COMO ENTENDER LA INMUNOLOGÍA DE LAS INMUNIZACIONES … EN 20´

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Grupo de Investigación en Vacunas (GENVIP)

Complexo Hospitalario Universitario de Santiago de Compostela

GENVIP

idis Instituto de Investigación Sanitaria de Santiago de Compostela

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Declaración de potenciales conflictos de interés

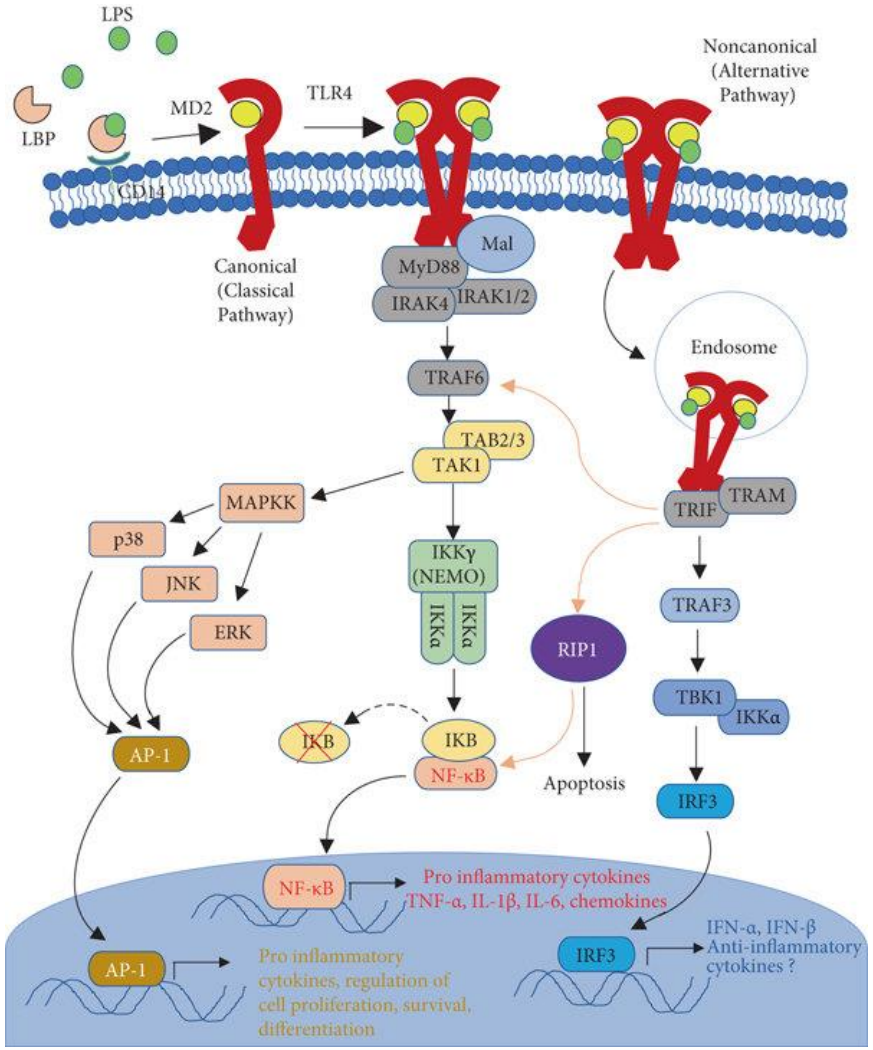
Desarrollo mi actividad profesional en el SERVICIO DE INMUNOLOGÍA y en la UNIDAD DE ENSAYOS CLINICOS DE VACUNAS PEDIATRICAS del HOSPITAL CLÍNICO UNIVERSITARIO DE SANTIAGO DE COMPOSTELA:

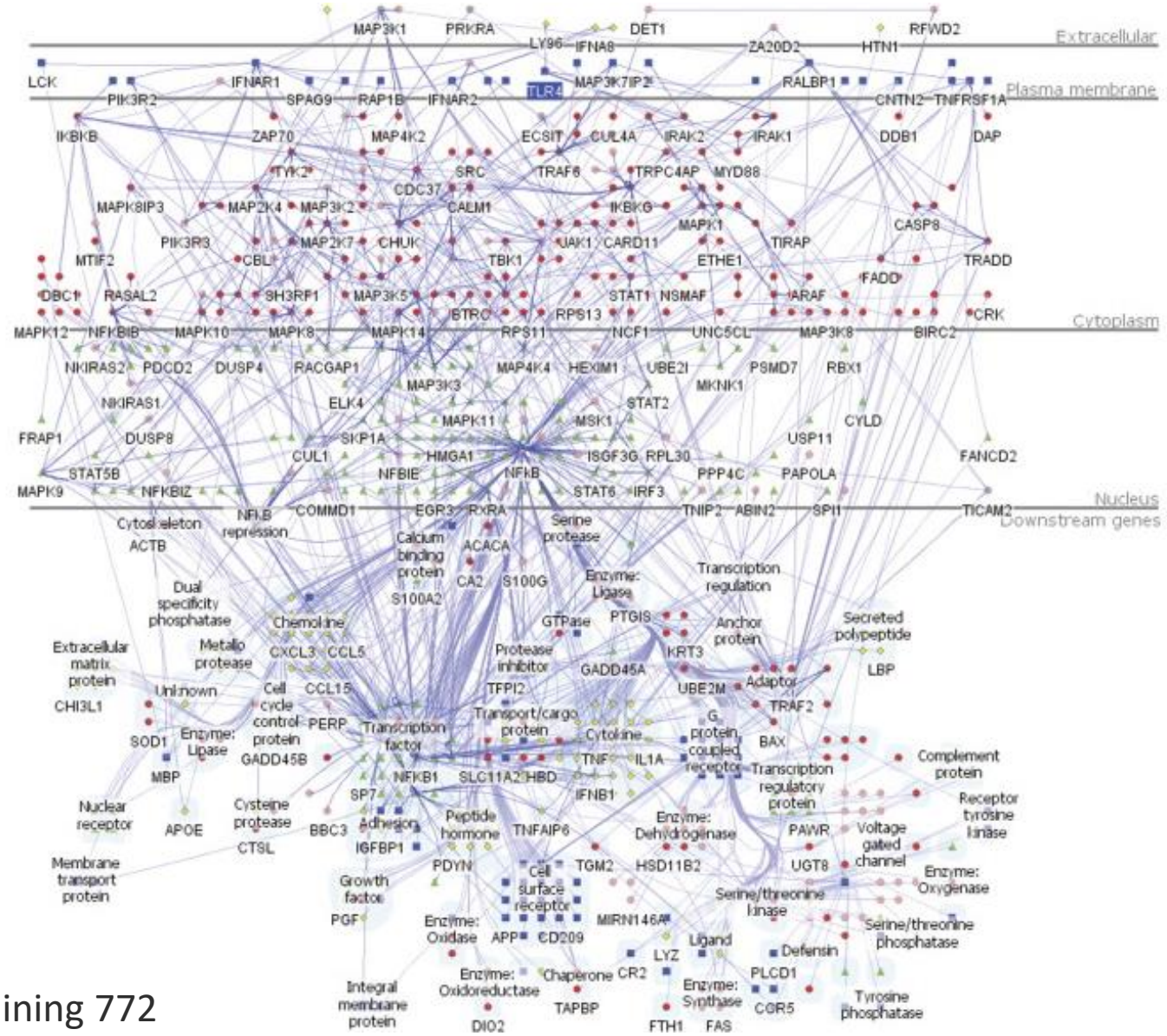
He recibido honorarios por conferencias de Pfizer, Moderna, Seqirus, AstraZeneca, GSK, Sanofi y MSD.

He recibido honorarios por asesoría científica de Pfizer, Moderna, Seqirus, GSK, Sanofi y MSD.

He recibido ayudas de investigación de Sanofi, GSK, MSD, Pfizer y Novartis.

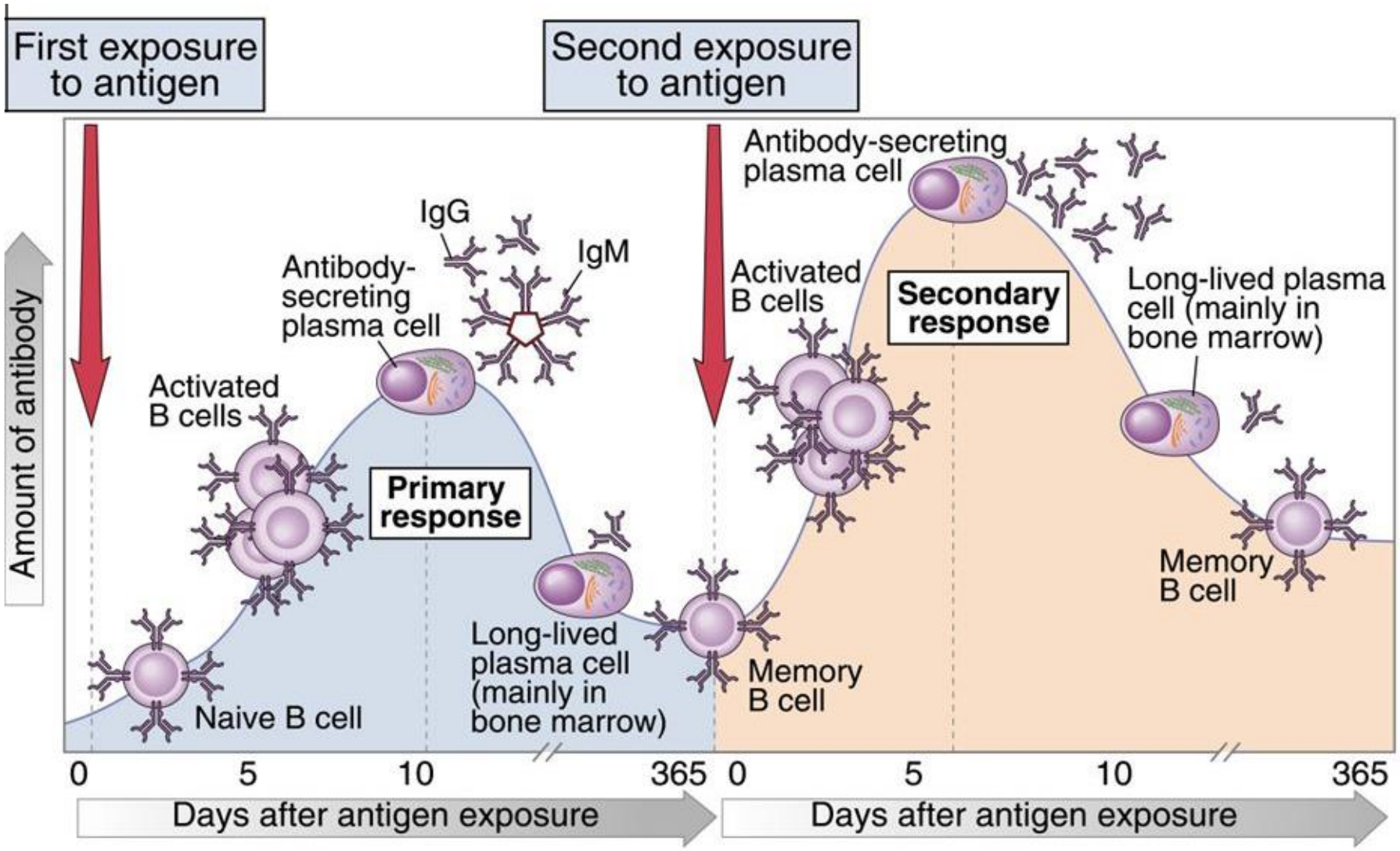
Participo en ensayos clínicos de vacunas de Sanofi, MSD, Pfizer, Roche, Medimmune, Novartis, Ablynx, Janssen y GSK.



