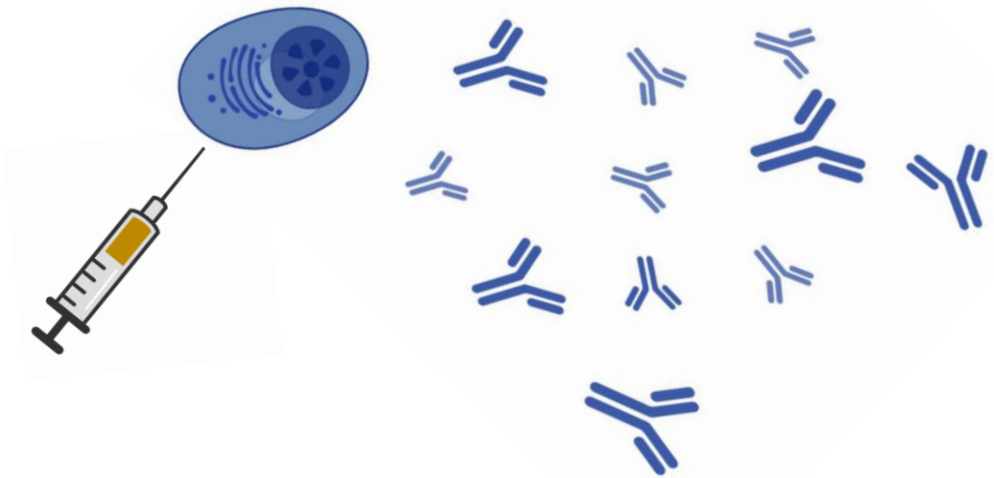
Vaccination chez les patients sous immunothérapie en immunologie

26/09/2024



Yannick Dieudonné

Immunologie Clinique et Médecine Interne
INSERM U1109 Immuno-Rhumatologie Moléculaire
Hôpitaux Universitaires de Strasbourg

Stratégie vaccinale

Cas n°1

Femme, 38 ans
Pas de co-morbidité

Polyarthrite rhumatoïde

Methotrexate 15mg/semaine

Cas n°2

Femme, 62 ans
Tabagique

Maladie de Crohn
Rhumatisme axial

Infliximab

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Patient, 68 ans
Cardiopathie post HTA

Vascularite ANCA
Atteinte pulmonaire et neuro périphérique

Rituximab

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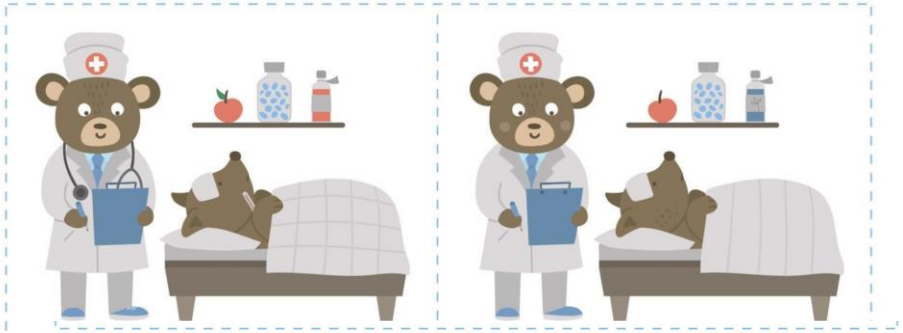
Différences ?



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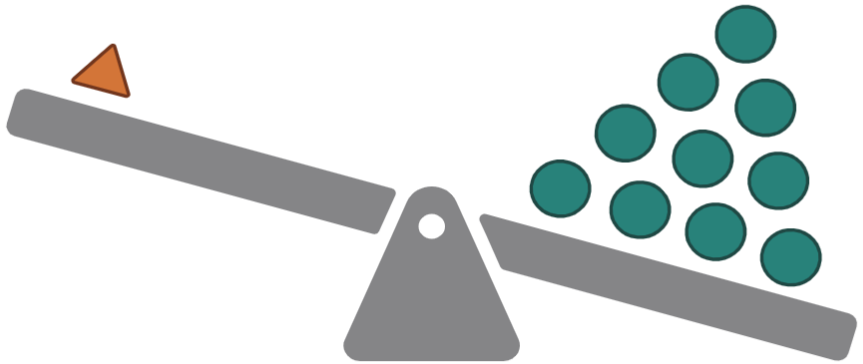
Peut-on généraliser?

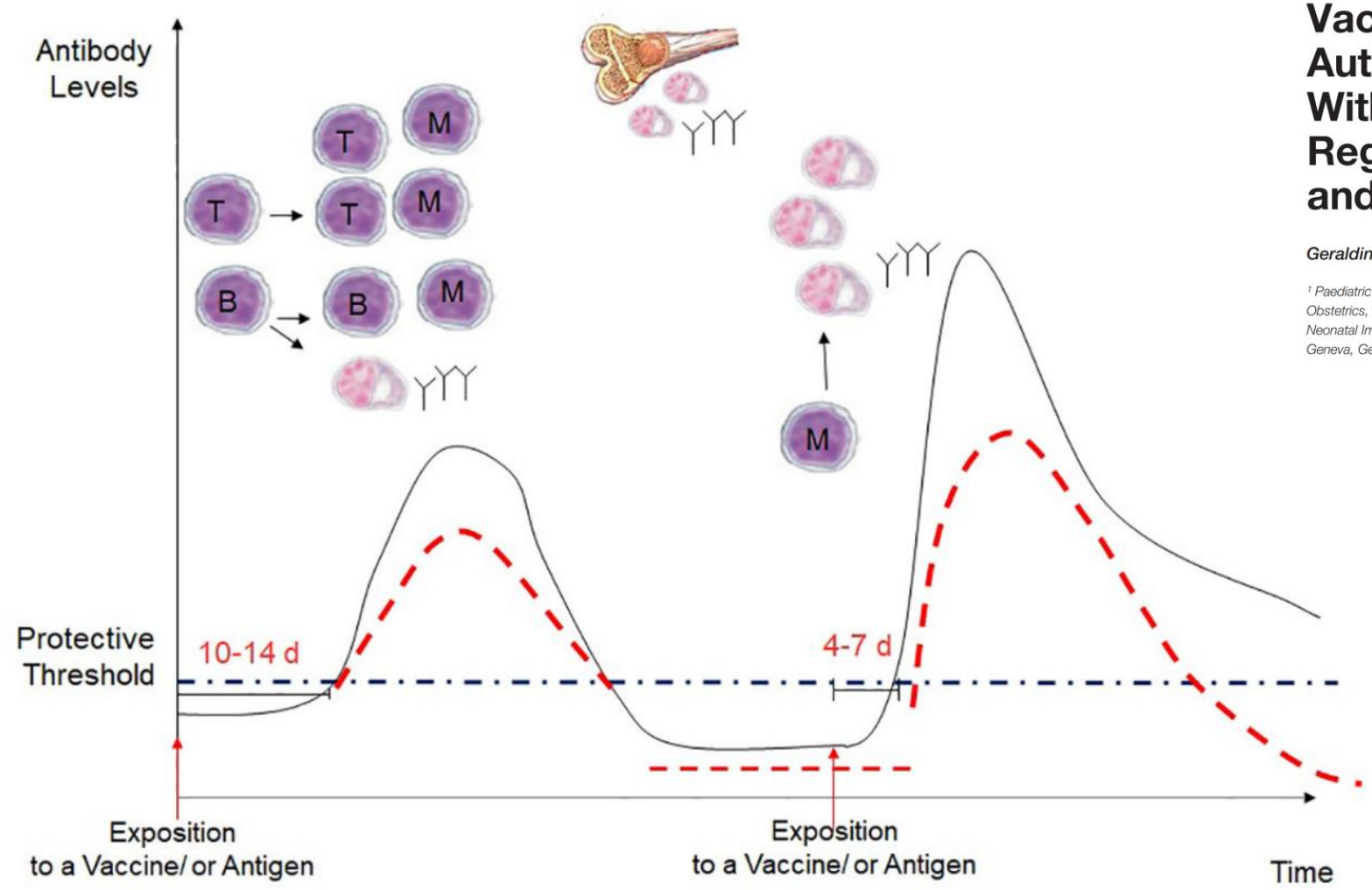
=

Déficit immunitaire secondaire

→ Réponse vaccinale altérée



Peut-on généraliser?



Vaccination in Children With Autoimmune Disorders and Treated With Various Immunosuppressive Regimens: A Comprehensive Review and Practical Guide

Geraldine Blanchard-Rohner[1,2*]

[1] *Paediatric Immunology and Vaccinology Unit, Division of General Paediatrics, Department of Paediatrics, Gynaecology and Obstetrics, Geneva University Hospitals and University of Geneva, Geneva, Switzerland,* [2] *Centre for Vaccinology and Neonatal Immunology, Department of Paediatrics and Pathology-Immunology, Medical Faculty and University Hospitals of Geneva, Geneva, Switzerland*

Peut-on généraliser?

=

Déficit immunitaire secondaire

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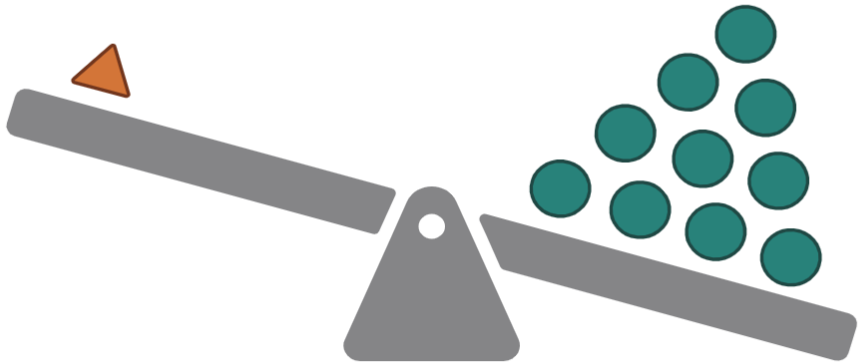


≠

Type de traitement
Type de maladie auto-immune
Terrain

→ Temporalité
→ Risque infectieux
→ Tolérance

Déficit immunitaire propre aux MAI

Maladie auto-immune

Lymphopénie

Hypogammglobulinémie

Consommation complément

Poussées +++

Déficit immunitaire primitif (Inborn errors of immunity)

