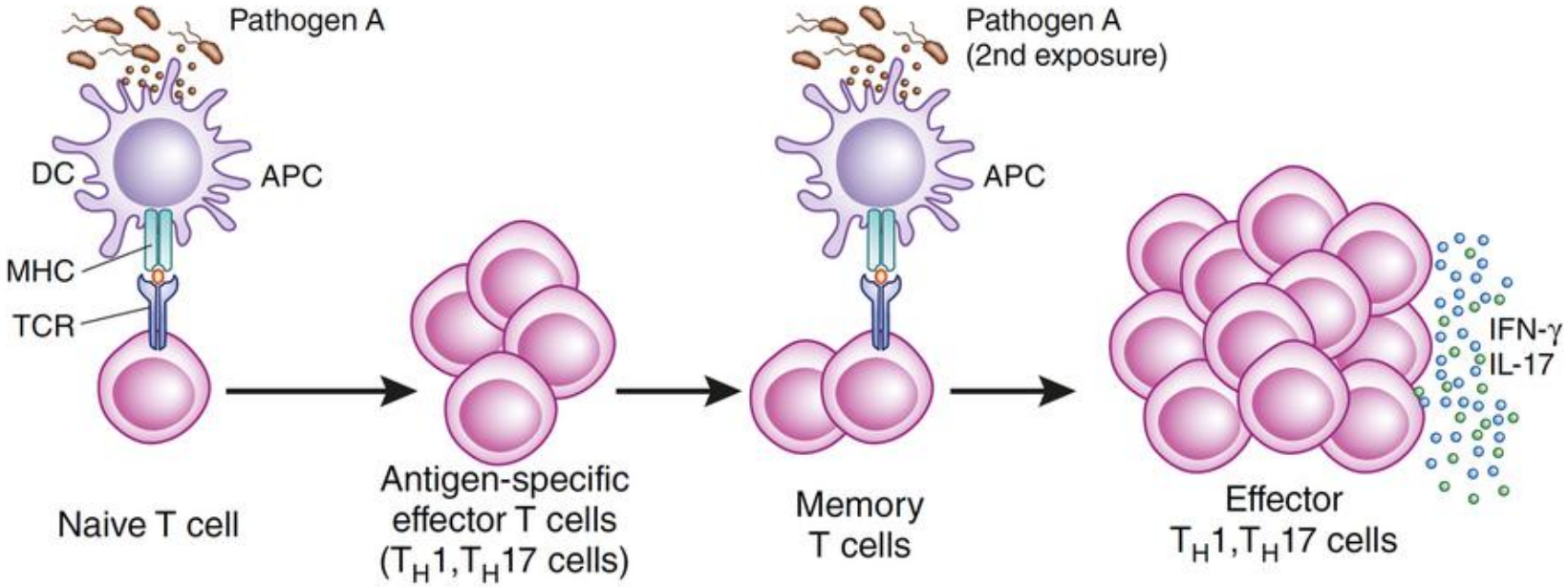
VACUNAS: IMITAN la acción del patógeno



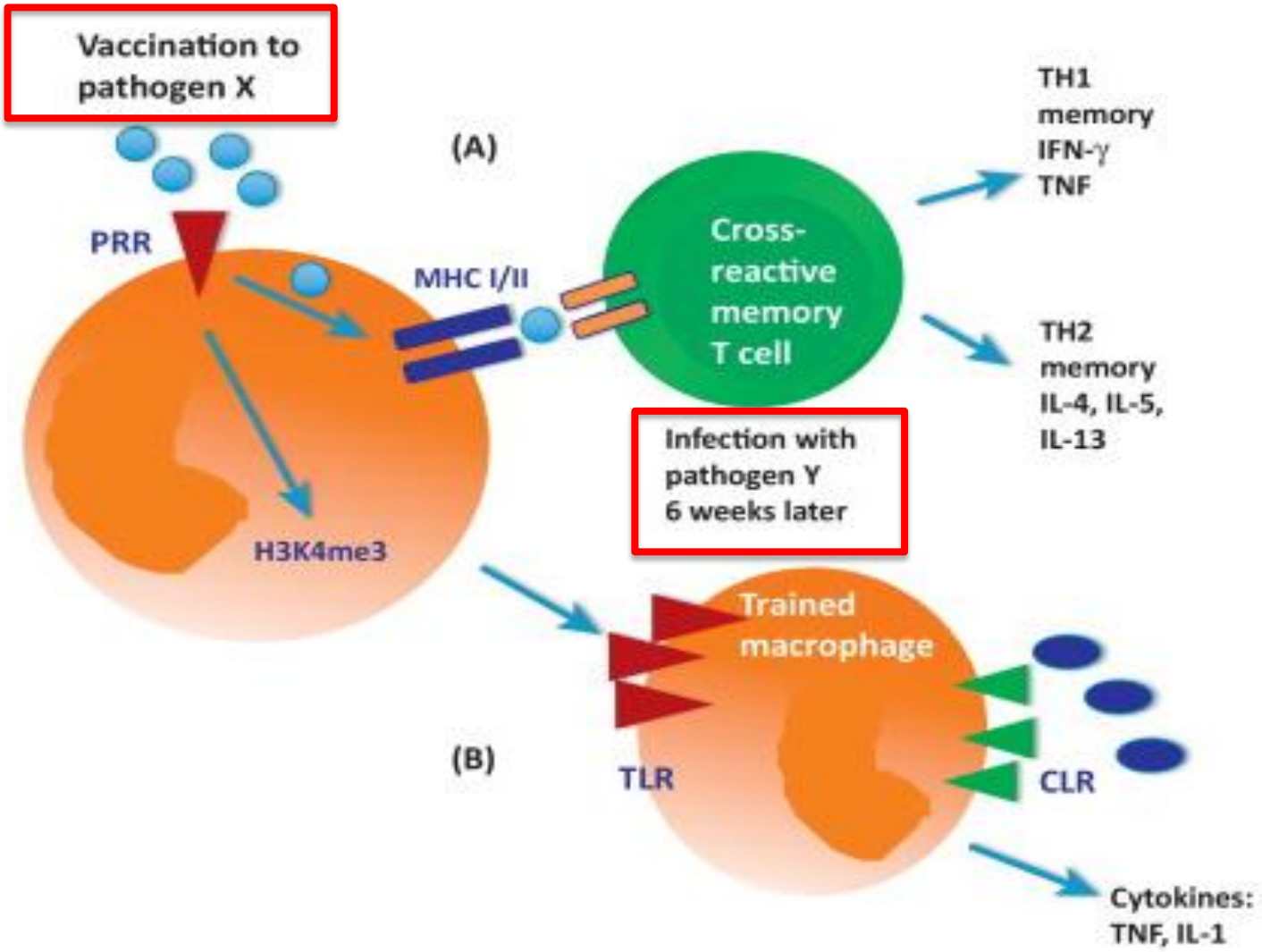
Dos componentes

- Antígenos Patógeno → Activar S.I. Específico
- Adyuvantes → Activar S.I. Innato