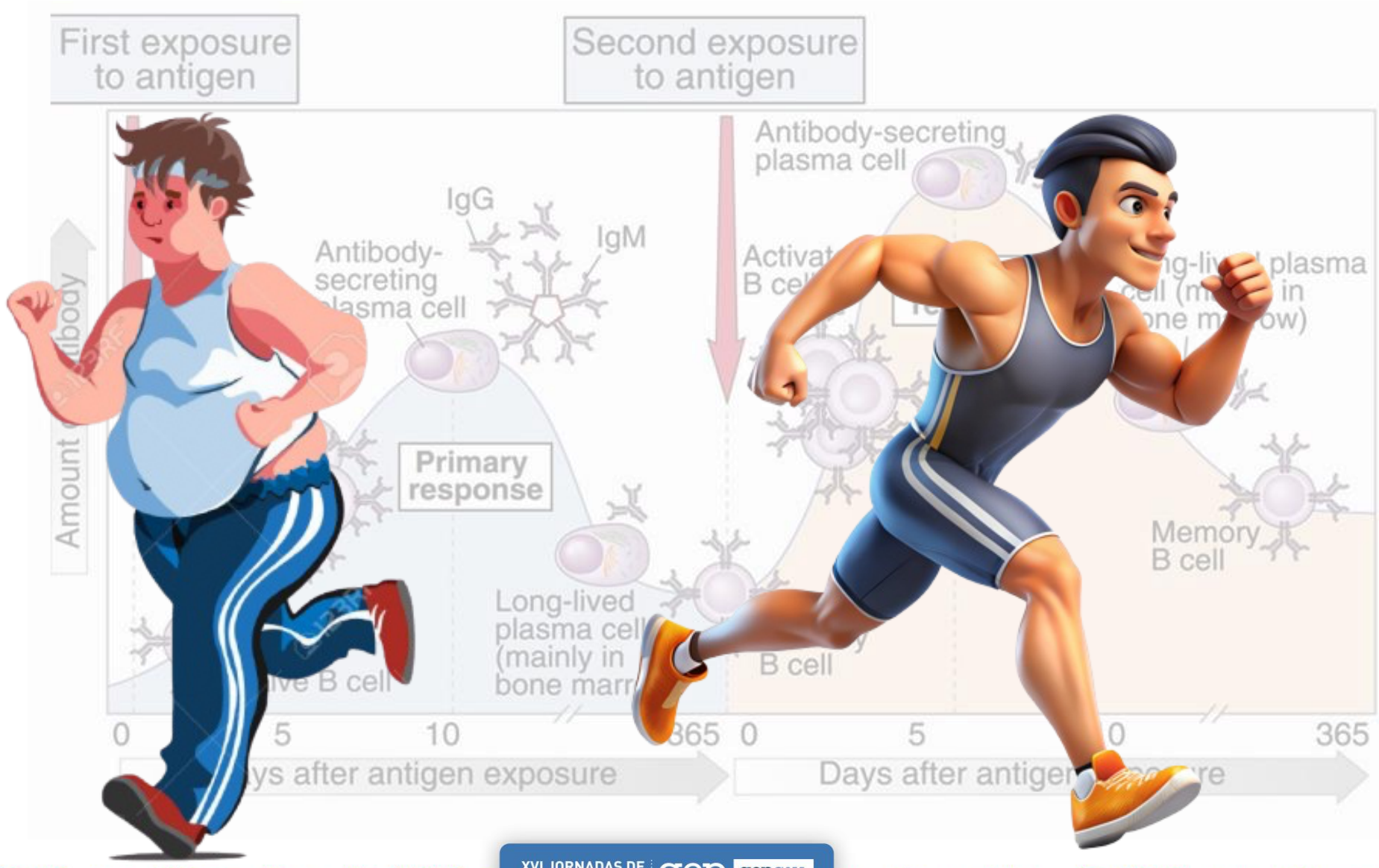


The TLR4–MAPK–NF-κB interaction network, containing 772 molecules and 1387 interacciones

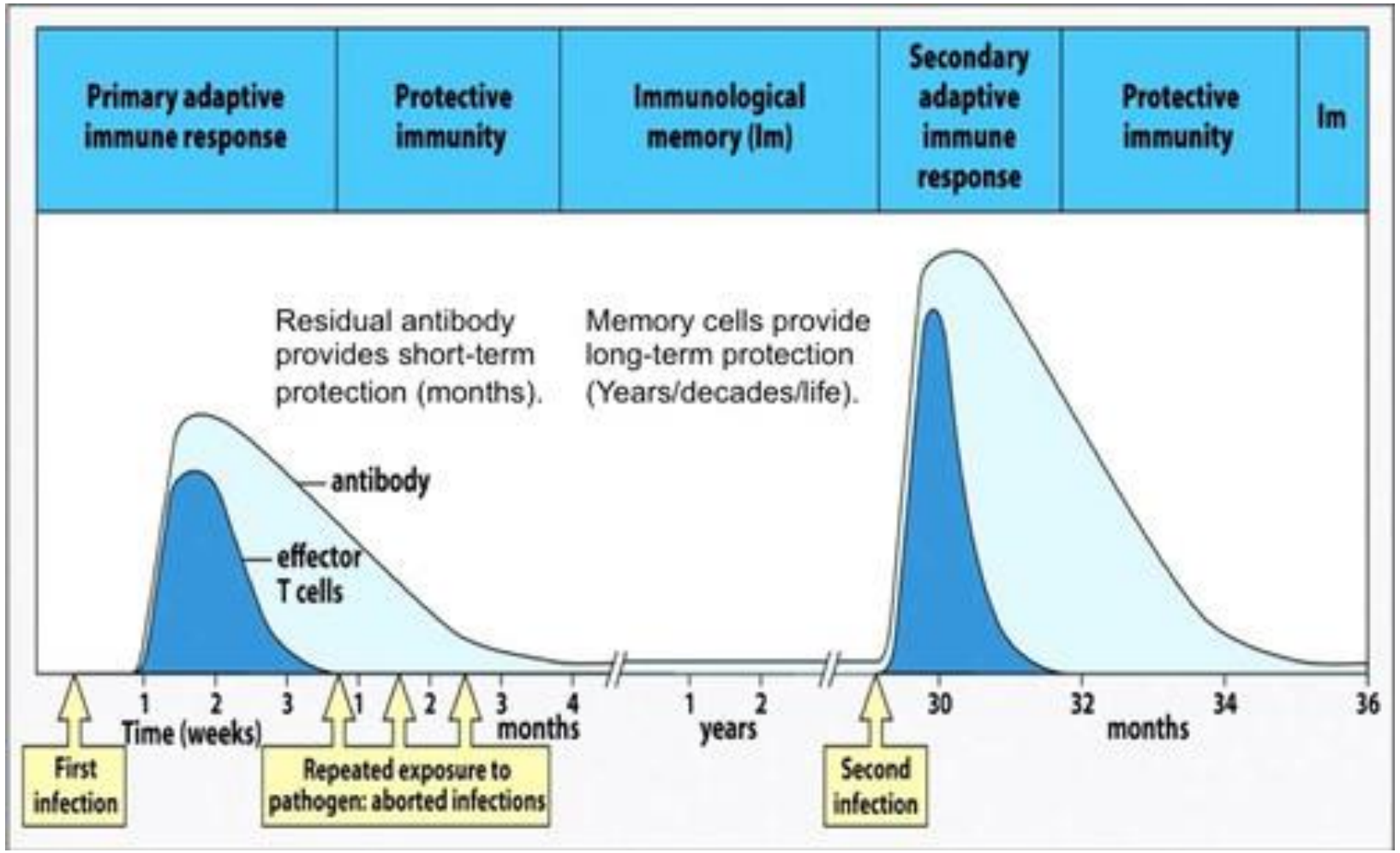
LO PRIMERO ES ENTENDER COMO FUNCIONAN LAS VACUNAS



VACUNAR ES ENTRENAR A NUESTRO SISTEMA INMUNITARIO



LO SEGUNDO ES DIFERENCIAR ENTRE INMUNIDAD PROTECTORA y MEMORIA INMUNOLÓGICA



Primera Infección

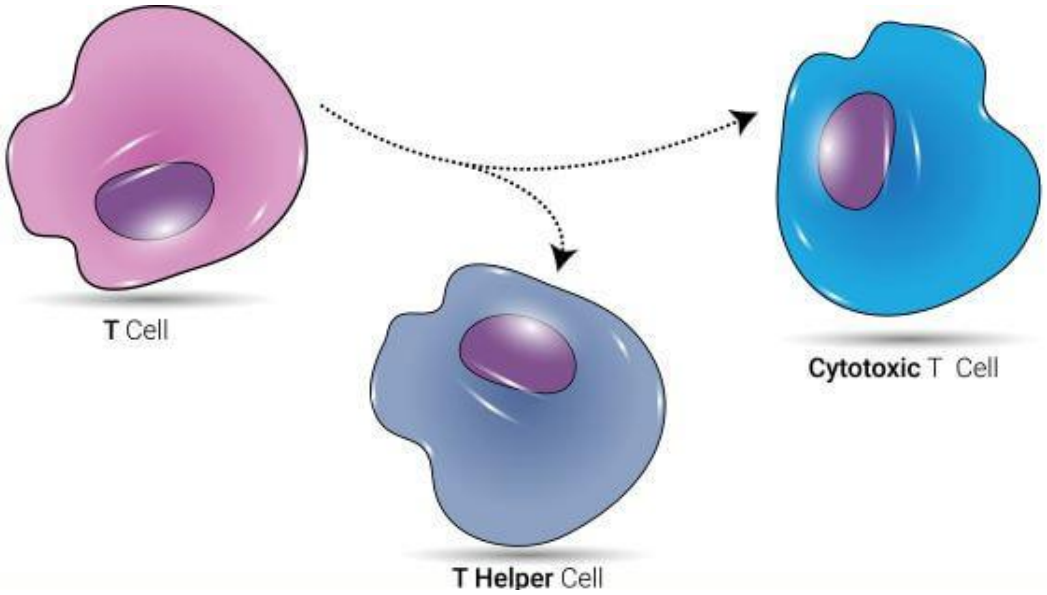
Exposición al patógeno: infección abortada

Segunda Infección

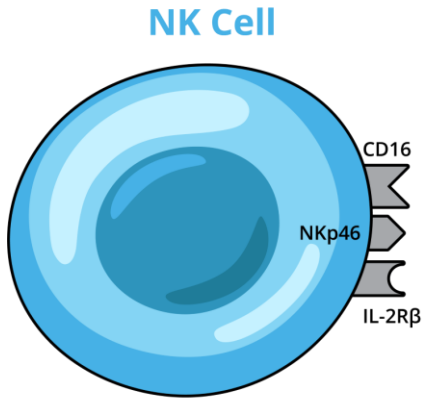
ENTRENAMOS A NUESTRO SISTEMA INMUNITARIO PARA COMPETIR …

NO PARA EVITAR LA COMPETICIÓN

¿QUIÉN HACE QUÉ?