Auto-immunité

granulome

Allergie

Lymphoprolifération

Stalman, JACI, 2024

Déficit immunitaire sous immunomodulateur

Classe médicamenteuse	Abréviation	Exemples de molécules
Conventional synthetic DMARD	csDMARD	• Méthotrexate • Léflunomide • Sulfasalazine • Hydroxychloroquine
Targeted synthetic DMARD (inhibiteurs de JAK)	tsDMARD	• Tofacitinib (Xeljanz) • Baricitinib (Olumiant) • Upadacitinib (Rinvoq)
Biological DMARD (anti-TNF, anti-IL-6R, anti-CD20, etc.)	bDMARD	• Adalimumab (anti-TNF) • Tocilizumab (anti-IL-6) • Rituximab (anti-CD20) • Abatacept (CTLA4-Ig)

Verdon, 2020

Déficit immunitaire sous biothérapie

Le déficit secondaire dépend du traitement…

TABLE 15 Summary of the risk of infectious complications of JAK inhibitors (Table view)

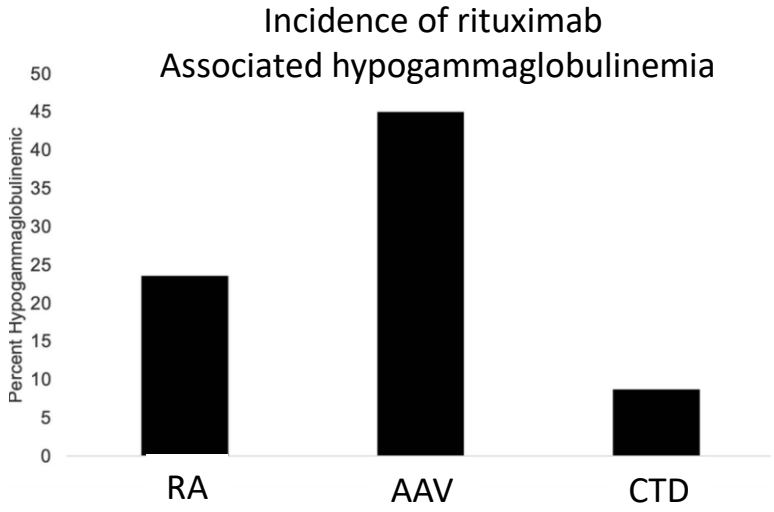
		No. of events/100 PY (reference[s]) with:		% of patients (reference[s]) receiving:	
Drug	**Type of infection**	**Drug**	**Placebo**	**Drug**	**Placebo**
Tofacitinib	All serious infections	3.1 (937), 2.7 (1248), 3.0 (1249), 2.6 (1250)			
	Herpes zoster	2.6 (1251), 4.3 (937), 3.9 (1248), 3.9 (1252)		3.6 (1251)	
	Tuberculosis	0.2 (1253), 0.2 (1254), 0.2 (1248)		0.2 (1253), 0.2 (1254), 0.2 (1248)	
Baricitinib	All serious infections			3 (1255), 1–2 (1256), 2 (1257)	3 (1255), 1 (1257)
	Herpes zoster	2.5 (1258)		4 (1255), 1–2 (1256), 2 (1257)	1 (1255), 0.4 (1257)
Ruxolitinib	All serious infections			2–6 (1258), 4–6 (1259)	
	Herpes zoster	3.5 (1260), 5.3 (1261)	1.0 (1260)	6.4 (1261)	0 (1261)
	Tuberculosis			1 (1262)	

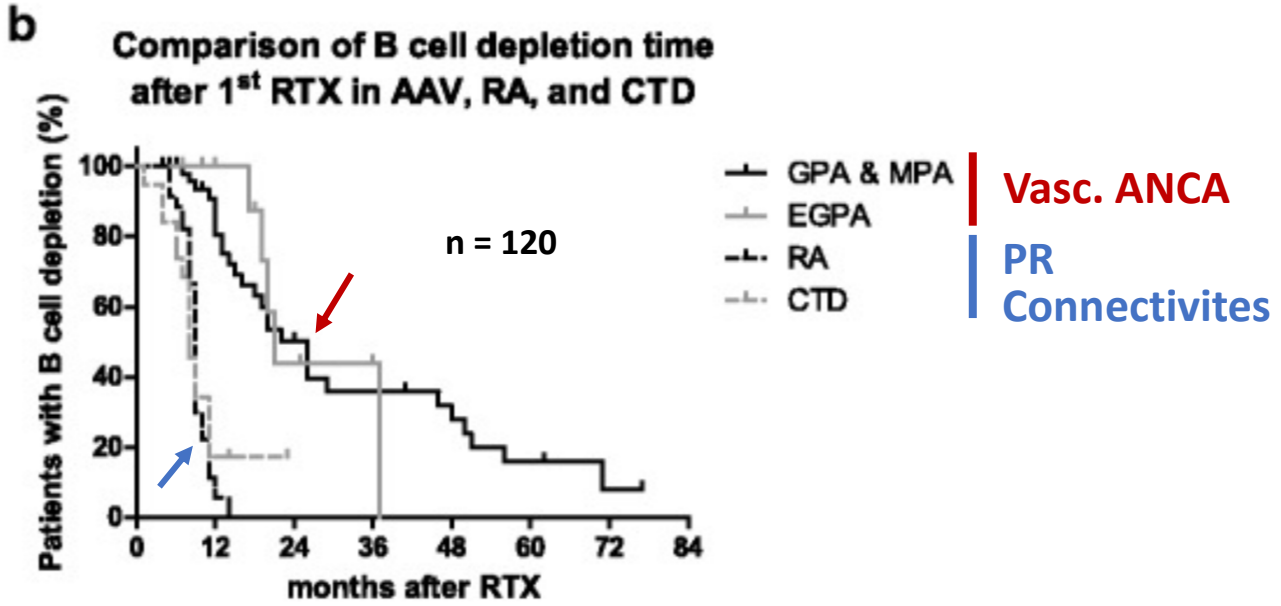
David, Clin Microbiol Rev, 2020

Déficit immunitaire sous biothérapie

Le déficit secondaire dépend du traitement…

Mais aussi du type de MAI





Thiel, Arthritis Res Ther, 2017
Wade, Rheumatol Int, 2021

Considérations générales

Recommandations

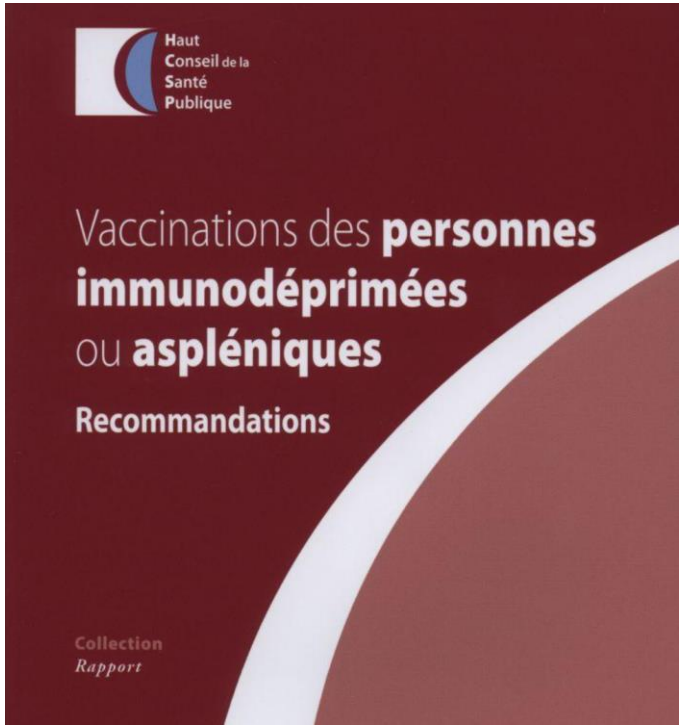
IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

Recommendation

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Victoria Furer ,[1,2] Christien Rondaan,[3,4] Marloes W Heijstek,[5] Nancy Agmon-Levin ,[2,6] Sander van Assen,[7] Marc Bijl,[8] Ferry C Breedveld,[9] Raffaele D'Amelio,[10] Maxime Dougados ,[11] Meliha Crnkic Kapetanovic ,[12] Jacob M van Laar ,[13] A de Thurah ,[14] Robert BM Landewé ,[15,16] Anna Molto ,[11] Ulf Müller-Ladner,[17] Karen Schreiber,[18,19] Leo Smolar,[20] Jim Walker,[21] Klaus Warnatz,[22] Nico M Wulffraat ,[23] Ori Elkayam [1,2]



Recommandations « générales »

Anticipation +++

Vacciner avant de débuter le traitement ou après pause (4 semaines)

Calendrier vaccinal de la population générale + adaptations

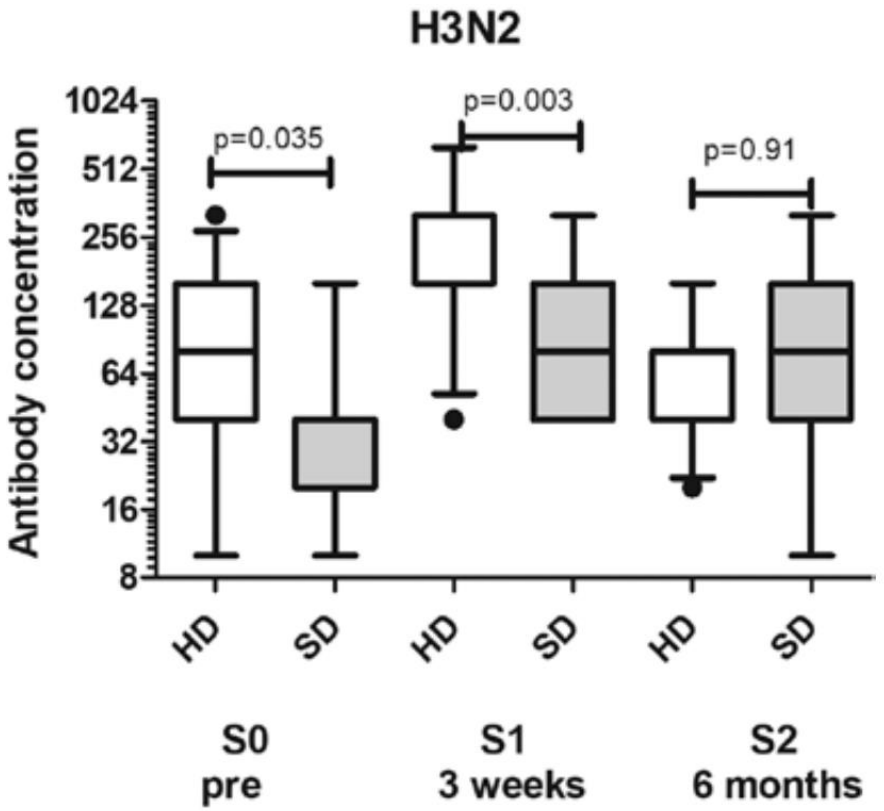
Contre-indication des vaccins vivants

Vaccination de l’entourage

Intérêt des sérologies post vaccinales

Recommendation
1. Influenza vaccination should be strongly considered for the majority of patients with AIIRD.
2. Pneumococcal vaccination should be strongly considered for the majority of patients with AIIRD.
3. Patients with AIIRD should receive toxoid tetanus vaccination in accordance with recommendations for the general population. Passive immunisation should be considered for patients treated with B cell depleting therapy.
4. Hepatitis A and hepatitis B vaccination should be administrated to patients with AIIRD at risk. In specific situations booster or passive immunisation is indicated.
5. Herpes zoster vaccination may be considered in high-risk patients with AIIRD.
6. Vaccination against yellow fever should be generally avoided in patients with AIIRD.
7. Patients with AIIRD, in particular patients with SLE, should receive vaccinations against HPV in accordance with recommendations for the general population.
8. Immunocompetent household members of patients with AIIRD should be encouraged to receive vaccines according to national guidelines with the exception of the oral polio vaccines.