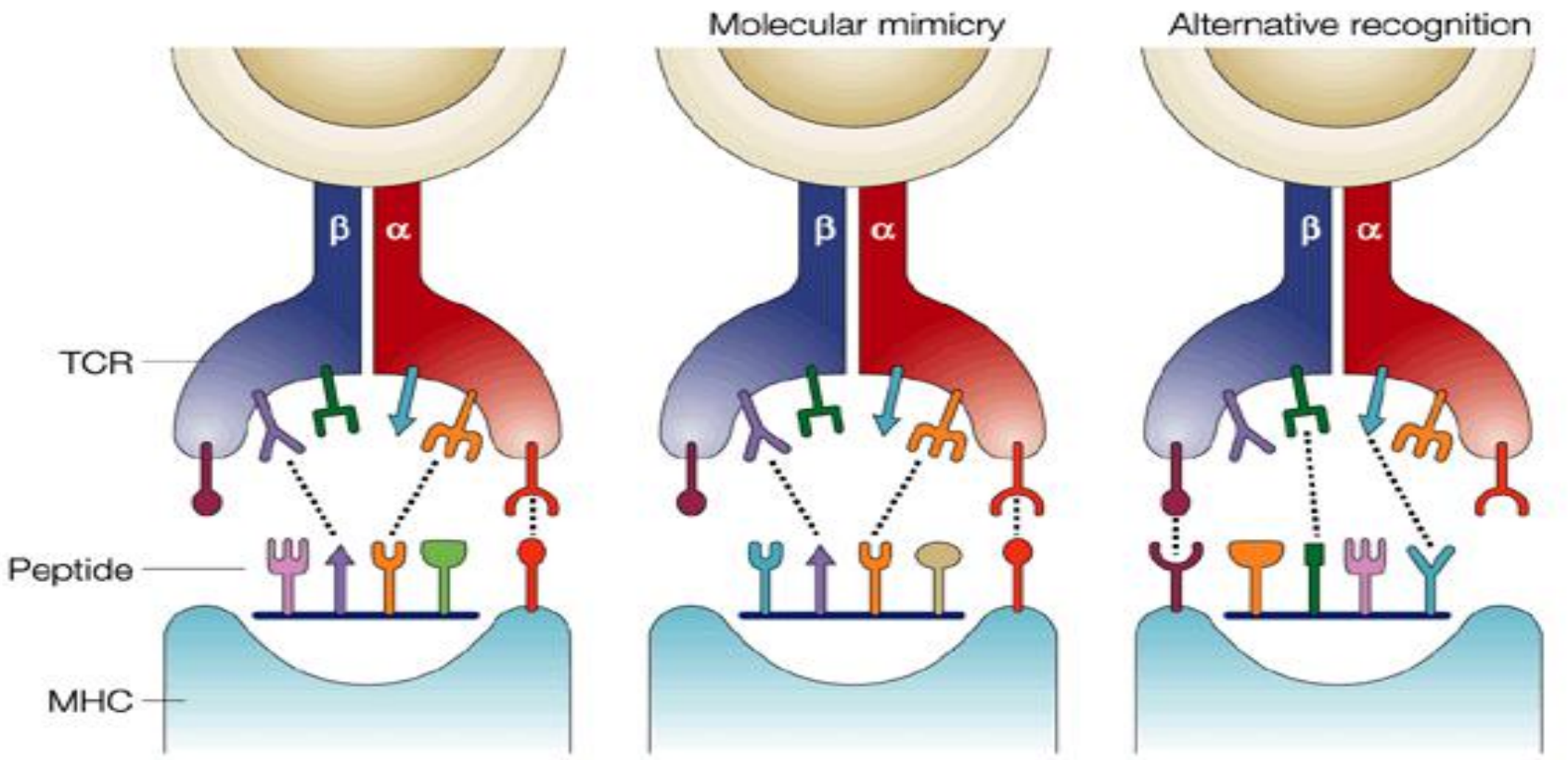
VACUNACIÓN: PROTECCIÓN ESPECÍFICA FRENTE A UN PATÓGENO



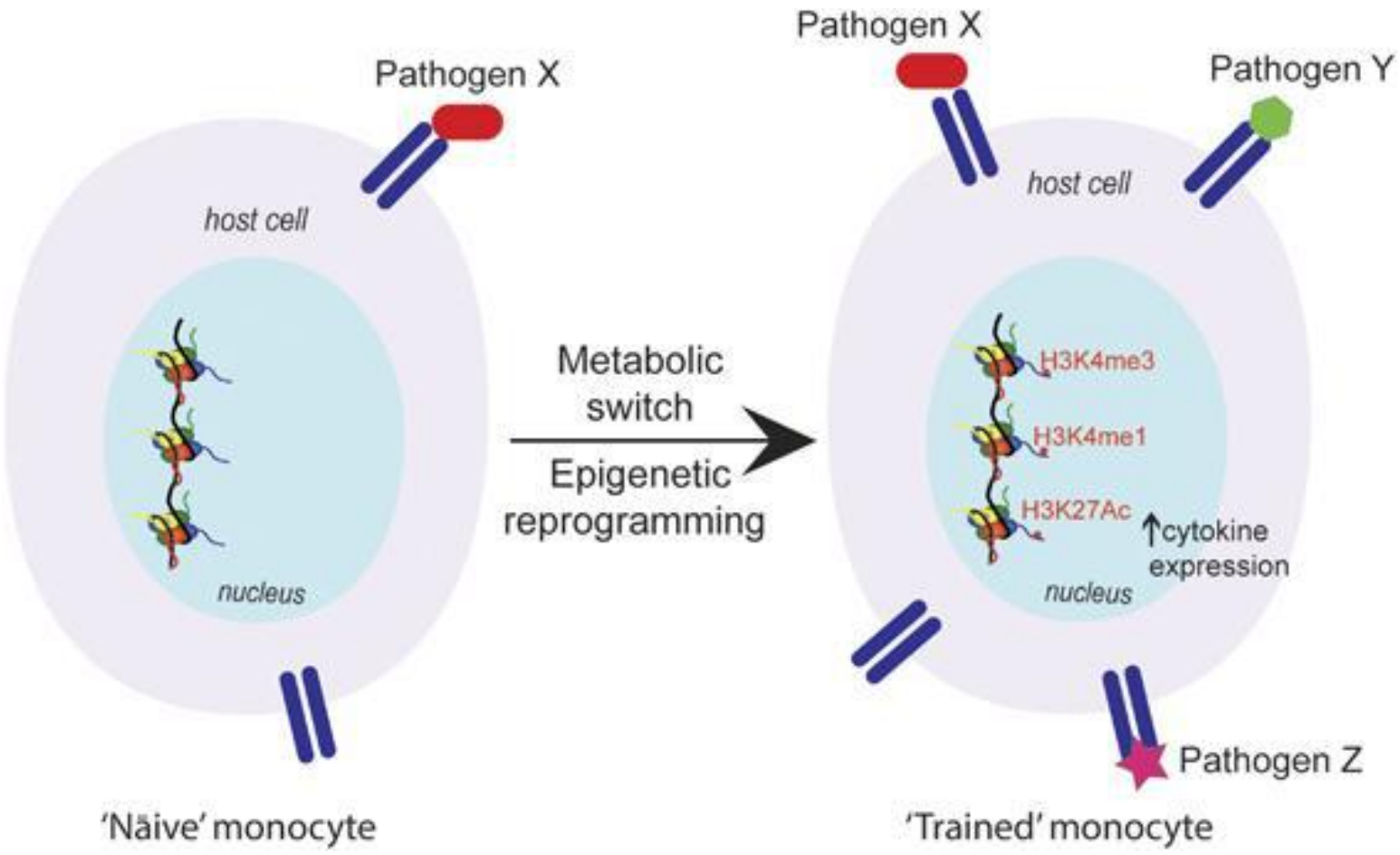