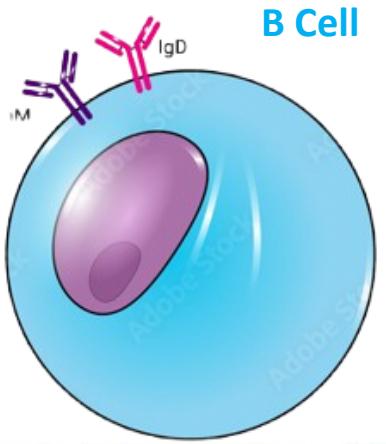
LINFOCITO T-CD8+ (CITOTÓXICO):
Destruir células infectadas por VIRUS
MICOBACTERIAS
Células TUMORALES



CÉLULA NK:
Destruir células infectadas por VIRUS
Células TUMORALES

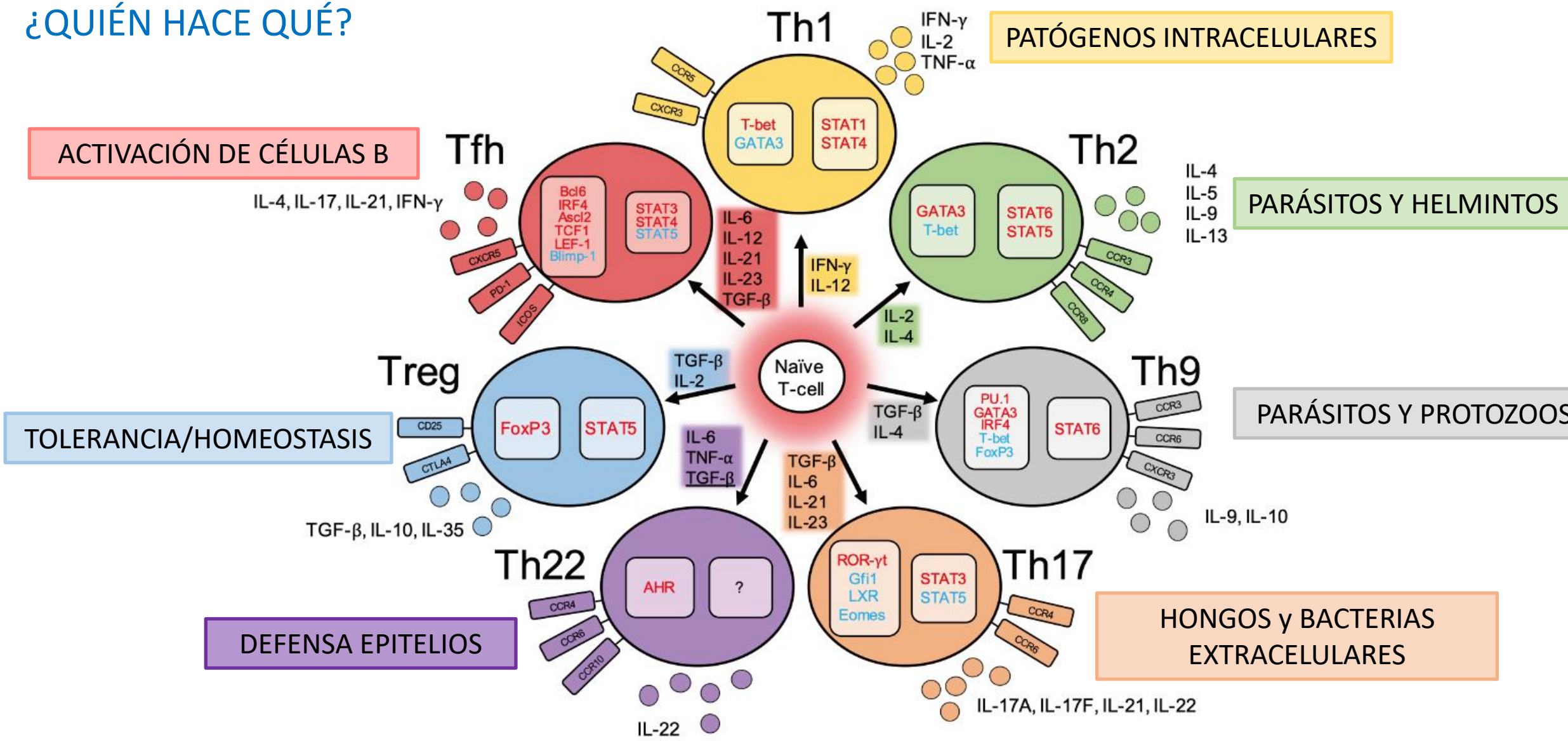
LINFOCITO T-CD4+ (COLABORADOR):

Asistir a otros linfocitos para madurar y diferenciarse



LINFOCITO B:
Producir Anticuerpos
Presentar antígenos a Linfocitos T

¿QUIÉN HACE QUÉ?



ACTIVACIÓN DE CÉLULAS B

PATÓGENOS INTRACELULARES

PARÁSITOS Y HELMINTOS

TOLERANCIA/HOMEOSTASIS

PARÁSITOS Y PROTOZOOS

DEFENSA EPITELIOS

HONGOS y BACTERIAS EXTRACELULARES

VACUNAS QUE FUNCIONAN

Trials in Vaccinology 3 (2014) 1–5

Contents lists available at ScienceDirect

Trials in Vaccinology

journal homepage: www.elsevier.com/locate/trivac

Neonatal BCG vaccination is associated with enhanced T-helper 1 immune responses to heterologous infant vaccines

Daniel H. Libraty[a,*], Lei Zhang[a], Marcia Woda[a], Luz P. Acosta[b], AnaMae Obcena[c], Job D. Brion[d], Rosario Z. Capeding[c,e]

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Curr Opin Immunol. 2013 June ; 25(3): 373–380. doi:10.1016/j.coi.2013.03.011.

Th17 cell based vaccines in mucosal immunity

Pawan Kumar, **Kong Chen**, and **Jay K. Kolls**
Richard King Mellon Foundation Institute for Pediatric Research, Children's Hospital of Pittsburgh of the University of Pittsburgh Medical Center, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA

HHS Public Access
Author manuscript
Vaccine. Author manuscript; available in PMC 2021 April 12.

Published in final edited form as:
Vaccine. 2020 February 11; 38(7): 1778–1786. doi:10.1016/j.vaccine.2019.12.023.

Peripheral CD4 T follicular cells induced by a conjugated pneumococcal vaccine correlate with enhanced opsonophagocytic antibody responses in younger individuals

Sarah Sterrett[1], Binghao J. Peng[1], Robert L. Burton[1], David C. LaFon[1], Andrew O. Westfall[2], Suddham Singh[4], Michael Pride[4], Annaliesa S. Anderson[4], Gregory C. Ippolito[5], Harry W Schroeder Jr[1,3], Moon H. Nahm[1,3], A. Krishna Prasad[4], Paul Goepfert[1,3,*], Anju Bansal[1,*]

PLOS ONE

RESEARCH ARTICLE

Circulating CXCR5$^+$CD4$^+$ T Follicular-Like Helper Cell and Memory B Cell Responses to Human Papillomavirus Vaccines

Ken Matsui[1], Joseph W. Adelsberger[2], Troy J. Kemp[1], Michael W. Baseler[2], Julie E. Ledgerwood[3], Ligia A. Pinto[1]*

Y OTRAS QUE NO TANTO

Clinical & Translational Immunology

Clinical & Translational Immunology 2024; **13**: e1491. doi: 10.1002/cti2.1491
www.wileyonlinelibrary.com/journal/cti

REVIEW

Fighting flu: novel CD8$^+$ T-cell targets are required for future influenza vaccines

Samuel Liwei Leong[1], Stephanie Gras[1,2] & Emma J Grant[1,2]

[1]Department of Biochemistry and Chemistry, La Trobe Institute for Molecular Science, La Trobe University, Bundoora, VIC, Australia
[2]Department of Biochemistry and Molecular Biology, Biomedicine Discovery Institute, Monash University, Clayton, VIC, Australia

Risk Management and Healthcare Policy

Dovepress
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REVIEW

Towards Eradication of Malaria: Is the WHO's RTS,S/AS01 Vaccination Effective Enough?

This article was published in the following Dove Press journal:
Risk Management and Healthcare Policy

npj | Vaccines

www.nature.com/npjvaccines

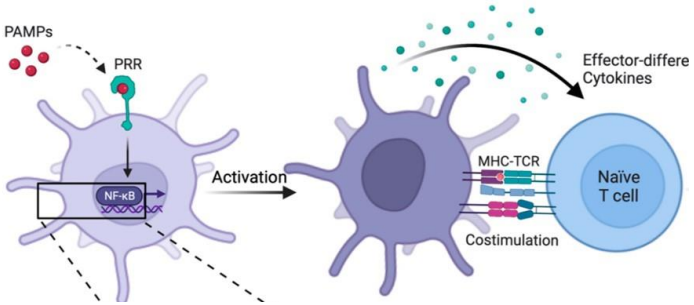
ARTICLE OPEN

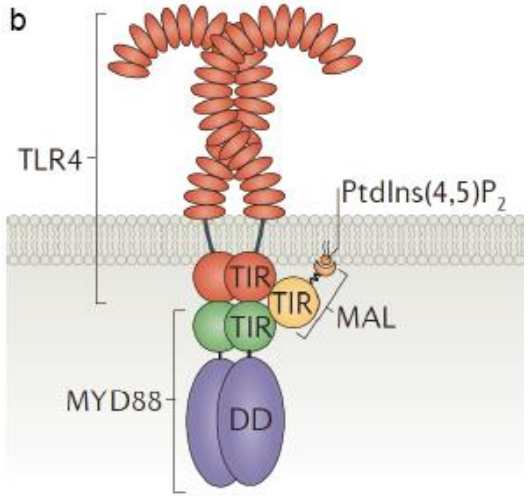
Check for updates

Suppression of mucosal Th17 memory responses by acellular pertussis vaccines enhances nasal *Bordetella pertussis* carriage