Vaccin haute dose ?



Furer, ARD, 2019
Caldera, IBD, 2020

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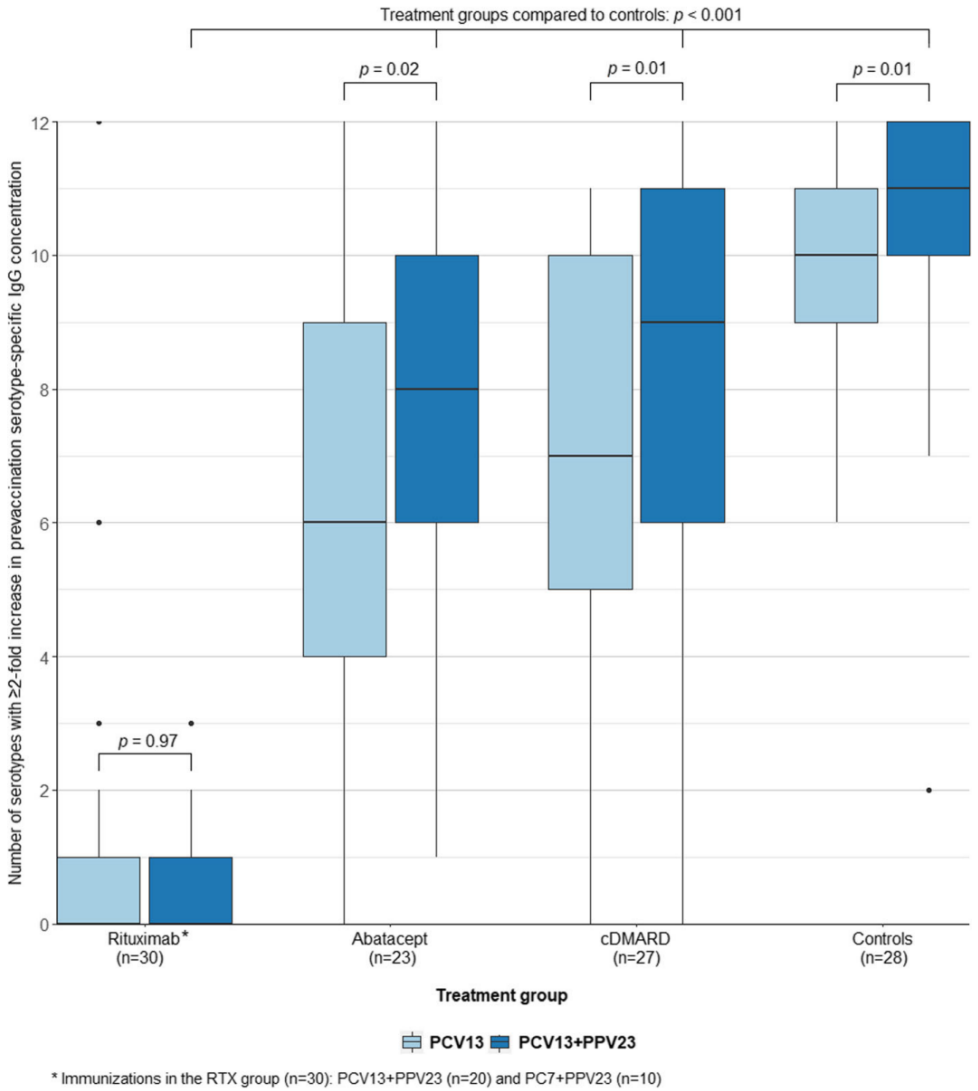
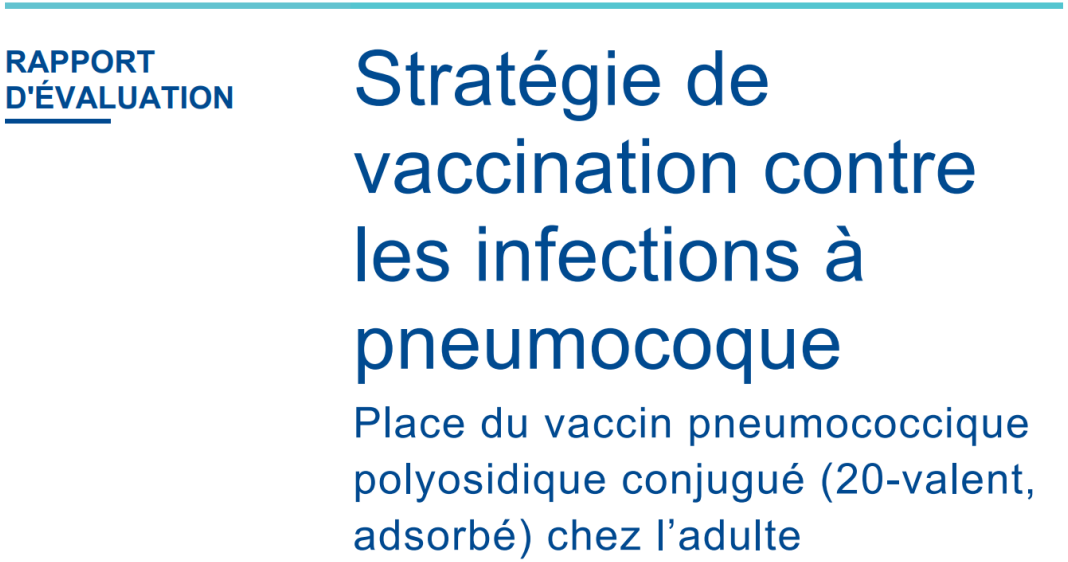


Fig. 2 The number of serotypes with positive antibody response after PCV13 and PCV13 + PPV23 in treatment groups and controls

Furer, ARD, 2019
Nived, Arthritis Res Ther, 2020

Place du vaccin pneumocoque 20-valent



Après P13 ou 23 : 1 an puis P20

Après schéma prime-boost : 5 ans après

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Calendrier des vaccinations et recommandations vaccinales 2024

Avril 2024

Vaccination dTP :

Tous les dix ans

Furer, ARD, 2019
Caldera, IBD, 2020

Recommendation
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Calendrier des vaccinations et recommandations vaccinales 2024

Avril 2024

Vaccination hépatite B :

Vaccination renforcée (40µg) schéma 4 dose (M0, M1, M2, M6)

Furer, ARD, 2019
Caldera, IBD, 2020

Recommendation
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Shingrix :

Chez les patients hématologiques (allogreffe/hémopathies):

Bonne réponse vaccinale

Baisse incidence zona

Efficace contre APZ

Furer, ARD, 2019

Bastidas JAMA 2019

Dagnew, Lancet Inf Disease 2019

Calendrier des vaccinations et recommandations vaccinales 2024

Avril 2024

Recommandations particulières

La vaccination contre le zona est recommandée **chez les personnes âgées de 18 ans et plus, immunodéprimées (déficit immunitaire primitif ou acquis, traitement immunosuppresseurs), avec le vaccin Shingrix®, selon un schéma à deux doses espacées de deux mois entre chaque dose (M0, M2),** lorsque ce vaccin sera pris en charge par l'assurance maladie dans cette indication.

Avant initiation d'une thérapie immunosuppressive, il est recommandé d'administrer le vaccin Shingrix® le plus en amont possible du début du traitement, afin que le schéma vaccinal soit complété idéalement 14 jours avant l'initiation du traitement. Dans cette situation, l'intervalle entre les deux doses de vaccin pourra être réduit à 1 mois.

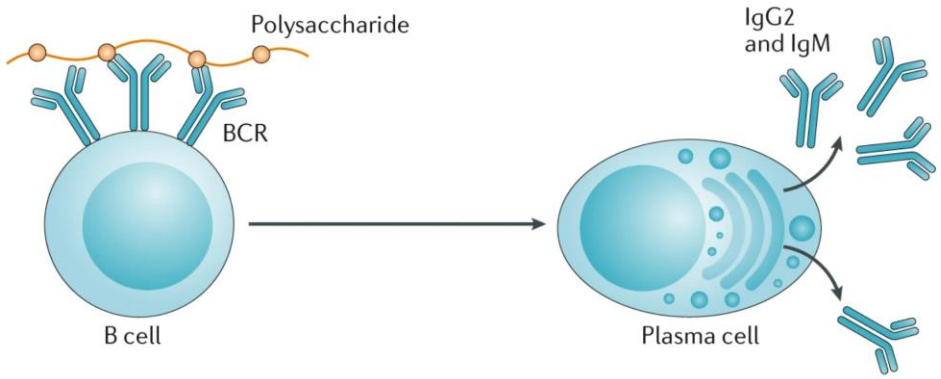
Chez les femmes allaitantes, l'administration du vaccin Shingrix® doit être évaluée au cas par cas, et dans le cadre d'une décision médicale partagée avec l'équipe soignante.

Furer, ARD, 2019
Caldera, IBD, 2020

Stratégie personnalisée ?

Quel vaccin ?