NUEVO CONCEPTO: PROTECCIÓN HETERÓLOGA (NO ESPECÍFICA) DE LAS VACUNAS



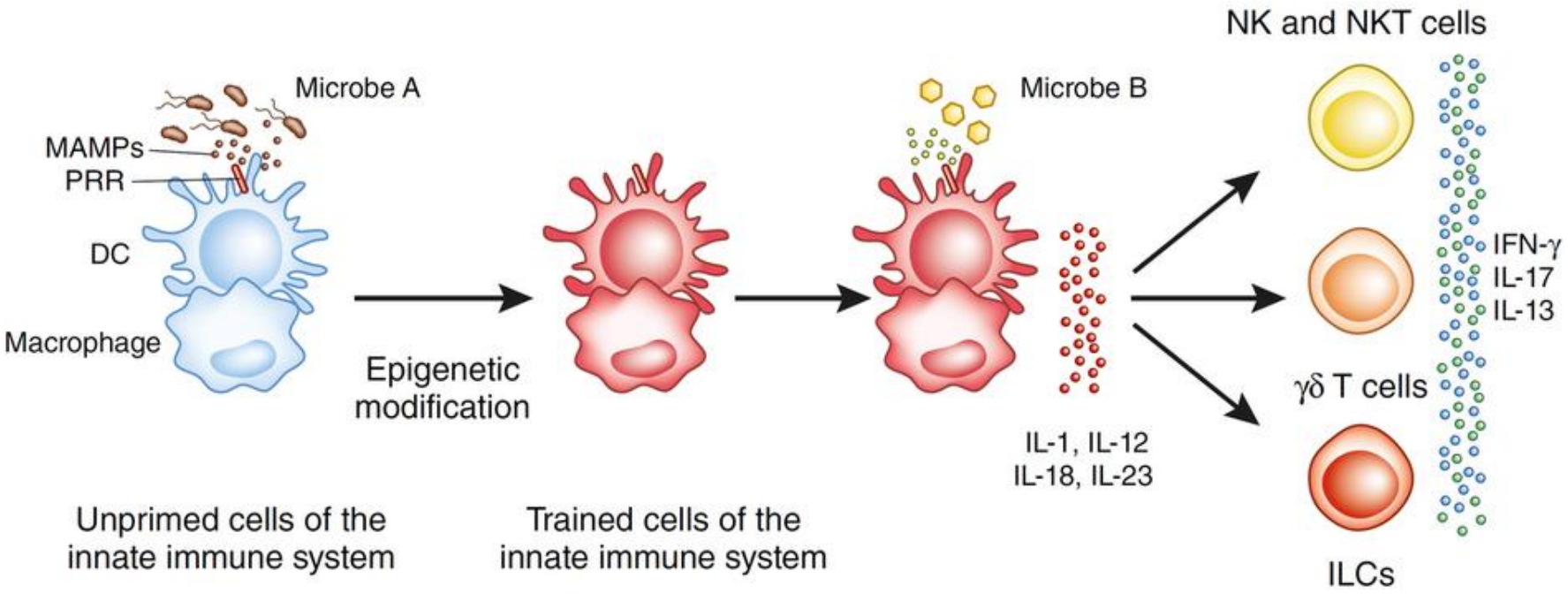
Protección heteróloga: Memoria *Cross-reactiva* del S.I. Específico