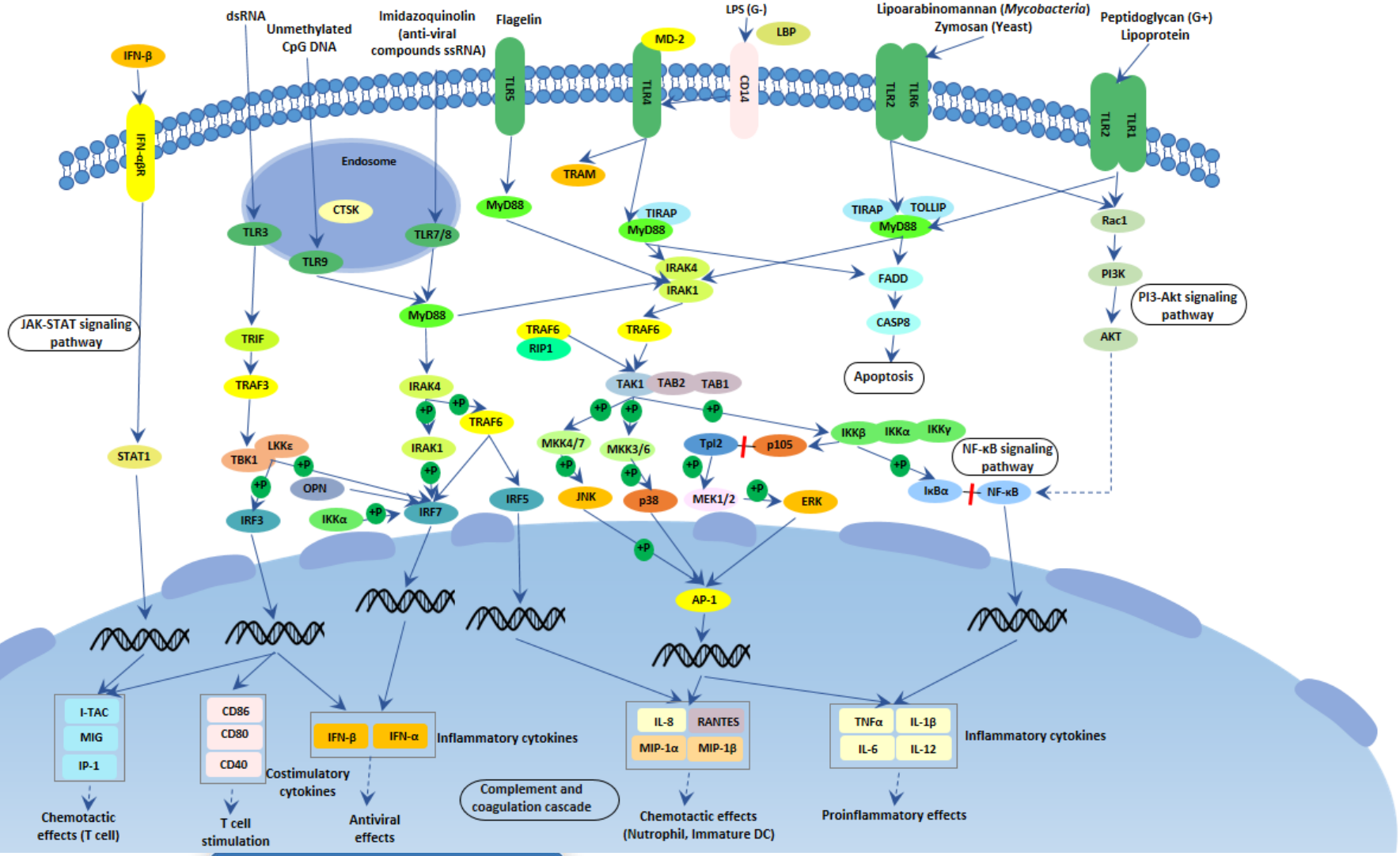
Violaine Dubois[1✉], Jonathan Chatagnon[1], Anaïs Thiriard[1], Hélène Bauderlique-Le Roy[2], Anne-Sophie Debrie[1], Loïc Coutte[1] and Camille Locht[1]

COMO SE ACTIVAN LAS CÉLULAS INMUNITARIAS: SISTEMA INMUNE INNATO

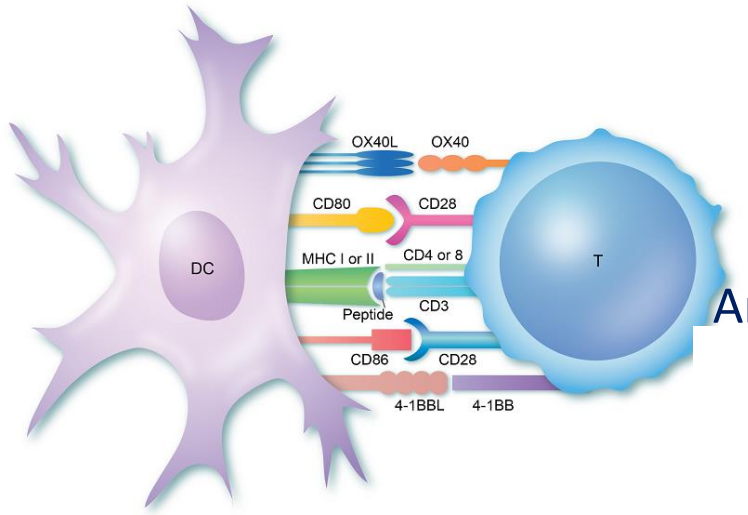




Vías TLRs



COMO SE ACTIVAN LAS CÉLULAS INMUNITARIAS: SISTEMA INMUNE ADAPTATIVO

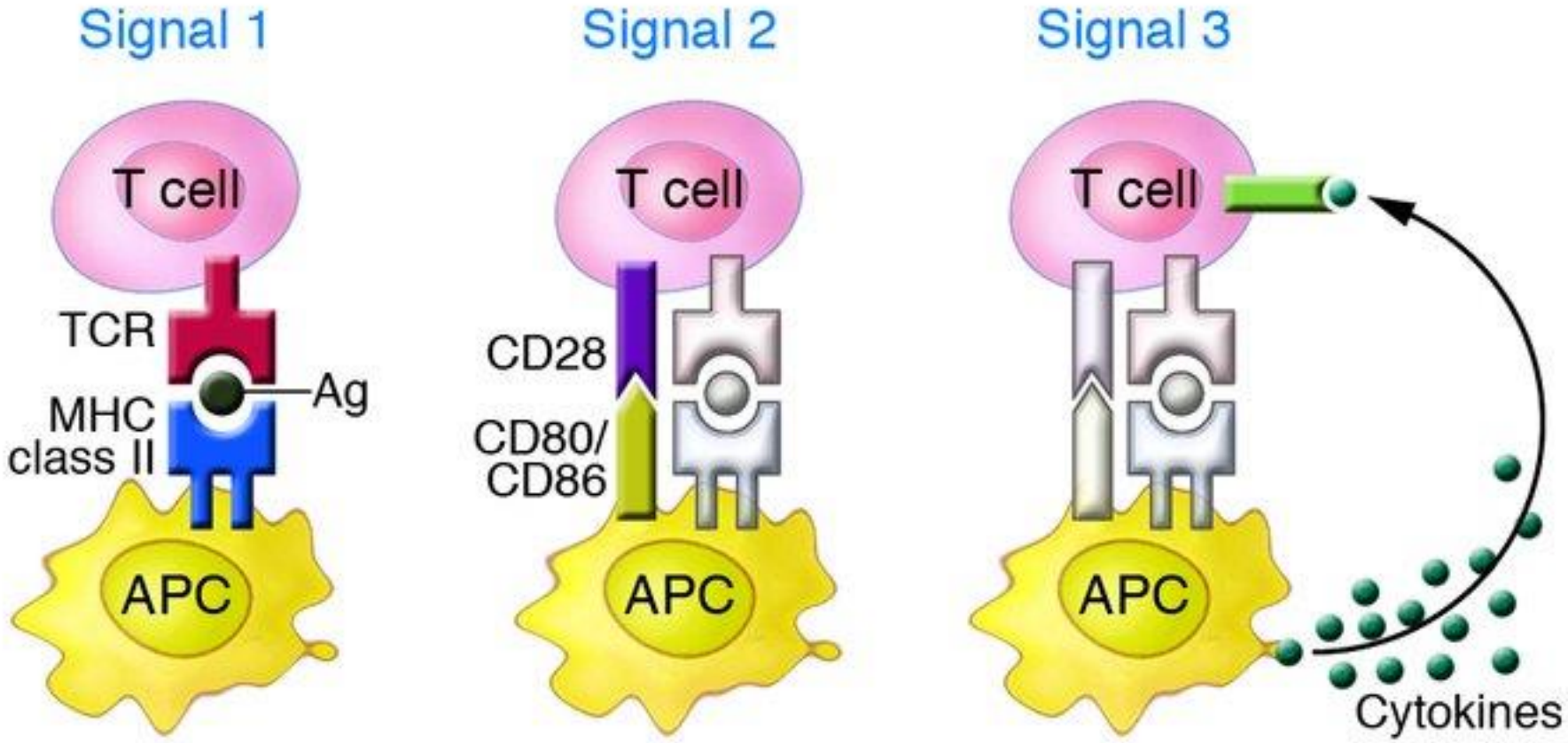


En la sinapsis inmunitaria formada por las células APC y las células T, se requieren <u>TRES SEÑALES para la activación de la célula T naive</u>

Antígeno Vacunal

Co-estimulación

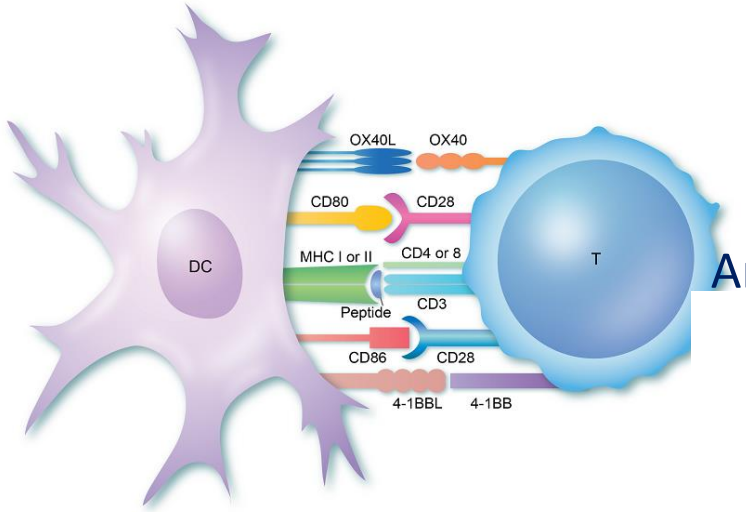
Inflamación



Teoría de las 3 señales

Gutcher I, Becher B. APC-derived cytokines and T cell polarization in autoimmune inflammation. The Journal of clinical investigation [Internet]. 2007 May 1;117(5):1119–27.