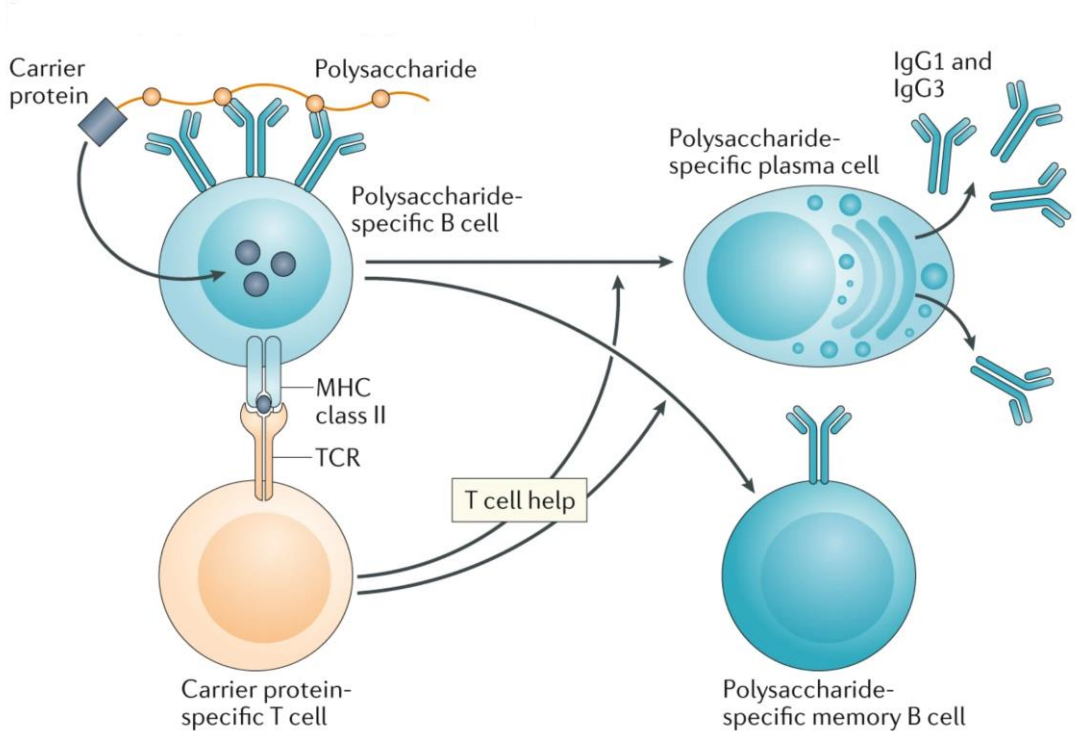
Vaccin polysaccharidique non conjugué



Réponse « T-indépendante »

- Mémoire : courte durée
- Antigènes : polysaccarides (germes encapsulés)
- Exemple : Pneumovax

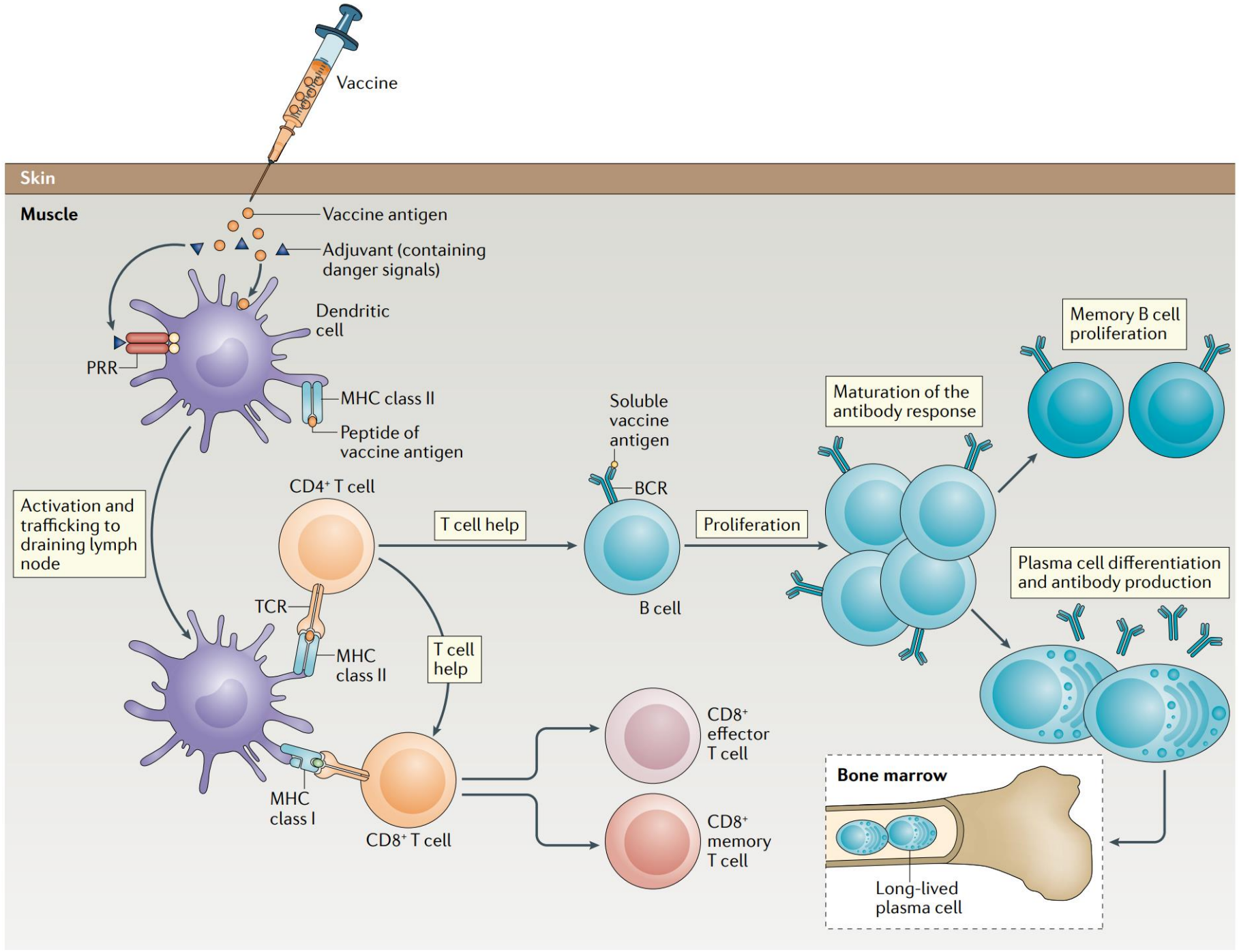
Vaccin polysaccharidique conjugué ou protéique



Réponse « T-dépendante »