Protección heteróloga: "ENTRENAMIENTO" del S.I. Innato



"TRAINED IMMUNITY": "MEMORIA" del S.I. INNATO



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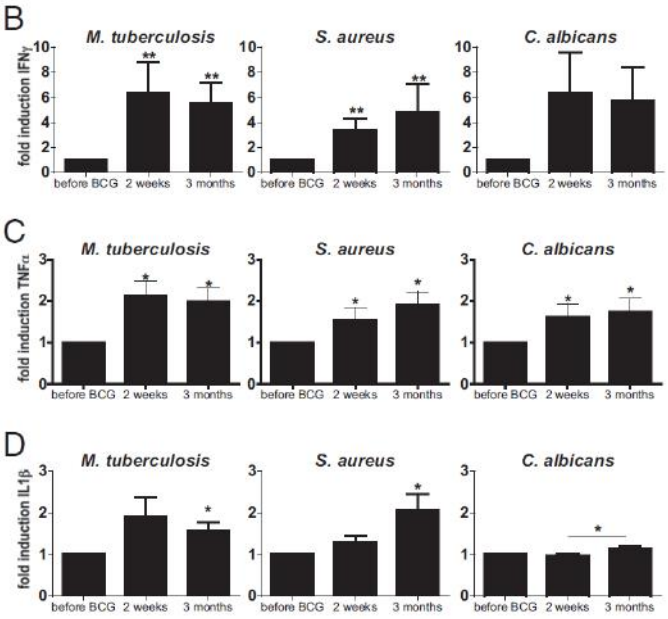
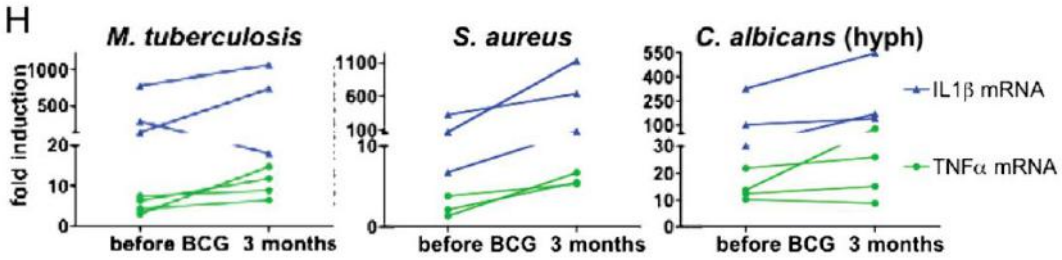
GENVIP idis

Bacille Calmette-Guérin induces NOD2-dependent nonspecific protection from reinfection via epigenetic reprogramming of monocytes

Johanneke Kleinnijenhuis[a,b,1], Jessica Quintin[a,b,1], Frank Preijers[c], Leo A. B. Joosten[a,b], Daniela C. Ifrim[a,b], Sadia Saeed[d], Cor Jacobs[a,b], Joke van Loenhout[e], Dirk de Jong[f], Hendrik G. Stunnenberg[d], Ramnik J. Xavier[g,h], Jos W. M. van der Meer[a,b], Reinout van Crevel[a,b], and Mihai G. Netea[a,b,2]





www.pnas.org/cgi/doi/10.1073/pnas.1202870109

Clin Infect Dis. 2015 Jun 1;60(11):1611-9. doi: 10.1093/cid/civ144. Epub 2015 Feb 27.

Nonspecific (Heterologous) Protection of Neonatal BCG Vaccination Against Hospitalization Due to Respiratory Infection and Sepsis.

de Castro MJ[1], Pardo-Seco J[2], Martinón-Torres F[3].

Author information

Abstract

BACKGROUND: Bacille Calmette-Guerin (BCG) vaccination has been suggested to have nonspecific beneficial effects in children from developing countries, reducing morbidity and mortality caused by unrelated pathogens.

OBJECTIVE: We aimed to assess the heterologous protective effects of BCG vaccination against respiratory infection (RI) and sepsis not attributable to tuberculosis in children born in Spain.

METHODS: We conducted a retrospective epidemiological study using data from the Official Spanish Registry of Hospitalizations (CMBD-HA) to identify differences in hospitalization rates (HR) in BCG-vaccinated children (Basque Country, where neonatal BCG is part of the immunization schedule and has a 100% coverage) as compared to non-BCG-vaccinated children (from the rest of Spain, where BCG is not used).

RESULTS: A total of 464 611 hospitalization episodes from 1992 to 2011 were analyzed. The HR due to RI not attributable to tuberculosis in BCG-vaccinated children was significant lower compared to non-BCG-vaccinated children for all age groups, with a total preventive fraction (PF) of 41.4% (95% confidence interval: 40.3-42.5; P-value <.001). According to age group, PF was 32.4% (30.9-33.9; P-value <.001) for children under 1 year old, 60.1% (58.5-61.7; P-value <.001) for children between 1 and 4 years old, 66.6% (62.8-70.2; P-value <.001) for children between 5 and 9 years old, and 69.6% (63.3-75.0; P-value <.001) for children between 10 and 14 years old. The HR due to sepsis not attributable to tuberculosis in BCG-vaccinated children under 1 year of age was also significantly lower, with a PF of 52.8% (43.8-60.7; P-value <.001).

CONCLUSIONS: BCG vaccination at birth may decrease hospitalization due to RI and sepsis not related to tuberculosis through heterologous protection.

KEYWORDS: BCG vaccination; children; heterologous effects; nonspecific effects

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PLoS one

Proof-of-Concept, Randomized, Controlled Clinical Trial of Bacillus-Calmette-Guerin for Treatment of Long-Term Type 1 Diabetes

Denise L. Faustman[1]*, Limei Wang[1], Yoshiaki Okubo[1], Douglas Burger[1], Liqin Ban[1], Guotong Man[1], Hui Zheng[2], David Schoenfeld[2], Richard Pompei[3], Joseph Avruch[3], David M. Nathan[3]

1 The Immunobiology Laboratory, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, United States of America, **2** Department of Biostatistics, Massachusetts General Hospital, Boston, Massachusetts, United States of America, **3** Diabetes Unit, Massachusetts General Hospital, Boston, Massachusetts, United States of America

glutamic acid decarboxylase (GAD) and other autoantibodies, and C-peptide, a marker of insulin secretion. BCG-treated patients and one placebo-treated patient who, after enrollment, unexpectedly developed acute Epstein-Barr virus infection, a known TNF inducer, exclusively showed increases in dead insulin-autoreactive T cells and induction of Tregs. C-peptide levels (pmol/L) significantly rose transiently in two BCG-treated subjects (means: 3.49 pmol/L [95% CI 2.95–3.8], 2.57 [95% CI 1.65–3.49]) and the EBV-infected subject (3.16 [95% CI 2.54–3.69]) vs.1.65 [95% CI 1.55–3.2] in reference diabetic subjects. BCG-treated subjects each had more than 50% of their C-peptide values above the 95th percentile of the reference subjects. The EBV-infected subject had 18% of C-peptide values above this level.