COMO SE ACTIVAN LAS CÉLULAS INMUNITARIAS: SISTEMA INMUNE ADPATATIVO



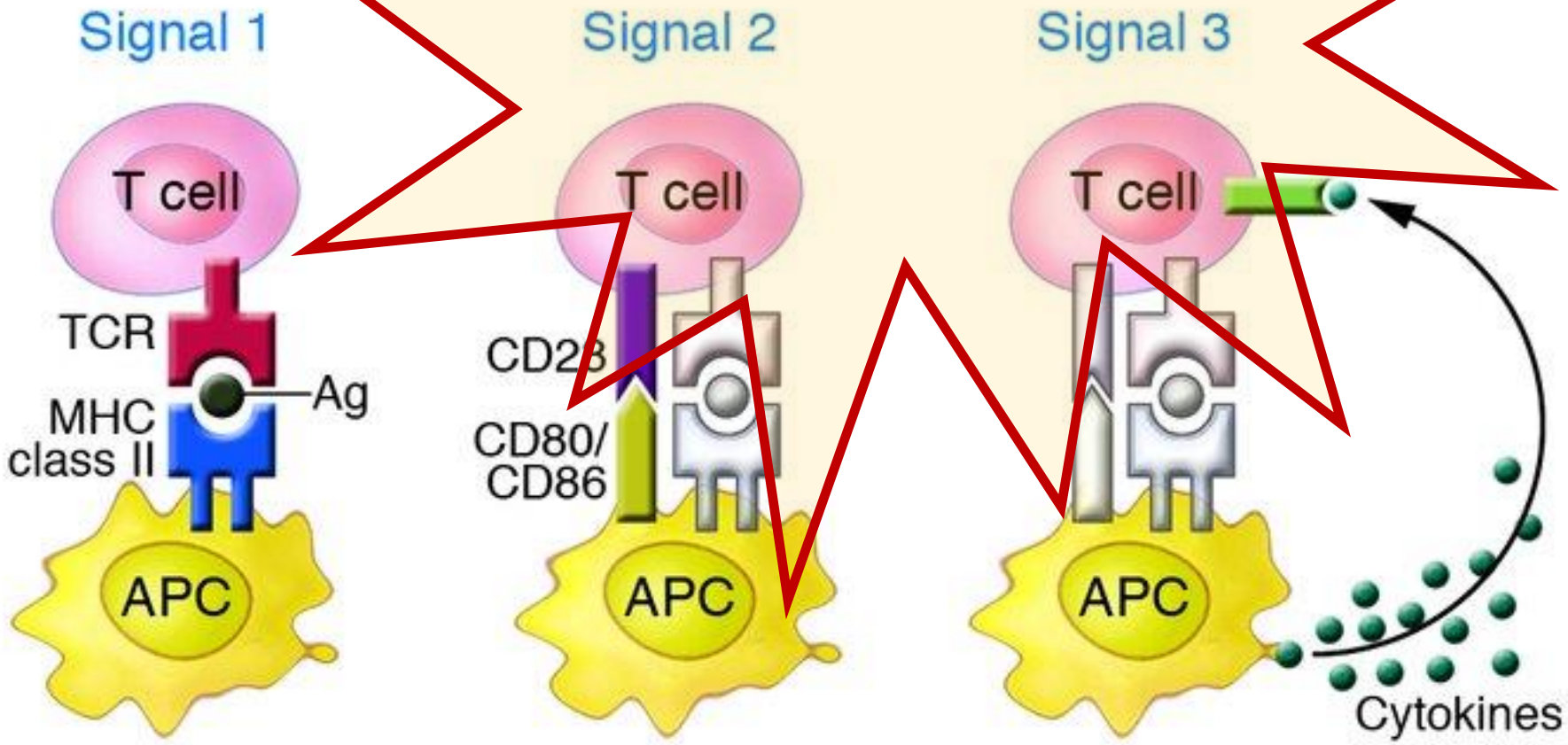
En la sinapsis inmunitaria formada por las células APC y las células T, se requieren TRES SEÑALES para la activación de la célula T naive

ADYUVANTE

Antígeno Vacunal

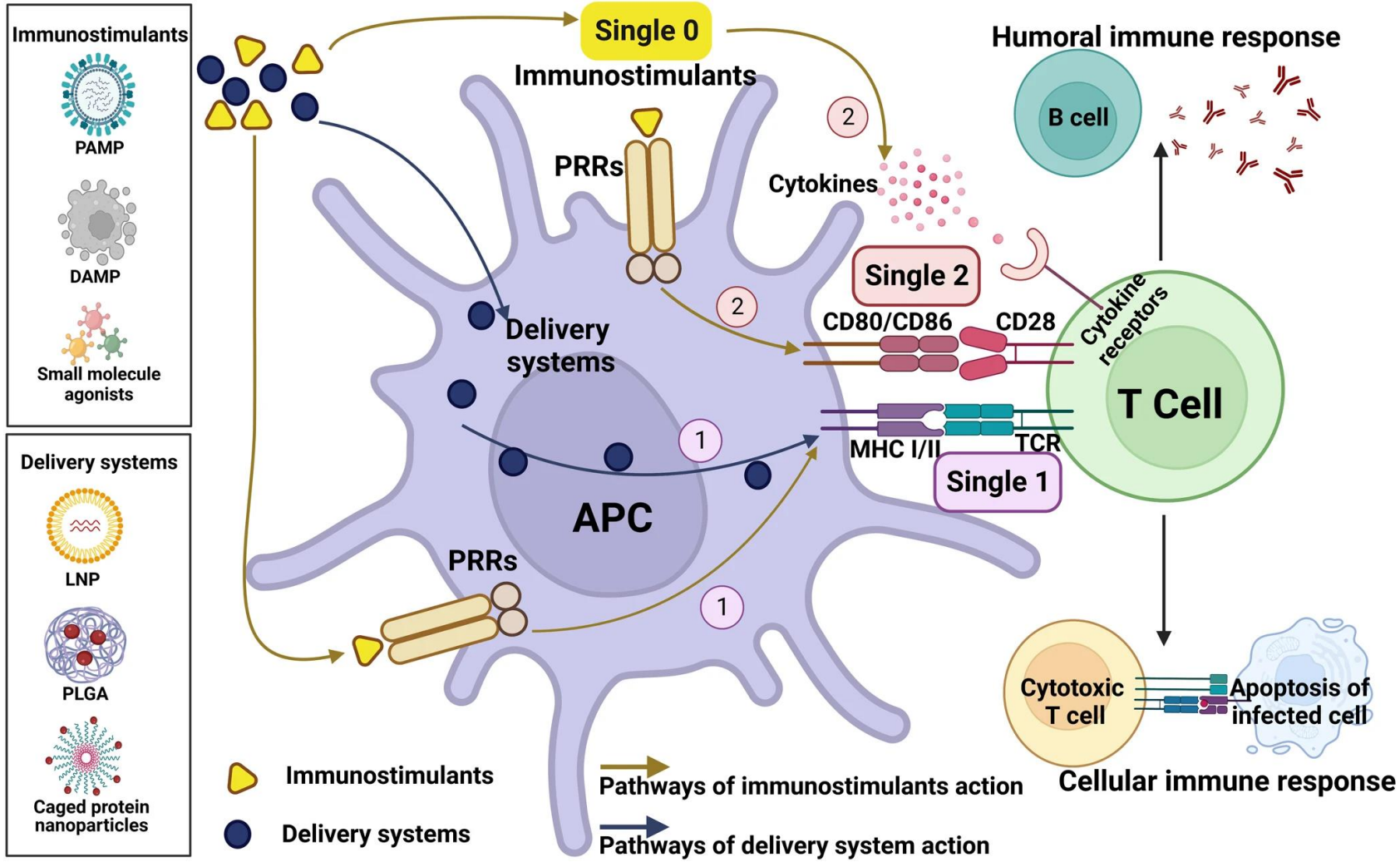
Co-estimulación

Inflamación

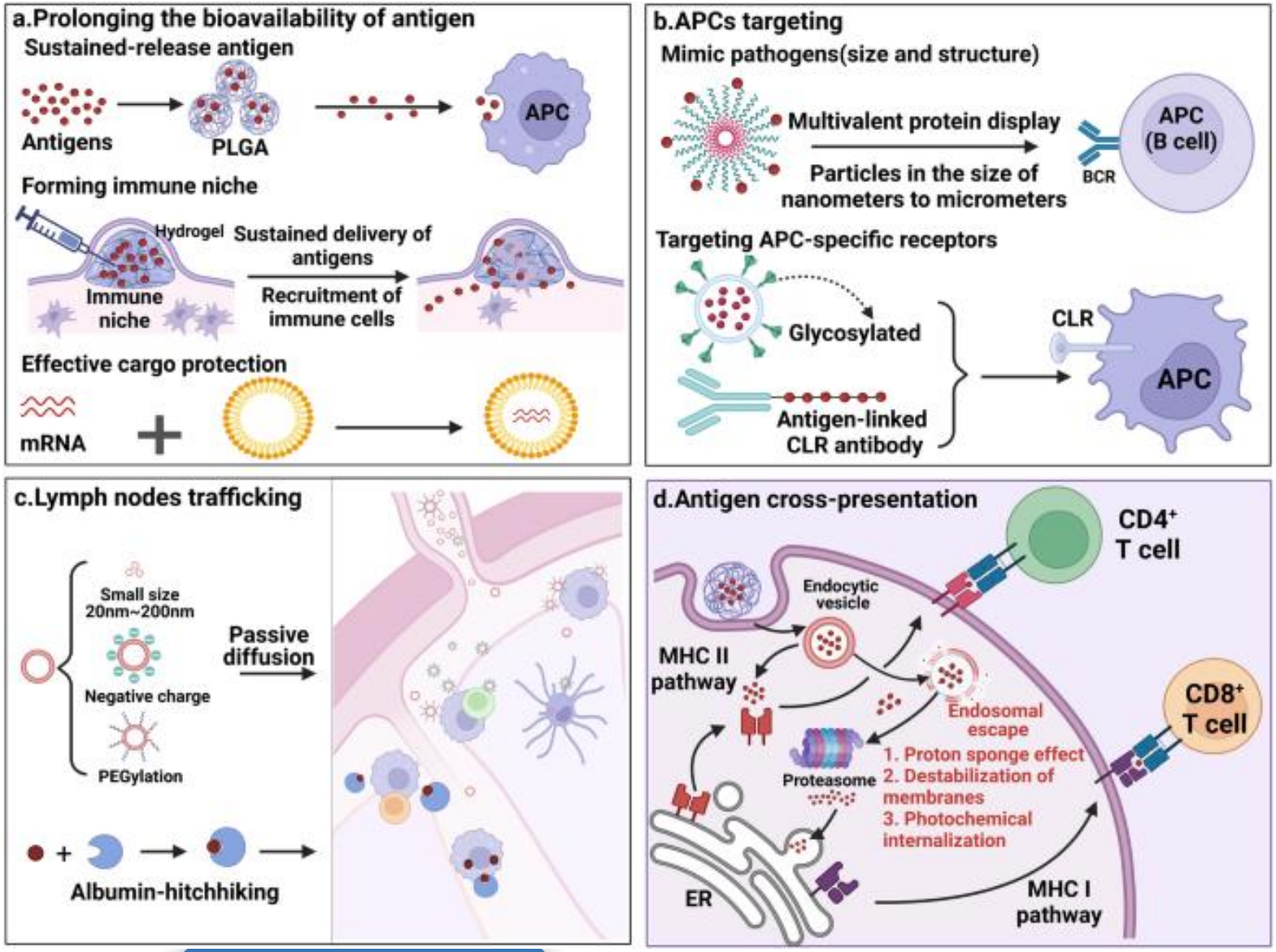


Gutcher I, Becher B. APC-derived cytokines and T cell polarization in autoimmune inflammation. The Journal of clinical investigation [Internet]. 2007 May 1;117(5):1119-27.

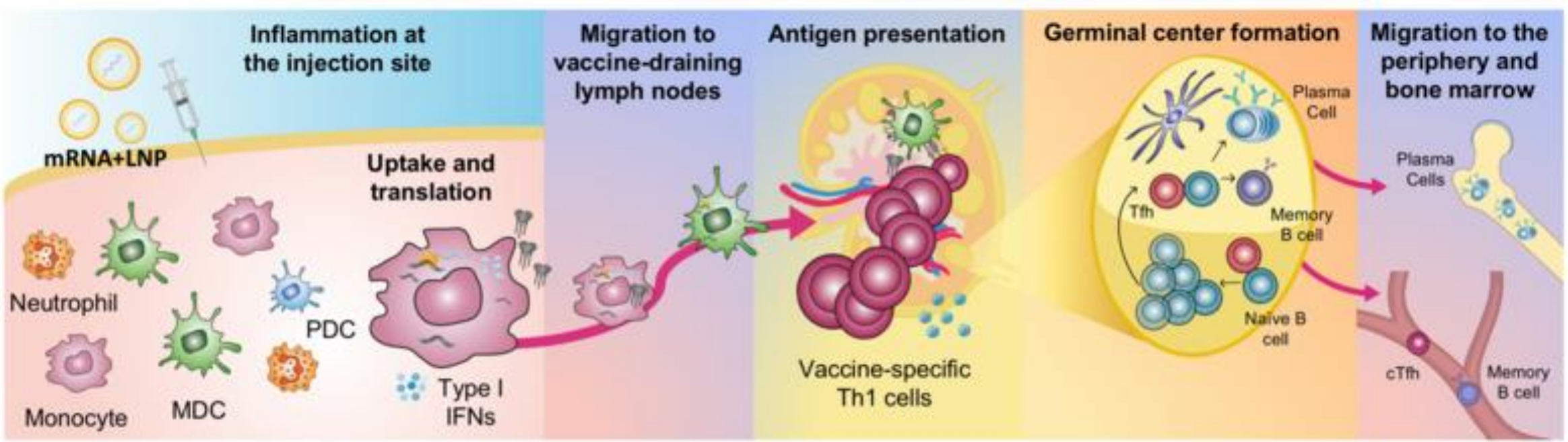
¿PARA QUE SIRVEN LOS ADYUVANTES?