- Mémoire ++ : longue durée
- Antigènes peptidiques
- Exemple : DTP

Polard, Nat Rev Immunol, 2021

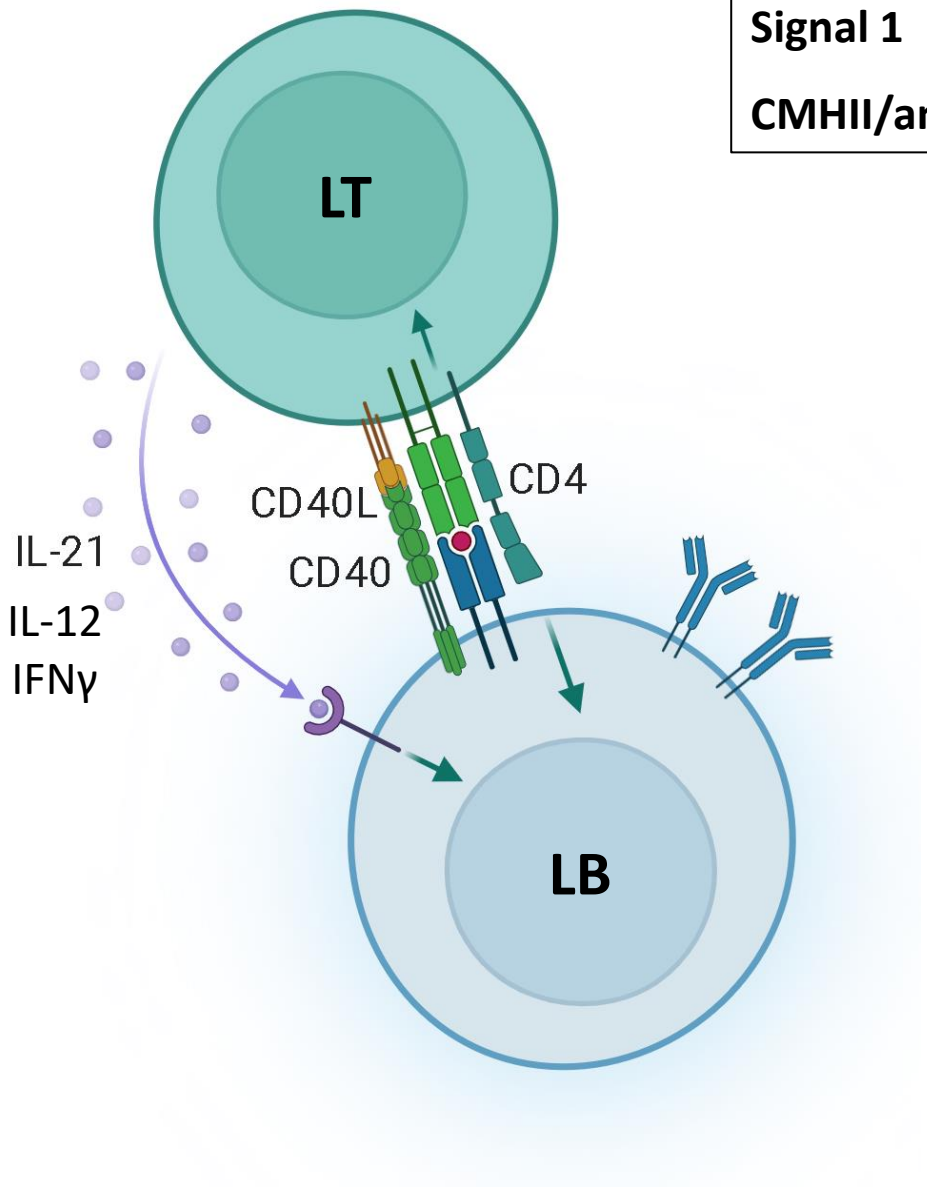


Polard, Nat Rev Immunol, 2021

La synapse immunologique

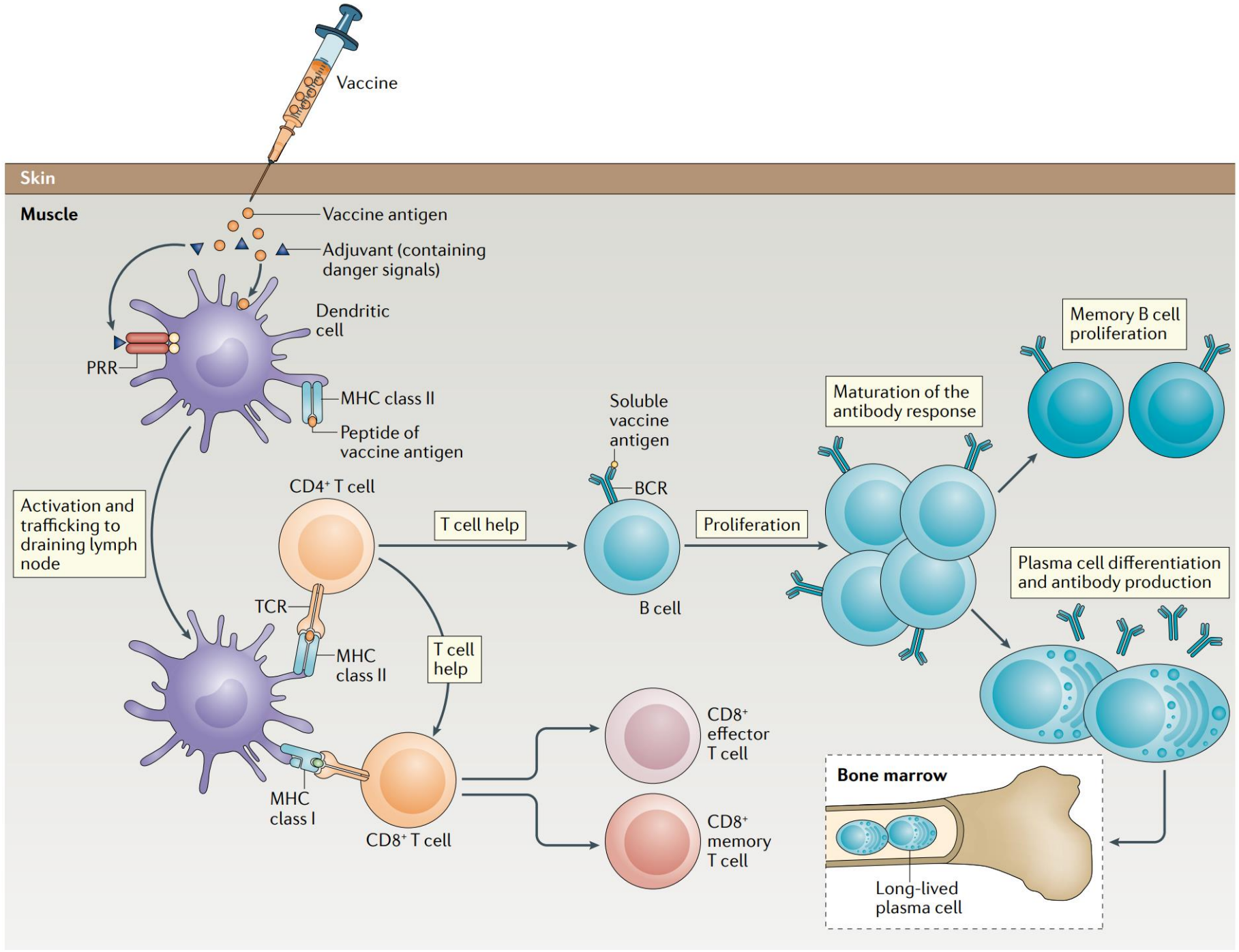
Signal 1

CMHII/antigène-TCR



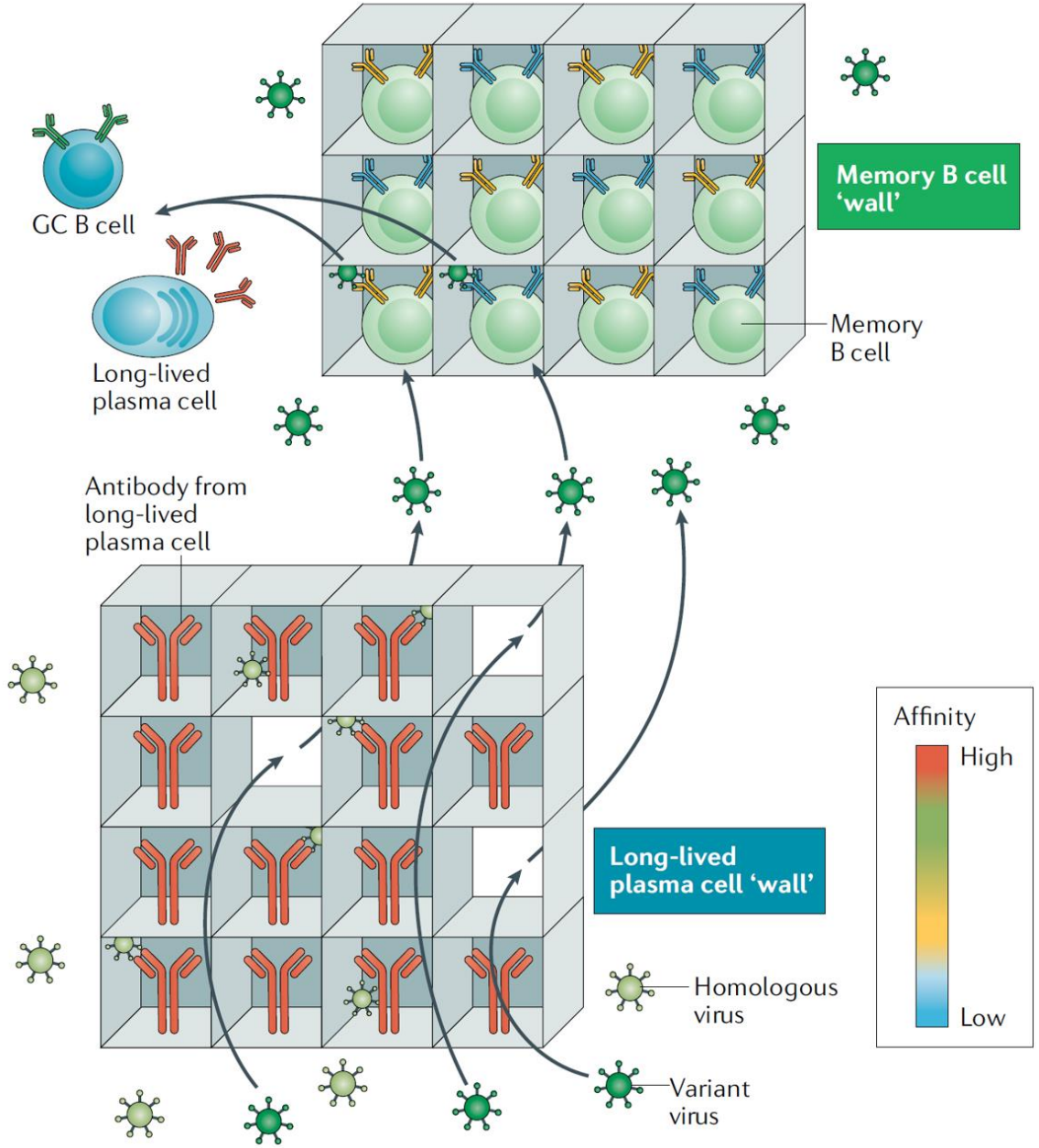
Signal 3
cytokines

Signal 2
Co-stimulation



Polard, Nat Rev Immunol, 2021

Le mur des cellules B mémoires



Akkaya, Nat Rev Immunol, 2021

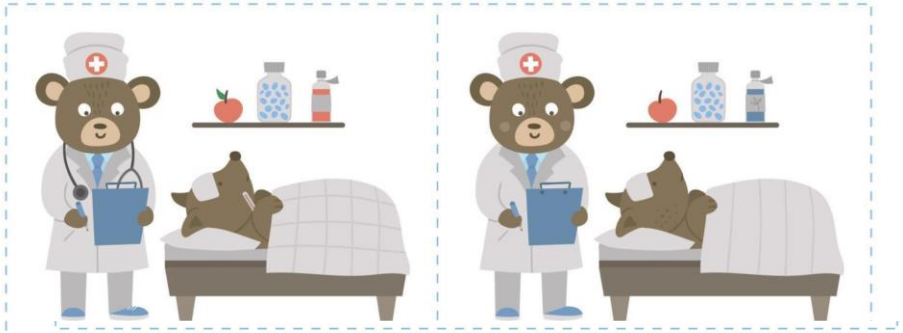
Cas n°2

Femme, 62 ans
Tabagique

Maladie de Crohn
Rhumatisme axial

Infliximab

Différences ?



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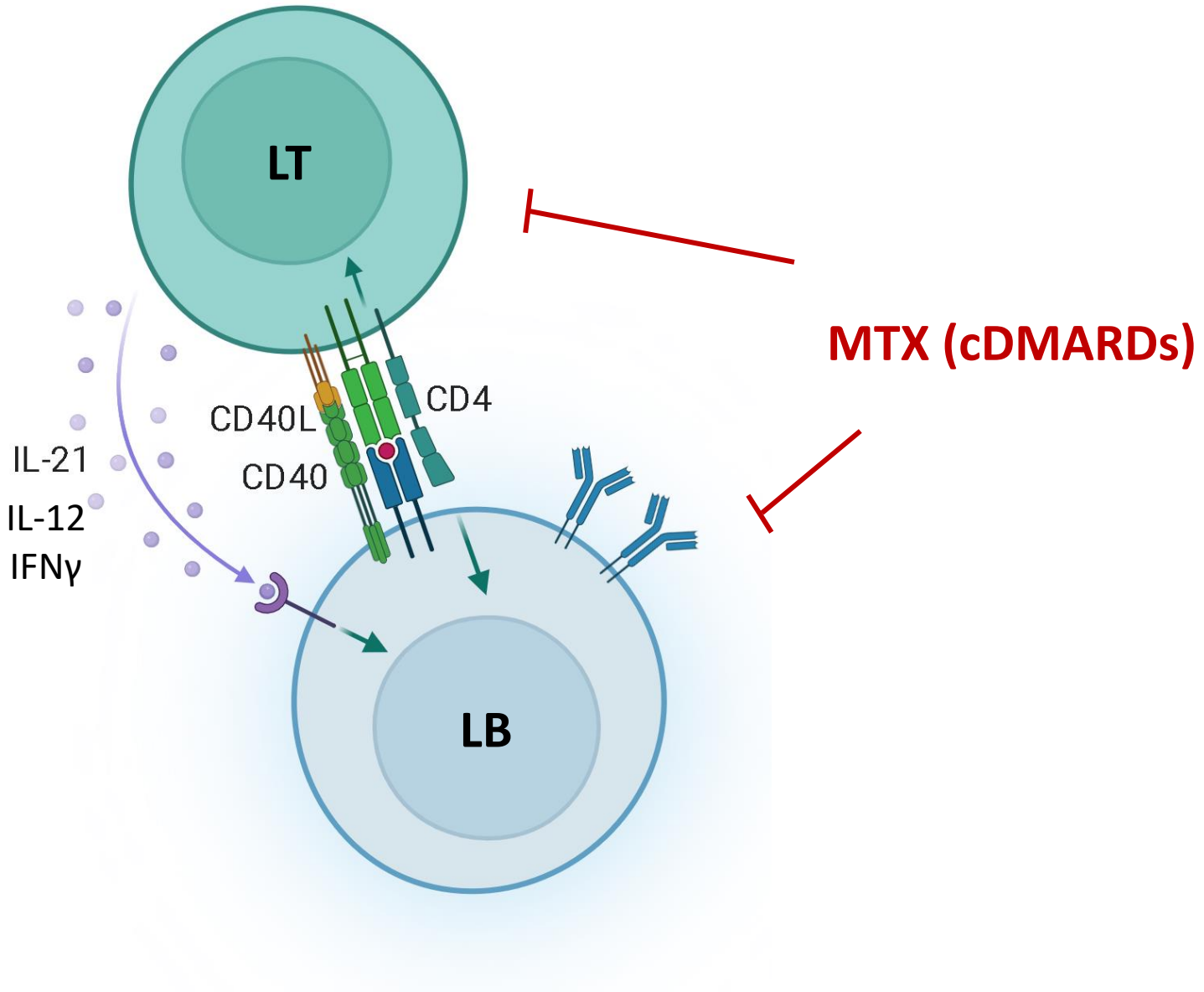
Methotrexate