Conclusions/Significance: We conclude that BCG treatment or EBV infection transiently modified the autoimmunity that underlies type 1 diabetes by stimulating the host innate immune response. This suggests that BCG or other stimulators of host innate immunity may have value in the treatment of long-term diabetes.

PUBLIC RELEASE: 7-JUN-2015

Massachusetts General Hospital launches phase II trial of BCG vaccine to reverse type 1 diabetes

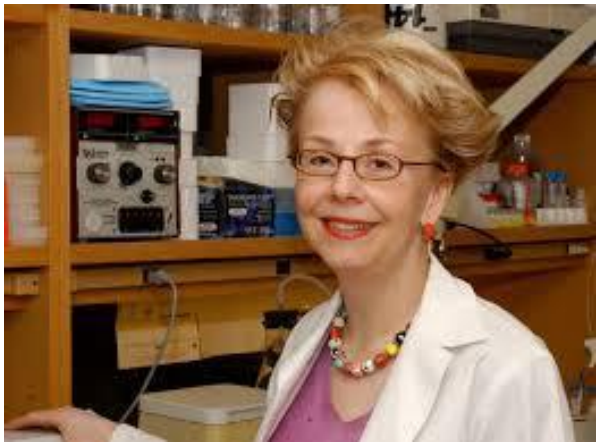
FDA approval of trial testing generic vaccine announced at ADA Scientific Sessions

MASSACHUSETTS GENERAL HOSPITAL

A phase II clinical trial testing the ability of the generic vaccine bacillus Calmette-Guérin (BCG) to reverse advanced type 1 diabetes has received approval from the U.S. Food and Drug Administration (FDA). The approval of this trial, which will shortly begin enrolling qualified patients, was announced today at the 75th Scientific Sessions of the American Diabetes Association (ADA) by Denise Faustman, MD, PhD, director of the Massachusetts General Hospital (MGH) Immunobiology Laboratory and principal investigator of the study.

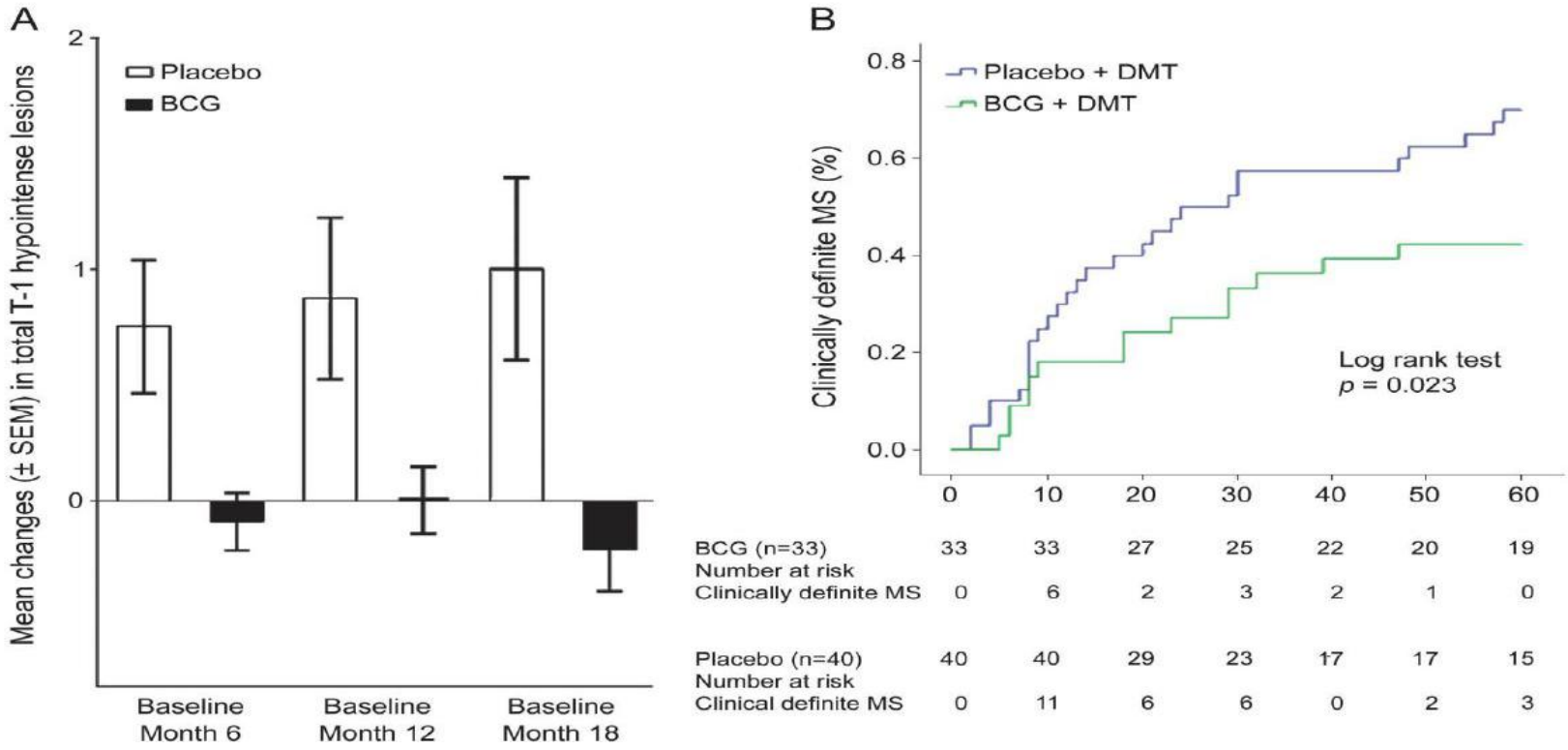
The five-year trial will investigate whether repeat BCG vaccination can clinically improve type 1 diabetes in adults between 18 and 60 years of age who have small but still detectable levels of insulin secretion from the pancreas. Faustman's research team was the first group to document reversal of advanced type 1 diabetes in mice and subsequently completed a successful phase I human clinical trial of BCG vaccination. She announced the FDA approval to launch the phase II trial during her ADA presentation, "Low Levels of C-Peptide Have Clinical Significance for Established Type 1 Diabetes."