¿PODEMOS MEJORAR LAS VACUNAS?



FASES DE LA INMUNIZACIÓN ACTIVA



FASE 1:
Activación inmunidad innata

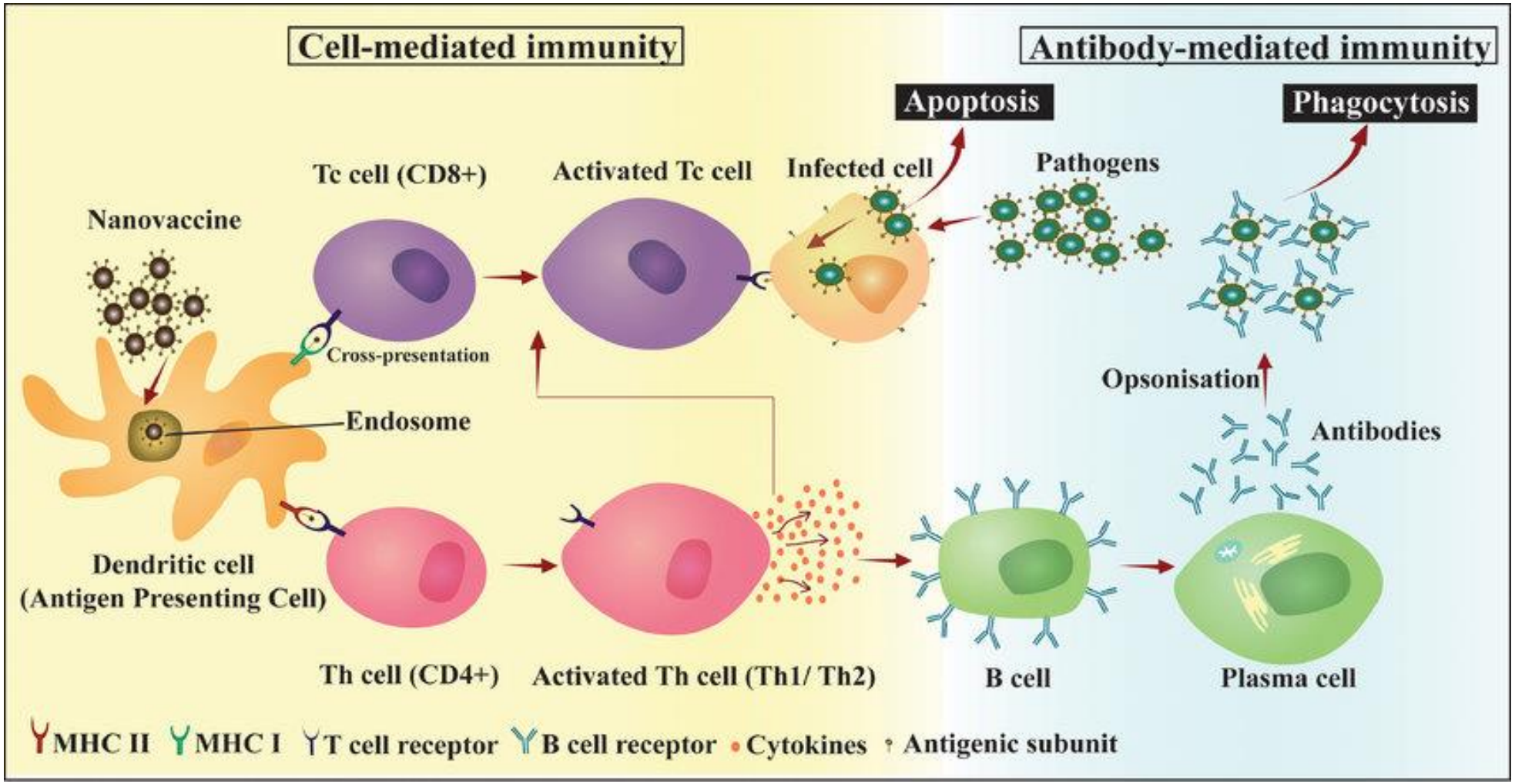
FASE 2:
Migración al ganglio linfático

FASE 3:
Activación inmunidad específica. Inmunidad celular Th1

FASE 4:
Activación inmunidad específica. Activación células B y formación Centro Germinal

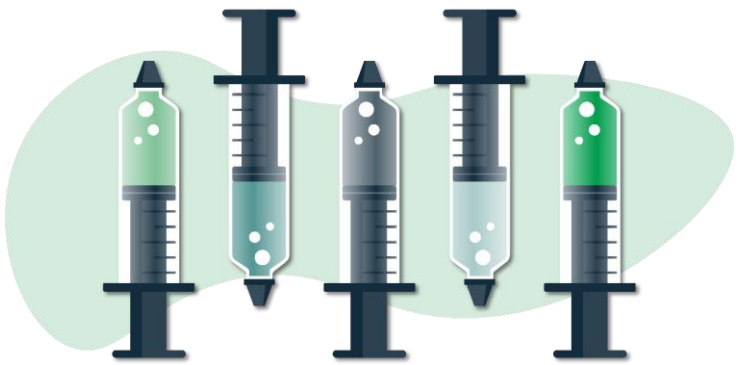
FASE 5:
Migración a periferia y médula ósea. Memoria.