Methotrexate

Epidemiology

OPEN ACCESS

TRANSLATIONAL SCIENCE

Methotrexate hampers immunogenicity to BNT162b2 mRNA COVID-19 vaccine in immune-mediated inflammatory disease

Rebecca H Haberman,[1,2] Ramin Herati,[3,4] David Simon ,[5,6] Marie Samanovic,[3,4] Rebecca B Blank,[1,4] Michael Tuen,[3,4] Sergei B Koralov,[7] Raja Atreya,[6,8] Koray Tascilar,[5,6] Joseph R Allen,[3] Rochelle Castillo,[1,2] Amber R Cornelius,[3] Paula Rackoff,[1] Gary Solomon,[1] Samrachana Adhikari,[9] Natalie Azar,[1] Pamela Rosenthal,[1] Peter Izmirly,[1] Jonathan Samuels,[1,10] Brian Golden,[1] Soumya M Reddy,[1,2] Markus F Neurath,[6] Steven B Abramson ,[4,11] Georg Schett ,[5,6] Mark J Mulligan,[3,4] Jose U Scher [1,2,4]

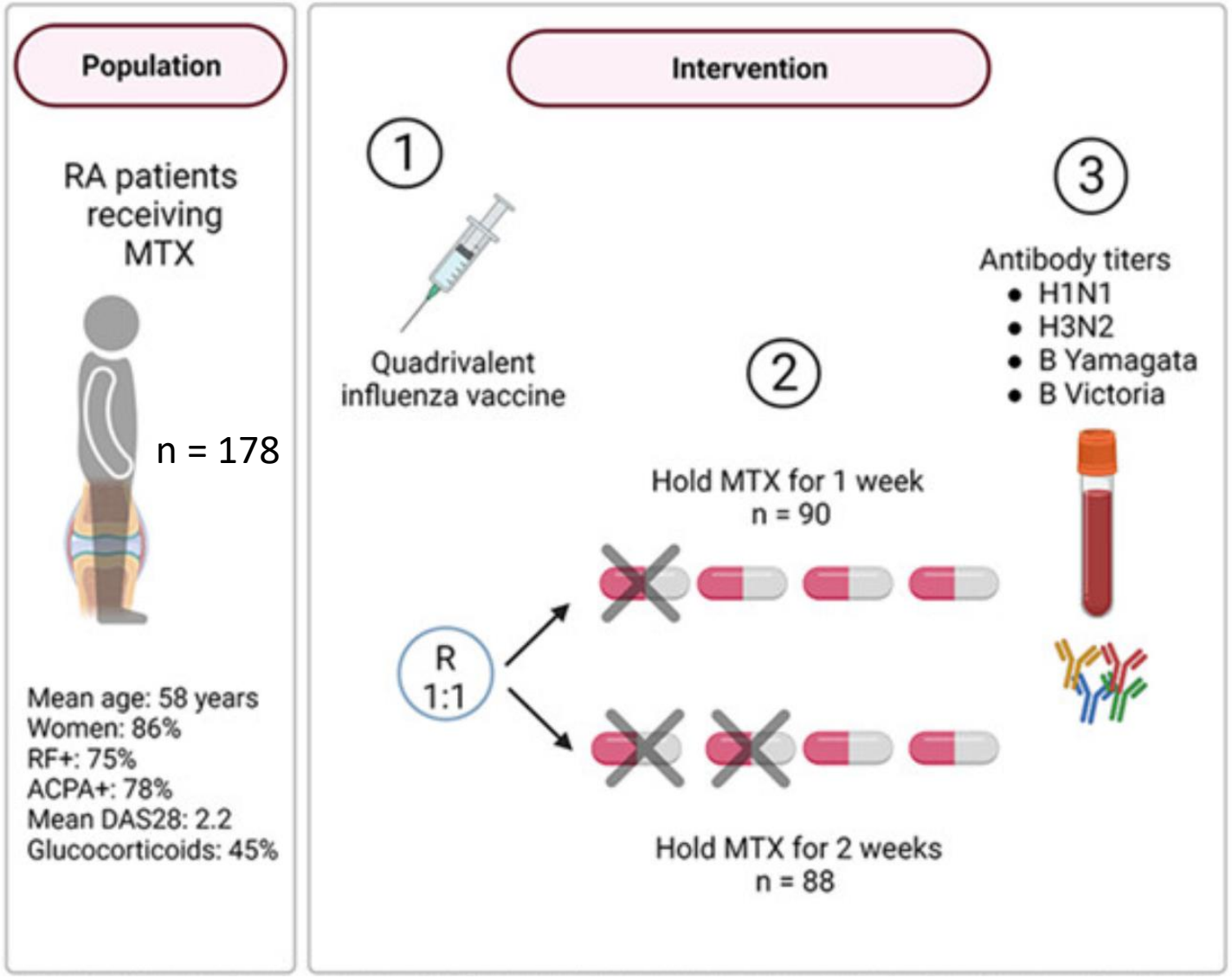
45 patients sous MTX
Vaccin ARNm

62% ont une réponse humorale adéquate (Spike, VS 90%)

Moins d'élévation des T et B spécifiques
Pas d'activation des T CD8

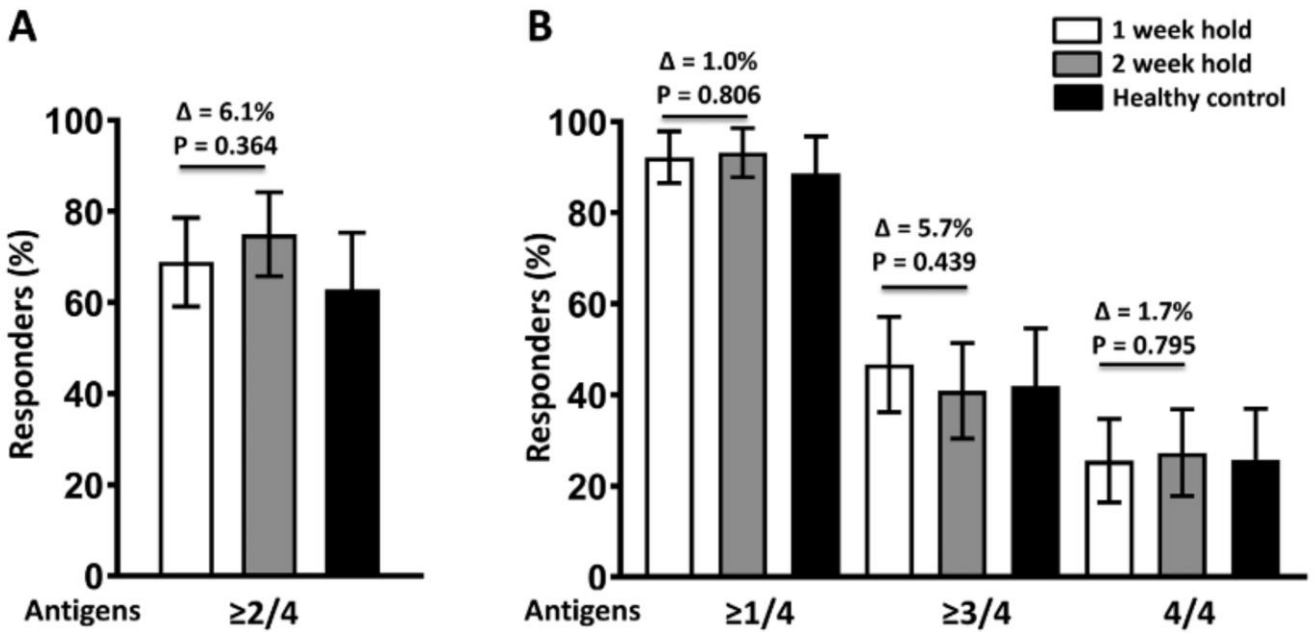
Haberman, ARD, 2021

Methotrexate



Park, Arthritis and Rheum, 2023

Methotrexate



Arrêt methotrexate :