"We have learned a lot since the early studies in mice - not just about how BCG works but also about its potential therapeutic benefits, similar to what are being seen in trials against other autoimmune diseases," says Faustman. "We are so grateful to all of the donors, large and small, who have made this trial possible - especially the Iacocca Foundation, which has believed in us and has been a supporter since our early days. Our goal is to complete enrollment and also to raise the remaining funds needed for the trial by the end of this year."

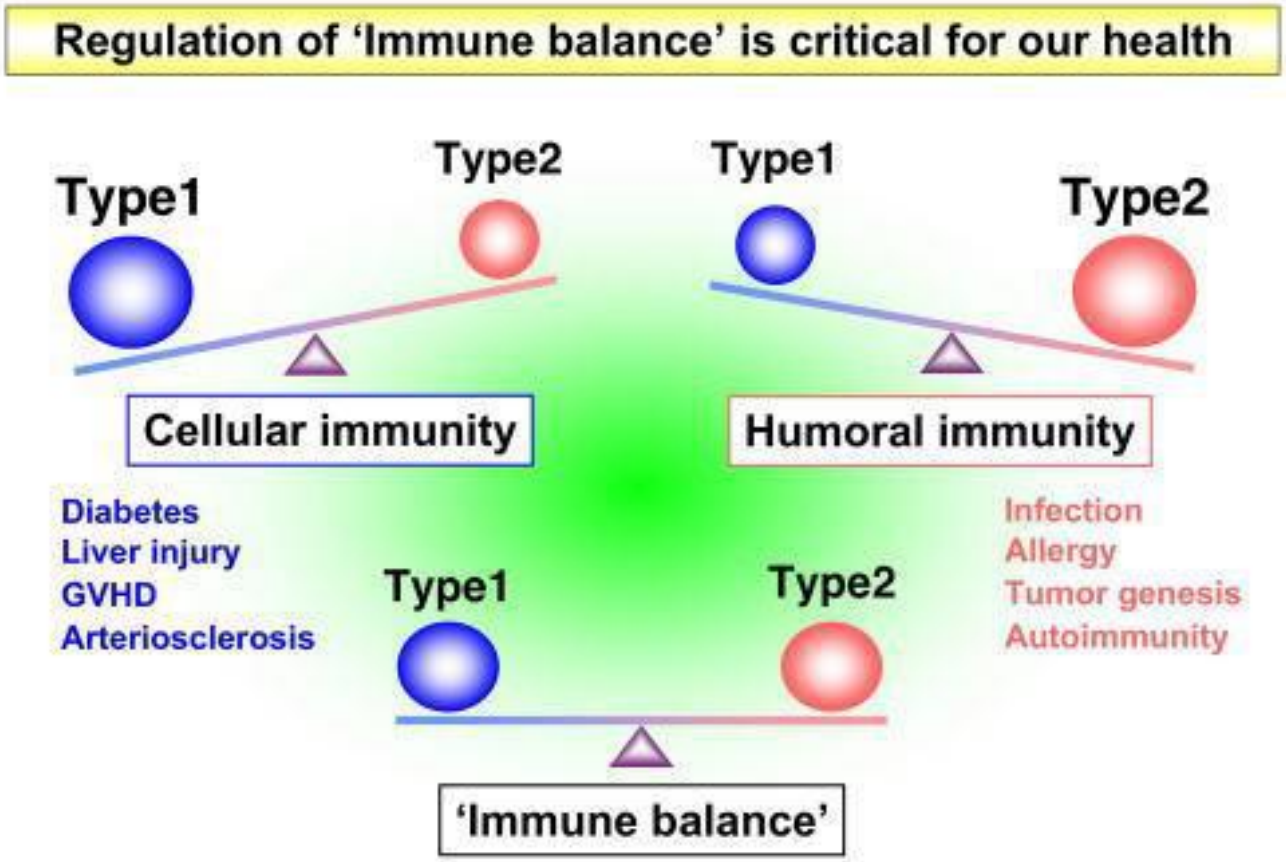


Dra. Denise L Faustman

Effects of Bacille Calmette-Guérin after the first demyelinating event in the CNS