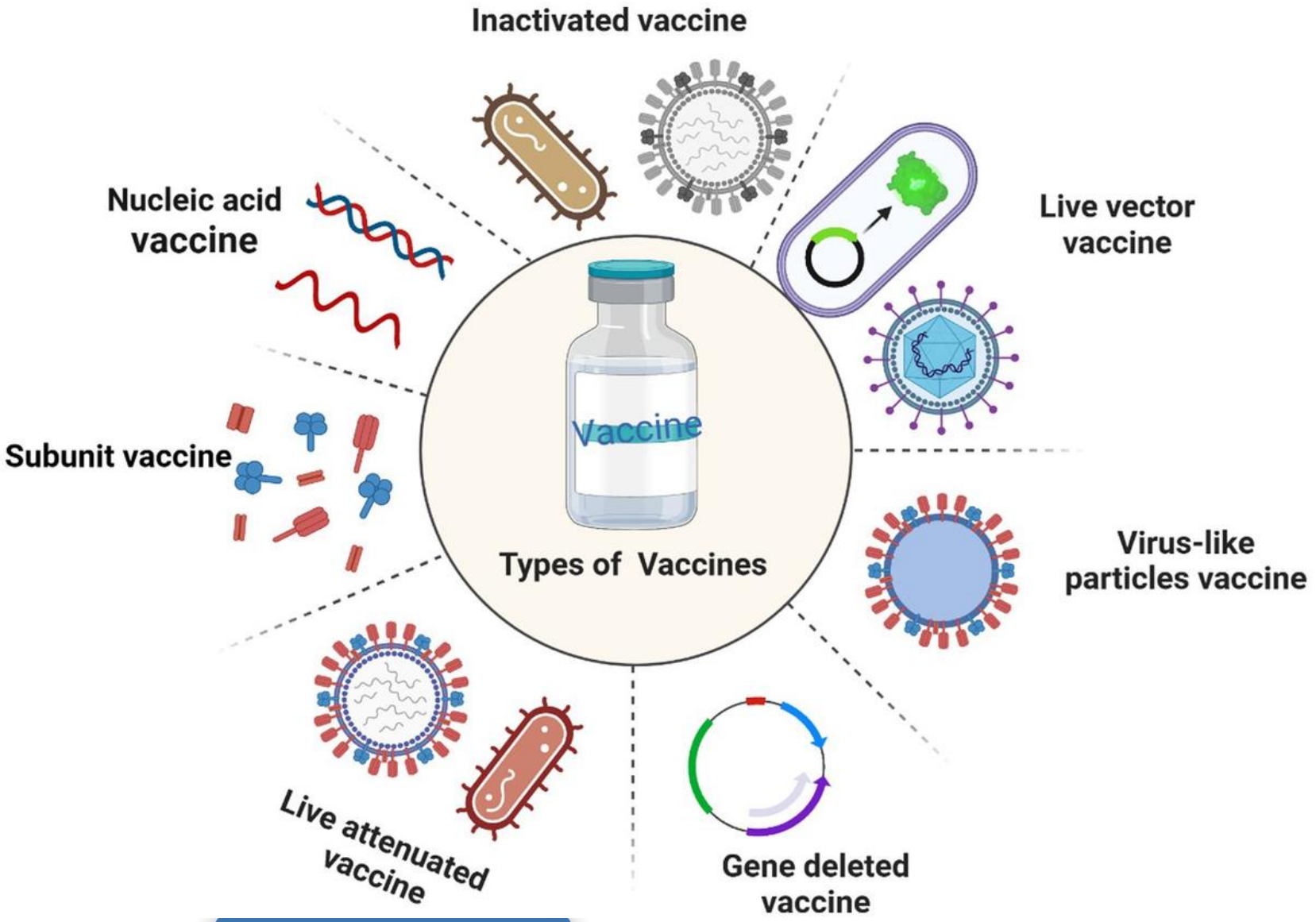
INMUNIDAD CELULAR vs INMUNIDAD HUMORAL



http://dx.doi.org/10.1016/j.actbio.2020.03.020

TIPOS DE VACUNAS: diferentes formas de presentar el antígeno vacunal





https://doi.org/10.3389/fvets.2023.1243835

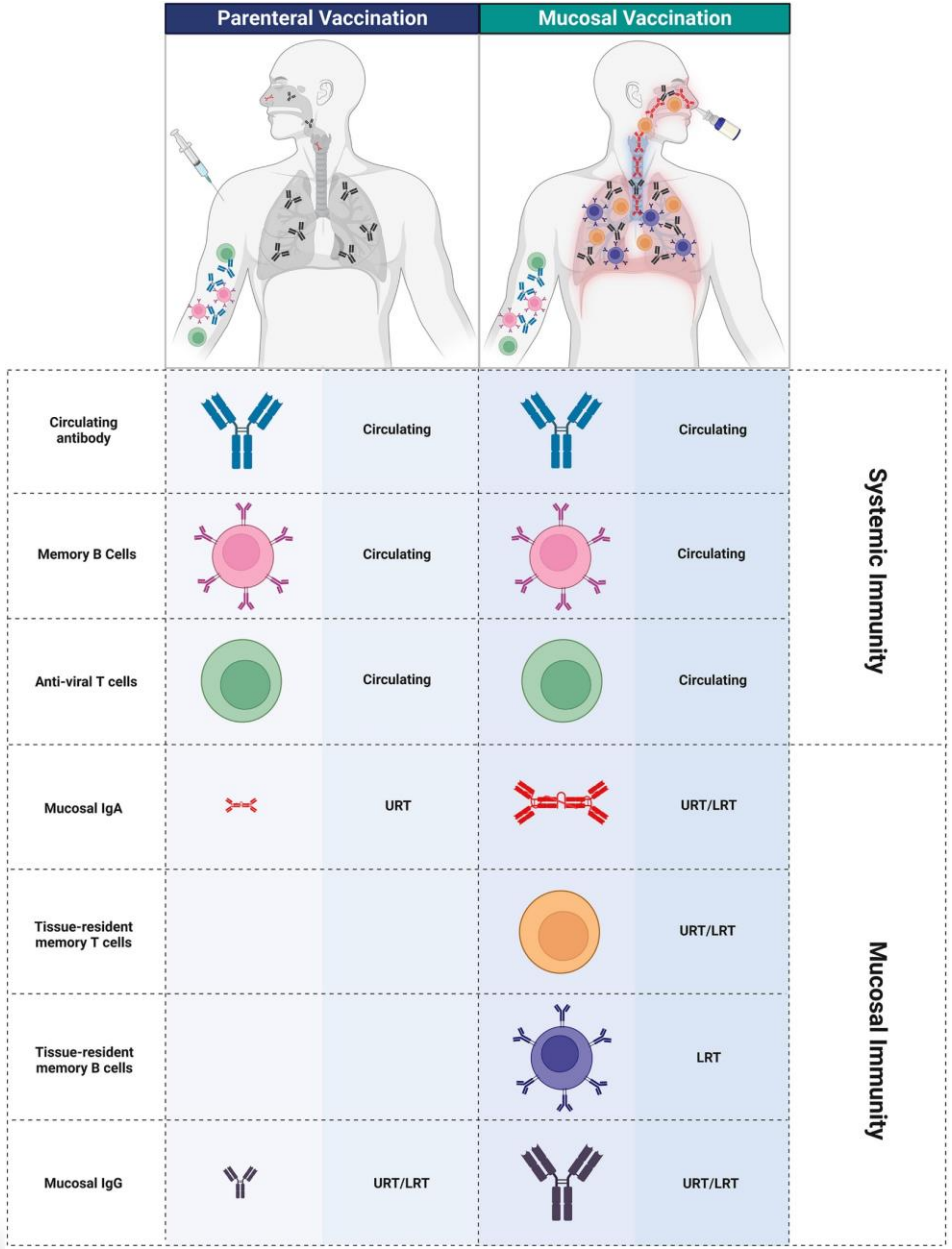
Mucosal vaccines for SARS-CoV-2: triumph of hope over experience

*Devaki Pilapitiya, Adam K. Wheatley, and Hyon-Xhi Tan**

Department of Microbiology and Immunology, University of Melbourne, at The Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, 3000, Australia

eBioMedicine
2023;92: 104585
Published Online 3 May 2023
https://doi.org/10.1016/j.ebiom.2023.104585

- Necesitamos Vacunas que actúen a nivel de la mucosa
- Impacto sobre la transmisión
- Impacto sobre portadores
- Dificultad en el desarrollo de Vacunas con acción mucosal



Flego et al. BMC Medicine 2013, 11:4
http://www.biomedcentral.com/1741-7015/11/4

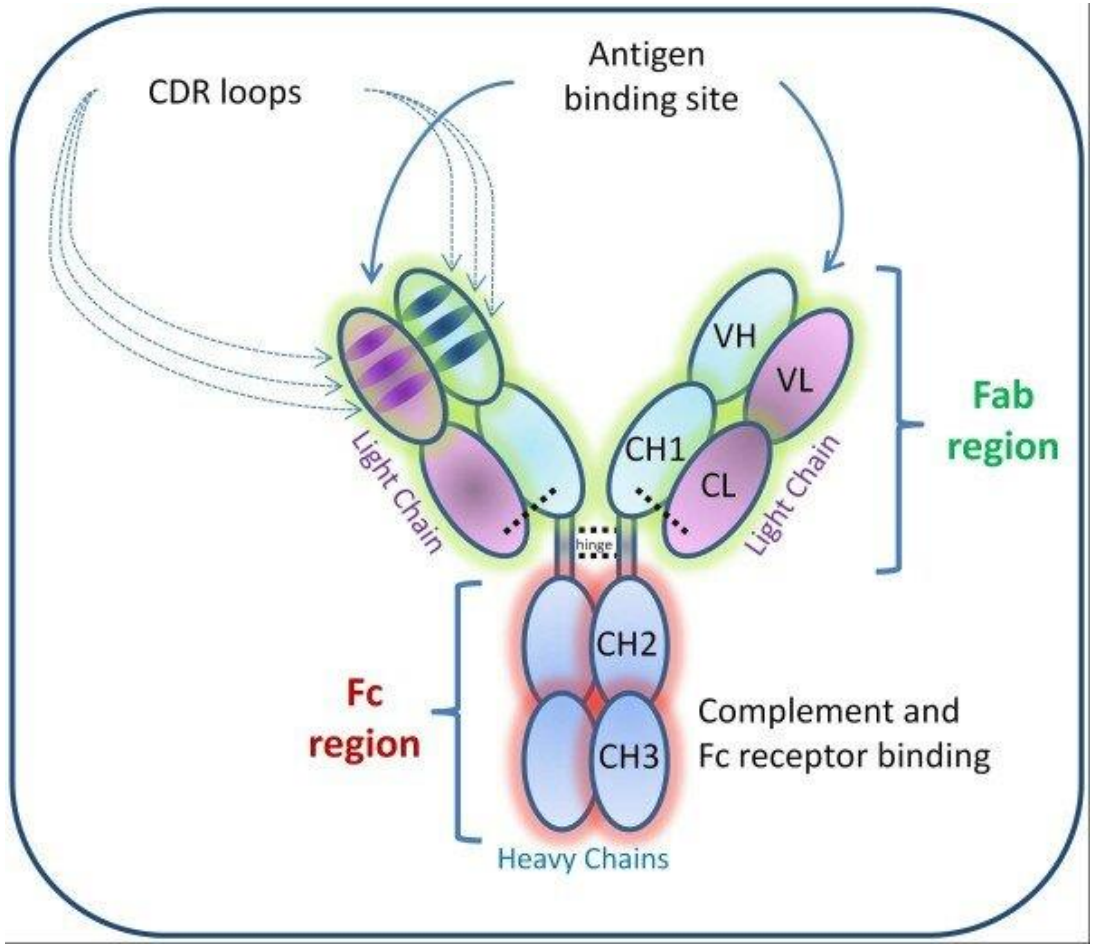
BMC Medicine

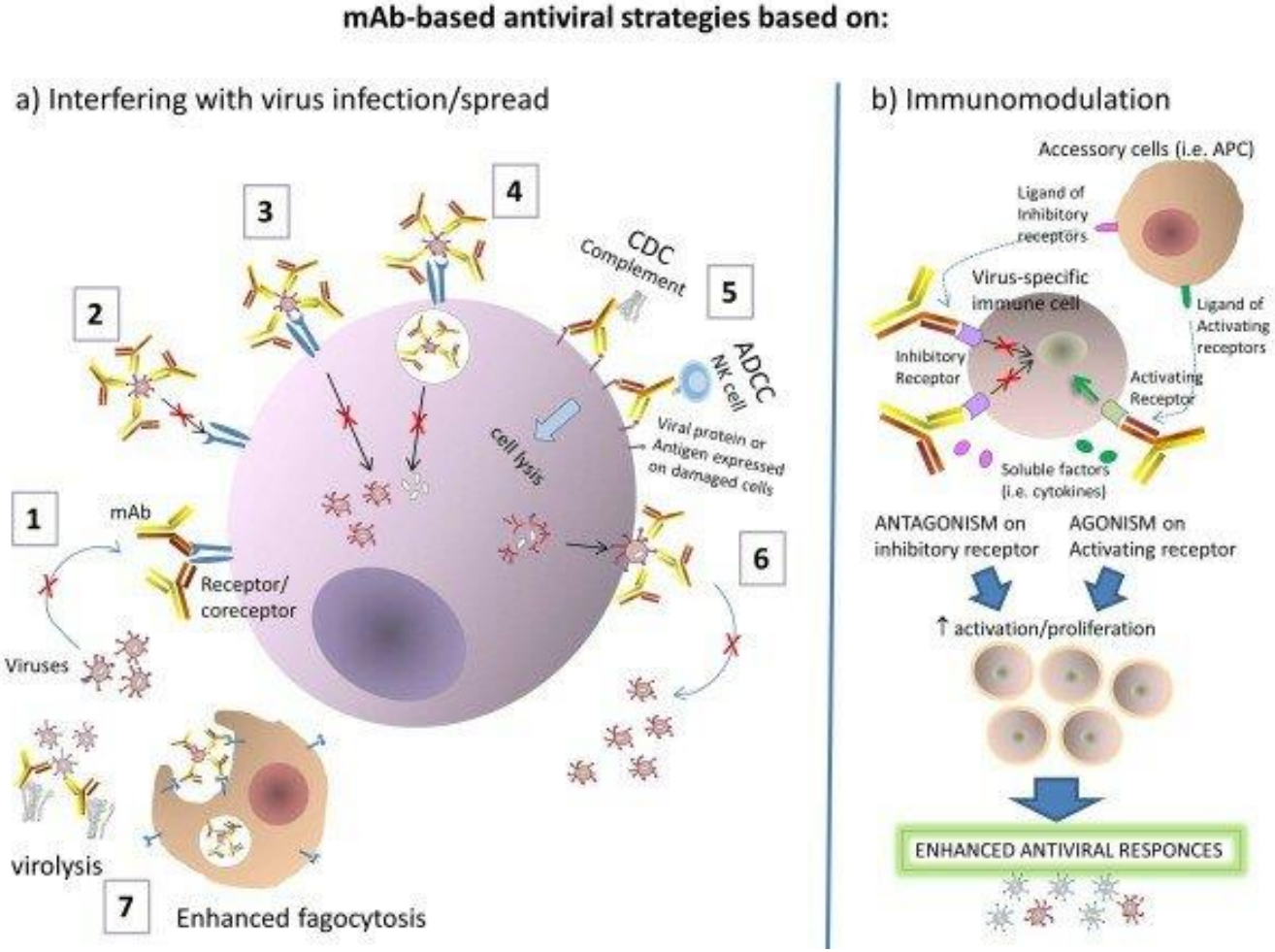
REVIEW Open Access

Clinical development of monoclonal antibody-based drugs in HIV and HCV diseases

Michela Flego*†, Alessandro Ascione†, Maurizio Cianfriglia and Stefano Vella

INMUNIZACIÓN PASIVA: Ac Mo





frontiers in Immunology

REVIEW
published: 07 June 2019
doi: 10.3389/fimmu.2019.01296

TABLE 1 | Fc modifications to enhance antibody effector function.