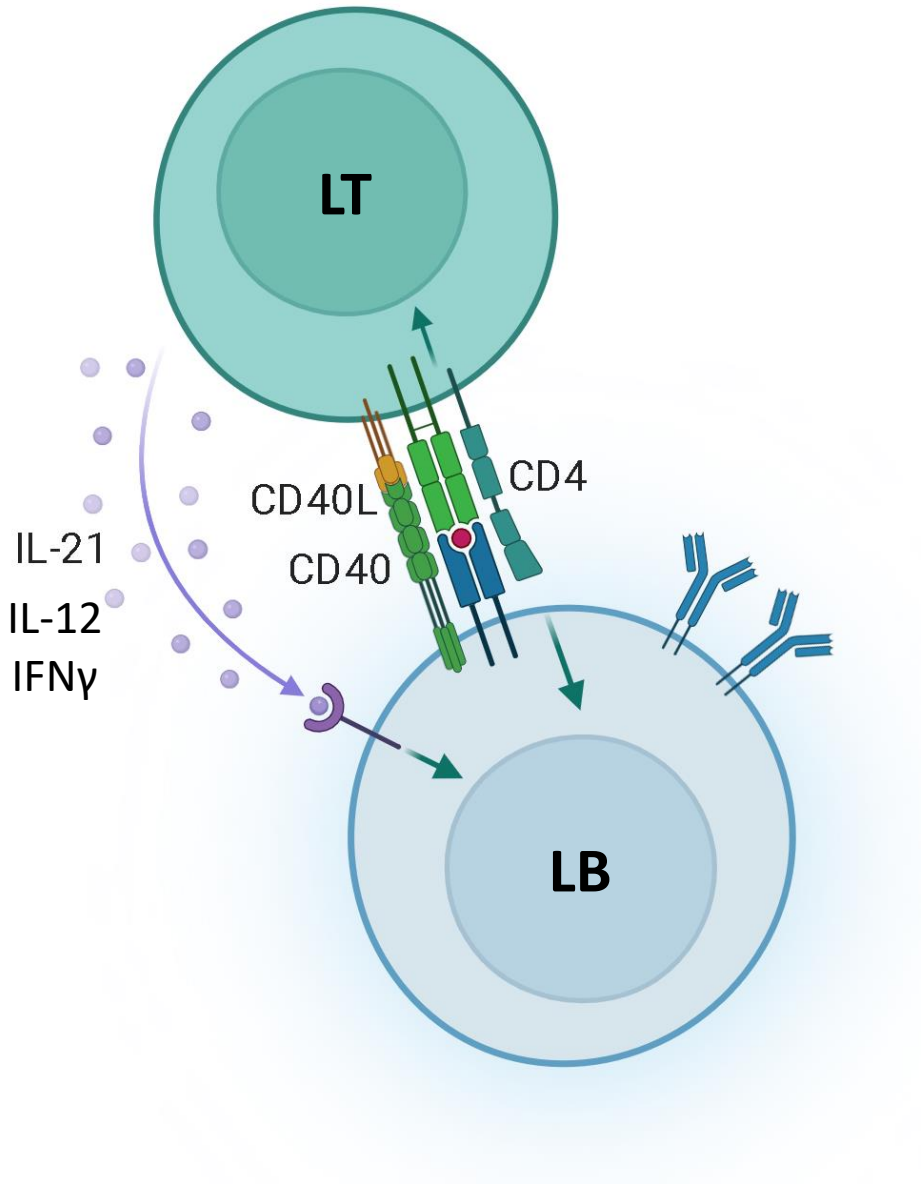
Arrêt MTX 1 sem = 2 sem > Poursuite MTX

Pas de poussée de la maladie

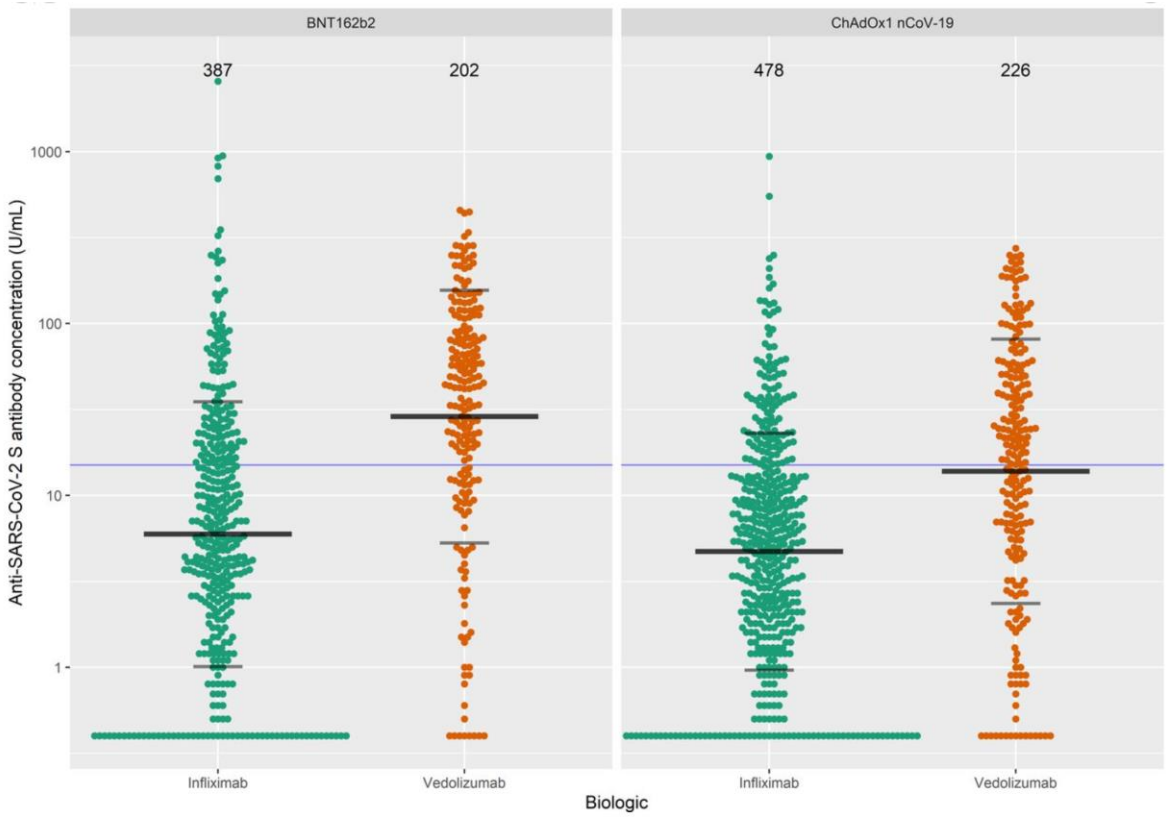
Park, Arthritis and Rheum, 2023

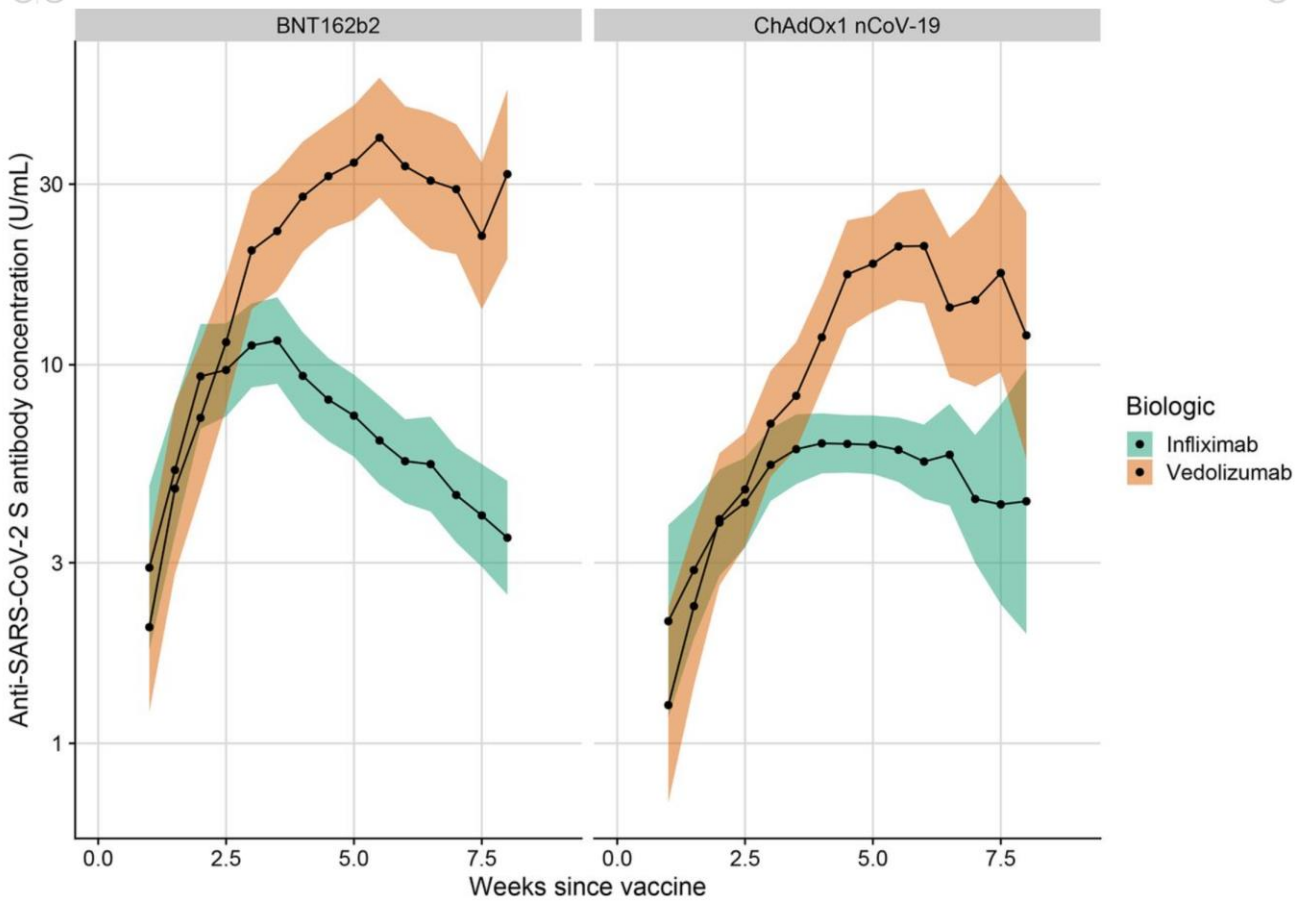
Les anti-TNF

Anti-TNF ⊣



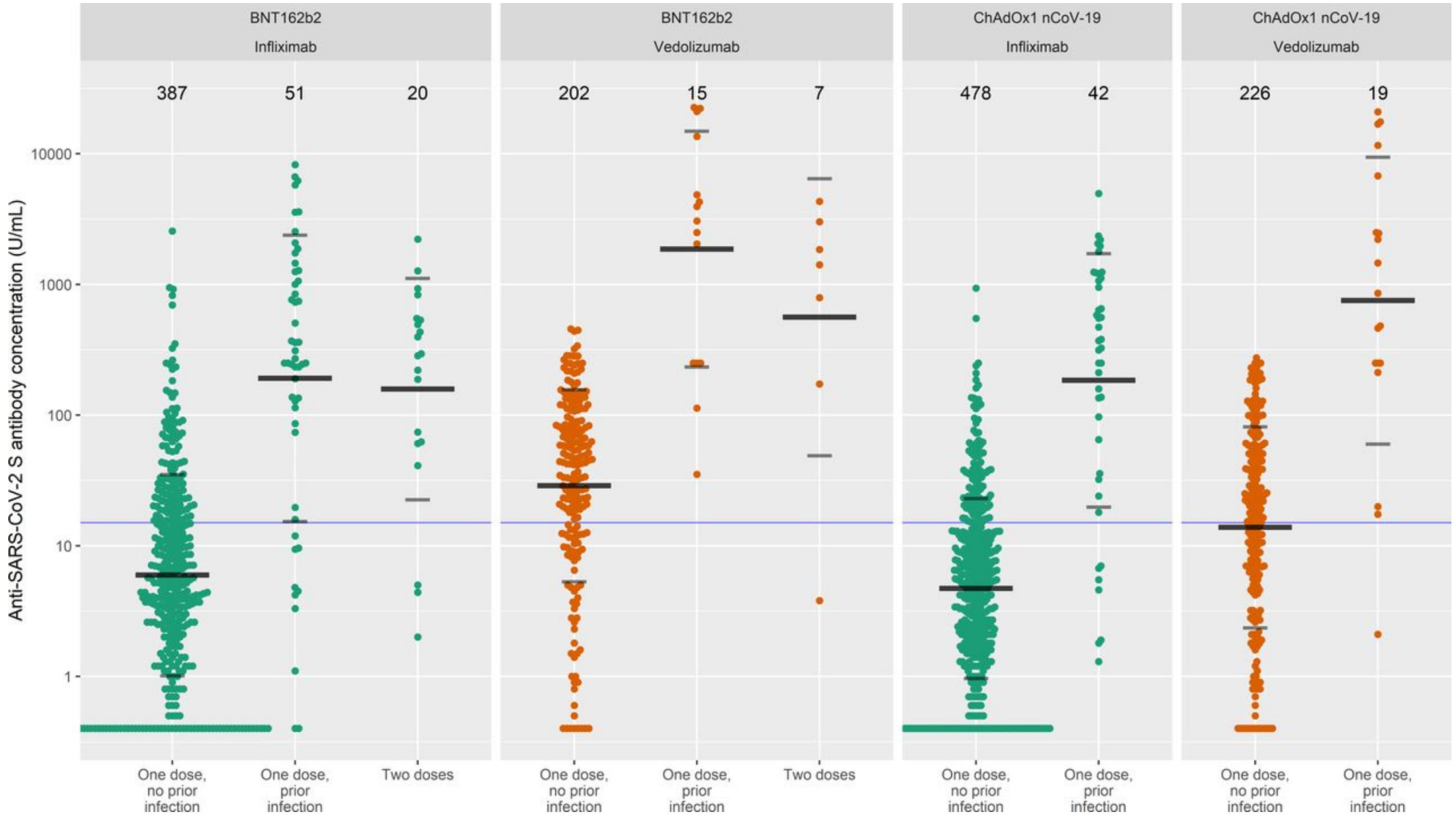