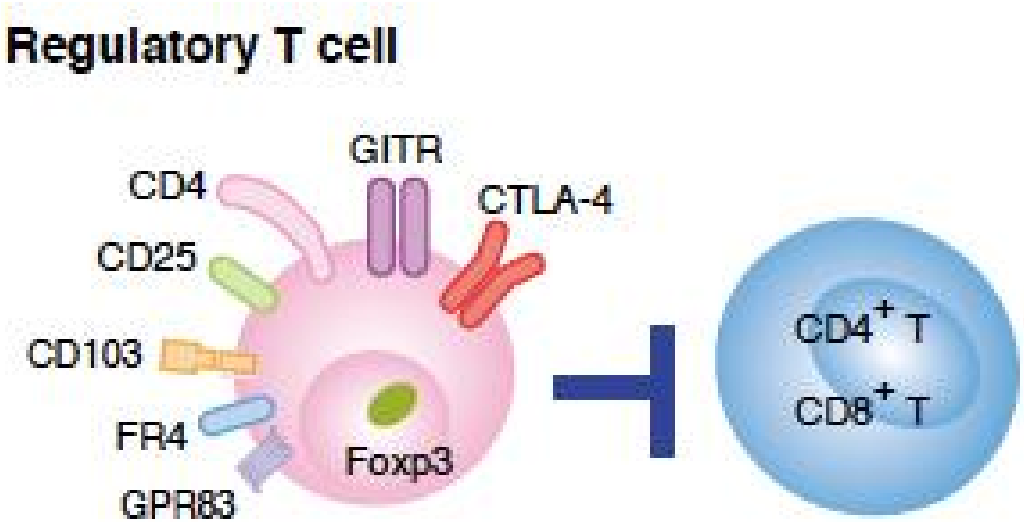


PROYECTO PNEUMO*REG*: Propiedades Inmunomoduladoras de la PCV13

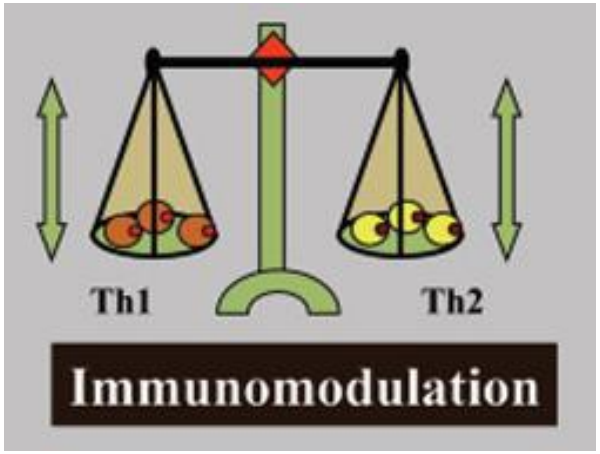


PCV13
Immuno-modulatory Effect

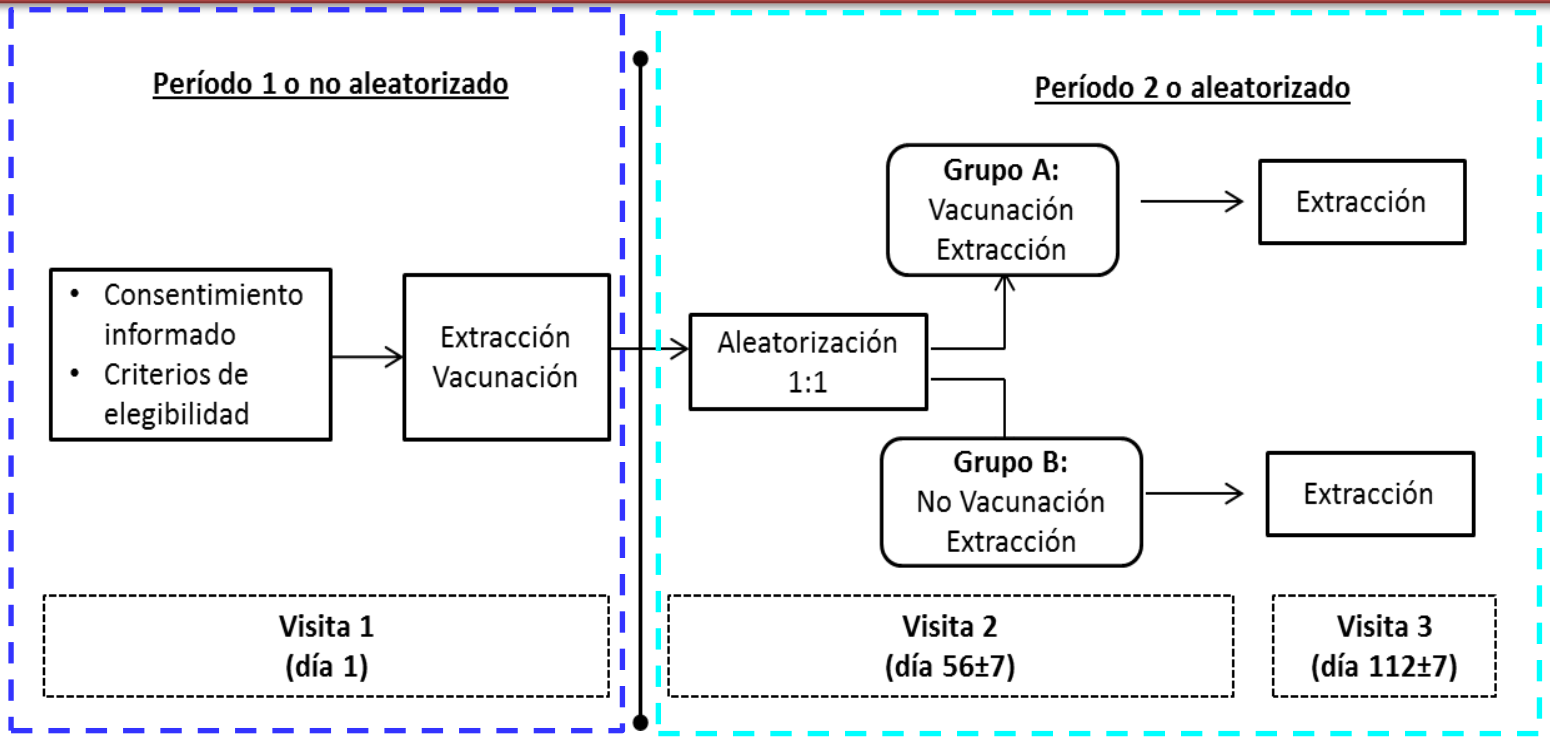
PROYECTO PNEUMO*REG*: Propiedades Inmunomoduladoras de la PCV13