Modifications or mutations (reference)	Abbreviated name	Phenotype	Enhanced effector function
Ser298Ala/Glu333Ala/Lys334Ala (38)	AAA	• Enhanced FcγRIIIa affinity	ADCC
Ser239Asp/Ala330Leu/Ile332Glu (39, 40)	DLE	• Increased FcγRIIIa affinity • Low binding to inhibitory FcγRIIb	ADCC ADCP
Ser239Asp/Ile332Glu (39, 40)	DE	• Increased FcγRIIIa • Strong binding to inhibitory FcγRIIb	ADCC ADCP
Gly236Ala/Ser239Asp/Ala330Leu/Ile332Glu (41–43)	GASDALIE	• Increased binding affinity to FcγRIIa and FcγRIIIa • Only a small increase to FcγRIIb	ADCC
Gly236Ala (40)	GA	• Increases FcγRIIa affinity • No change in FcγRIIb affinity • Decreased FcγR1	ADCP
Ser239Asp/Ile332Glu/Gly236Ala (40)	DAE	• Recovers FcγRI binding lost by Gly236Ala • Increases FcγRIIIa and FcγRIIa • Enhanced FcγRIIb binding	ADCC ADCP
Leu234Tyr/Gly236Trp/Ser298Ala (44)	YWA	• Improved FcγRIIIa affinity when present in 1 heavy chain constant region • Used in asymmetric Fc design with DLE	ADCC
Phe243Leu, Arg292Pro, Tyr300Leu, Val305Ile, and Pro396Leu (45)	Variant 18	• Enhanced FcγRIIa and FcγRIIIa off-rates • Less than 2 fold enhancement of FcγRIIb	ADCC
Lys326Trp/Glu333Ser (46)		• Increased C1q binding • CDC activity was comparable to Lys326Trp, but improved versus wildtype Fc • Decreased ADCC activity	CDC
Lys326Ala/Glu333Ala (46)		• Increased C1q binding • Preserved ADCC activity	CDC
Lys326Met/Glu333Ser (46)		• Increased CDC activity • Preserved ADCC activity	CDC
Cys221Asp/Asp222Cys (47)		• Increased C1q binding • Preserves FcγRIII affinity and ADCC	CDC
Ser267Glu, His268Phe, and Ser324Thr (48)	EFT	• Increased C1q binding • Ser267Glu increased inhibitory FcγRIIb affinity • Decreased ADCC/ADCP	CDC
His268Phe and Ser324Thr (48)	FT	• Improved CDC • Functions with ADCC and ADCP enhancing mutations • Less potent CDC than EFT	CDC
Glu345Arg (49)	Arg345	• Increased C1q binding • IgG1 hexamer formation	CDC
IgG1/IgG3 cross-subclass (50)	1133 1131	• Increased C1q binding • Preserves ADCC activity	CDC
IgG2/IgG3 cross-subclass (51)	IgG 3-3-3/2-3 IgG 2-2-3-2	• Increases C1q and C4b binding	CDC
4-domain cross-isotype (52)	γγγα	• Decreased FcγRI binding • Decreased Polymeric Ig receptor binding • Decreased half-life	CDC
Tandem cross-isotype (53)	IgG1/IgA2	• Bound to FcγRs, FcαRI, and FcRn • Decreased C1q binding	ADCC
Chimeric cross-isotype (54)	IgGA	• Bound to FcγRI, FcγRIIa, FcαRI • Lost FcRn	ADCC ADCP CDC
Multimeric IgG (55)		• Increased C1q • Increased FcγRI and FcγRIII	CDC
Galactosylation (56, 57)		• Increased C1q	CDC
Biantennary glycan at N297 (58, 59)		• Improved binding to FcγRIIIa	ADCC
Afucosylated glycan at N297 (60)		• Increased binding to FcγRIIIa	ADCC

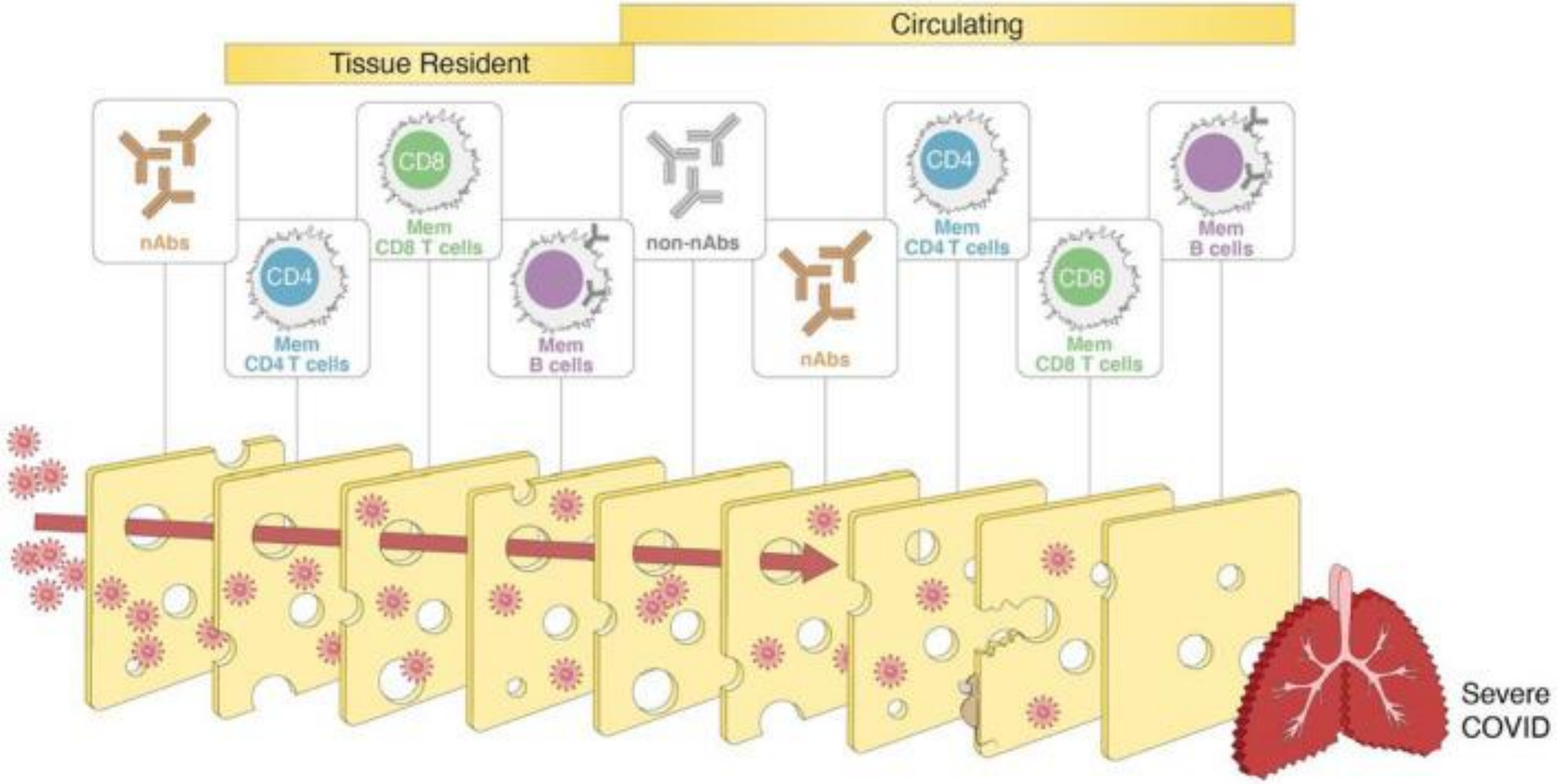
TABLE 2 | Fc modifications to improve antibody circulation half-life.

Modifications or mutations (reference)	Abbreviated name	Phenotype	Enhanced function
Arg435His (110)	His435	• Increased binding to FcRn at low pH	Extended half-life
Asn434Ala (38)	A	• Increased binding to FcRn at pH6	Extended half-life
Met252Tyr/Ser254Thr/Thr256Glu (111)	YTE	• Slowed off-rate for Fc and FcRn • Increased FcRn affinity • Decreased ADCC	Extended half-life
Met428Leu/Asn434Ser (112)	LS	• Increased affinity to and slowed off-rate for FcRn at pH6 • No change in ADCC	Extended half-life
Thr252Leu/Thr253Ser/Thr254Phe (113)	LSF	• Increased binding to FcRn at pH < 6.5	Extended half-life
Glu294delta/Thr307Pro/Asn434Tyr (114)	C8A-66	• Increased binding to FcRn at pH < 6 • No binding to FcRn at pH7.4 • Decreased FcγRIIa binding and ADCC	Extended half-life
Thr256Asn/Ala378Val/ Ser383Asn/Asn434Tyr (114)	C8A-78	• Increased binding to FcRn at pH < 6 • No binding to FcRn at pH7.4	Extended half-life
Glu294delta (114, 115)	Del	• Increased sialylation	Extended half-life

TABLE 3 | Fc modifications to silence antibody effector function.

Modifications or mutations (reference)	Abbreviated name	Phenotype	Reduced effector function
Leu235Glu (129)	LE	• Decreased binding to cell surface FcγRs	ADCC
Leu234Ala/Leu235Ala (130–132)	LALA	• Decreased binding to FcγRI, II, III	ADCC ADCP CDC
Ser228Pro/Leu235Glu (133)	SPLE in IgG4	• Decreased FcγRI binding • Half-life was unchanged	
Leu234Ala/Leu235Ala/Pro329Gly (134)	LALA-PG	• Eliminated binding to FcγRI, II, III, C1q	ADCP
Pro331Ser/Leu234Glu/Leu235Phe (135, 136)	TM	• Decreased binding to FcγRI, II, III and C1q	CDC
Asp265Ala (134, 137)	DA	• Decreased binding to FcγRI, II, III	ADCC ADCP
Gly237Ala (138)		• Decreased binding to FcγRII	ADCP
Glu318Ala (138)		• Decreased binding to FcγRII	ADCP
Glu233Pro (38)		• Decreased binding to FcγRI, II, and III	
Gly236Arg/Leu328Arg (139, 140)	GRLR	• Decreased binding to all FcγR	ADCC
IgG2-IgG4 cross-subclass (141, 142)	IgG2/G4	• Decreased binding to FcγRs and C1q	
His268Gln/Val309Leu/Ala330Ser/Pro331Ser (143, 144)	IgG2m4	• Decreased binding to all FcγR • Decreased C1q binding	ADCC ADCP CDC
Val234Ala/Gly237Ala/Pro238Ser/ His268Ala/Val309Leu/Ala330Ser/Pro331Ser (144)	IgG2σ	• Near complete elimination of FcγRI, IIa, IIb, and IIIa binding • Decreased C1q binding • Binds FcRn	ADCC ADCP CDC
Leu234Ala/L235Ala/Gly237Ala/P238Ser/ His268Ala/Ala330Ser/Pro331Ser (144–146)	IgG1σ	• Near complete elimination of FcγRI, IIa, IIb, and IIIa binding • Binds FcRn	ADCC CDC
Ala330Leu (89)	AL	• Decreased C1q binding • Part of DLE mutations	CDC
Asp270Ala (89)		• Decreased C1q binding	CDC
Lys322Ala (89)		• Decreased C1q binding	CDC
Pro329Ala (89)		• Decreased C1q binding	CDC
Pro331Ala (89)		• Decreased C1q binding	CDC
IgG2-IgG3 cross-subclass (51)		• Decreased C1q binding	CDC
High mannose glycosylation (147, 148)		• Decreased C1q binding	CDC
Val264Ala (137)		• Decreased C1q binding	CDC
Phe241Ala (137)		• Decreased C1q binding	CDC
Asn297Ala or Gly or Gln (32, 149–152)		• Decreased binding to FcγRI and IIIa • Decreased C1q binding	ADCC ADCP CDC
S228P/Phe234Ala/Leu235Ala (144)	IgG4 PAA	• Decreased binding to FcγRI, IIa and IIIa	ADCC CDC

VACUNA: MULTIPLES CAPAS DE PROTECCIÓN



COMO ENTENDER LA INMUNOLOGÍA DE LAS INMUNIZACIONES … EN 20´

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