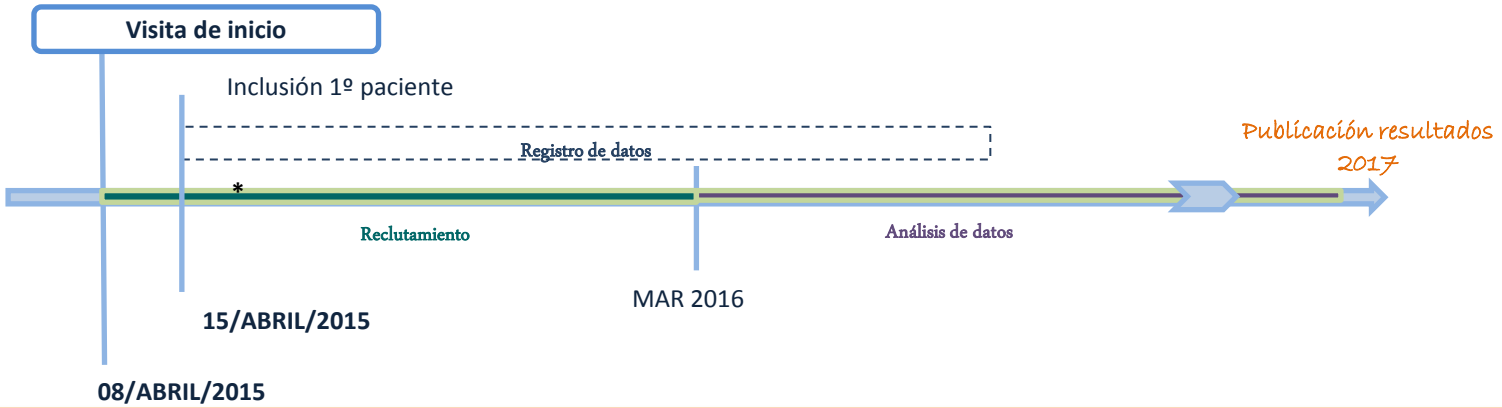


PCV13
Immuno-modulatory Effect



PROYECTO PNEUMO*REG*: Propiedades Inmunomoduladoras de la PCV13





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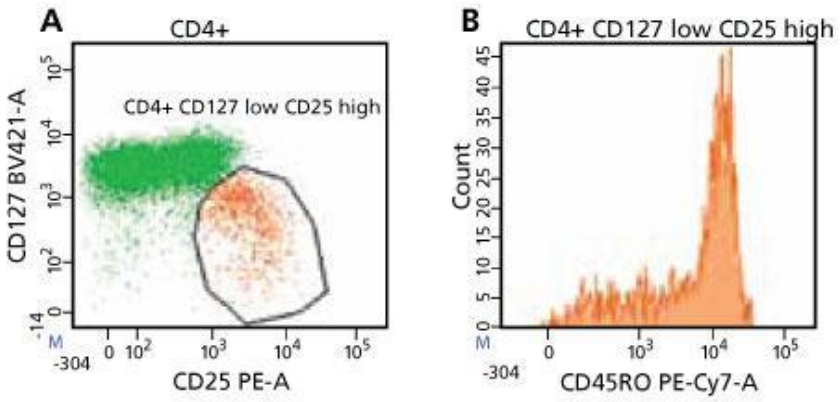
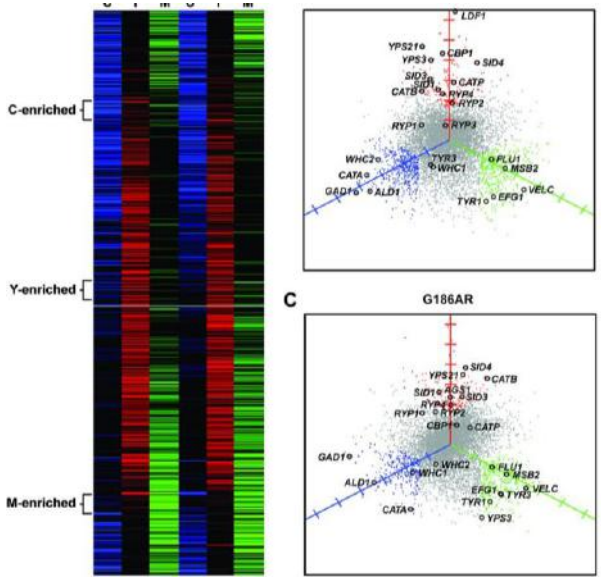
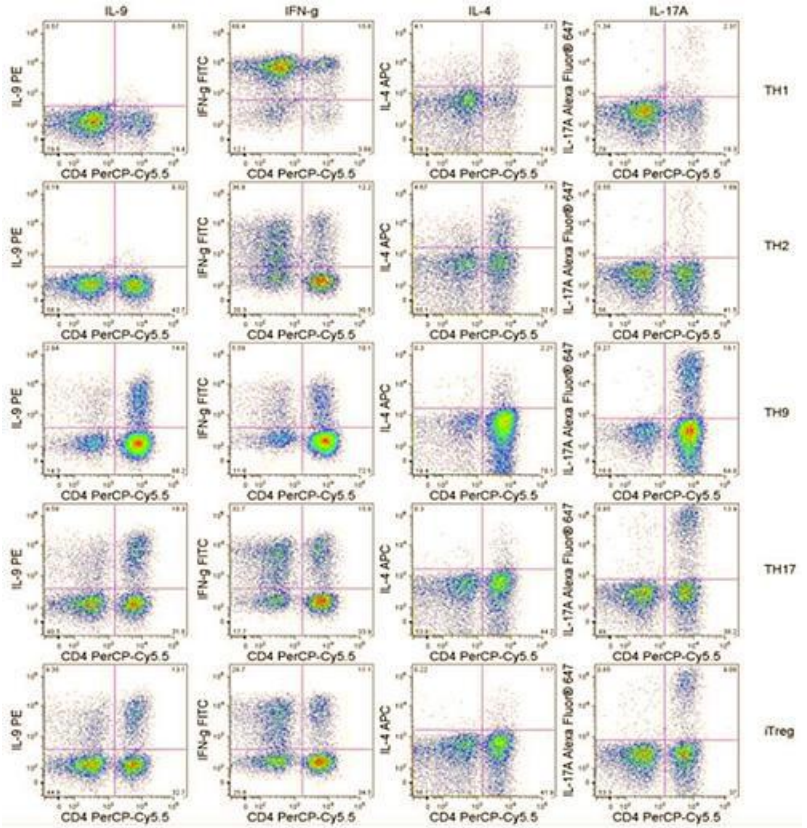
PROYECTO PNEUMO*REG*: Propiedades Inmunomoduladoras de la PCV13







Translational Pediatrics and Infectious Diseases

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