Anti-TNF et réponse humorale





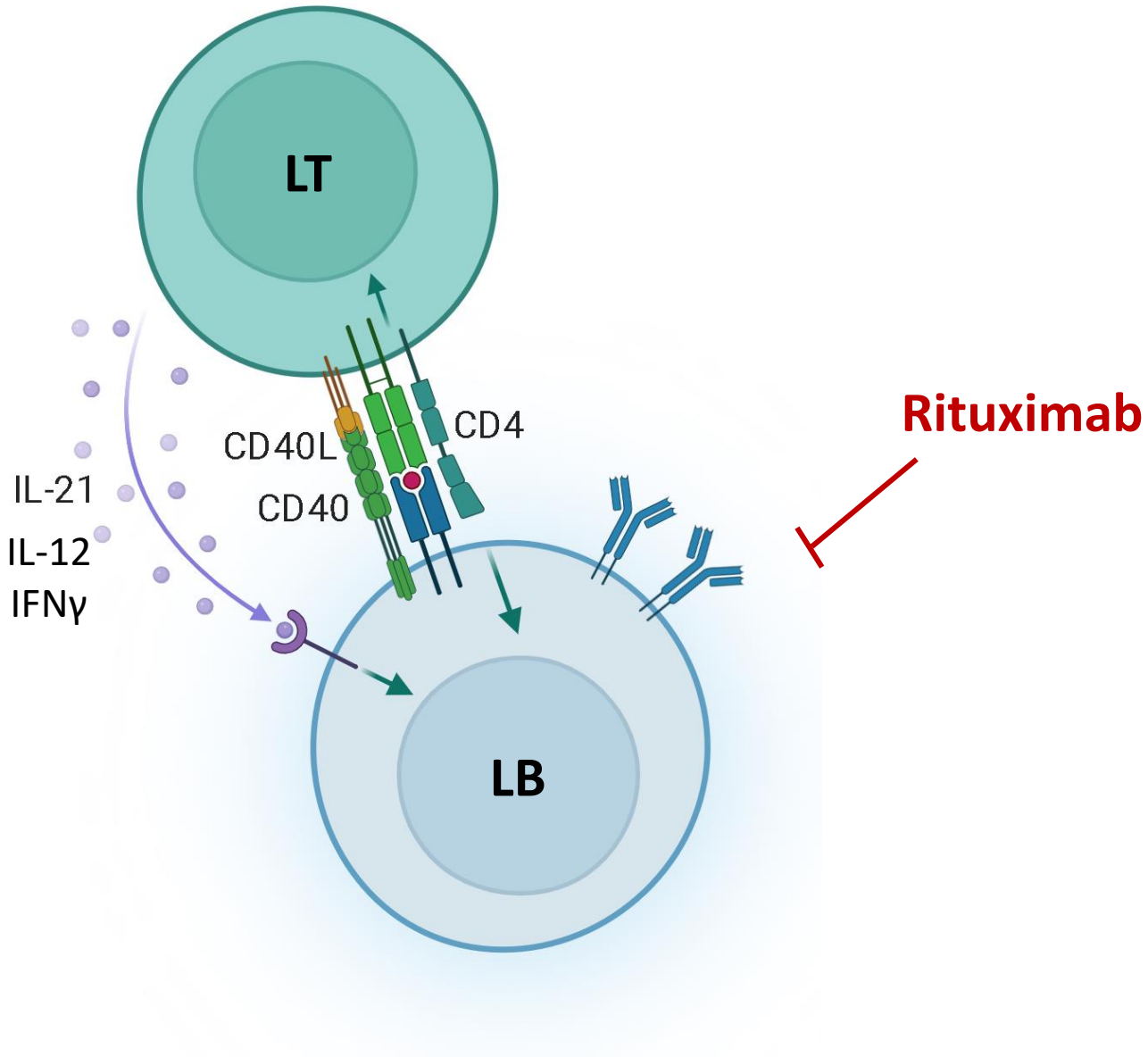
Kennedy, Gut, 2020

Anti-TNF et réponse humorale

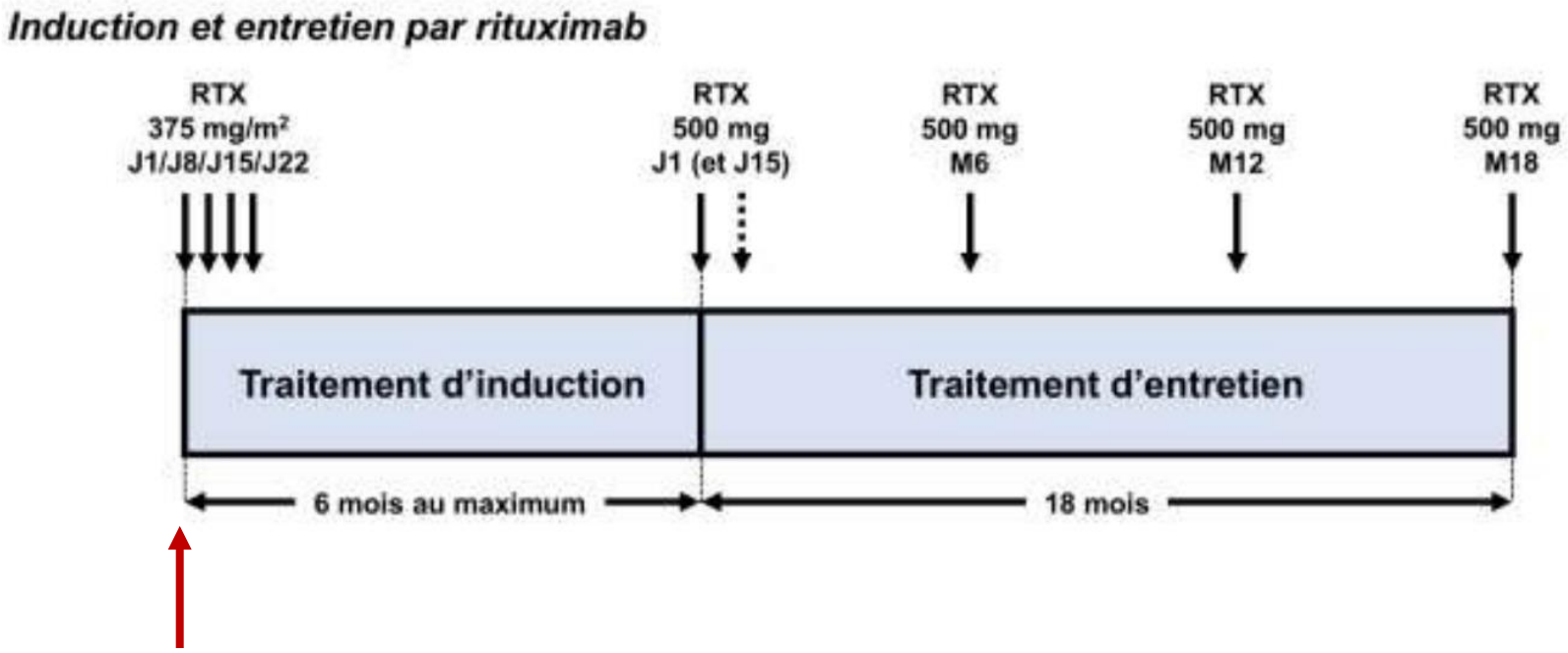


Kennedy, Gut, 2020

Rituximab



Rituximab dans les vascularites à ANCA



Lymphopénie B naïve
Lymphocytes B hypo-répondeurs

PNDS vascularites nécrosantes

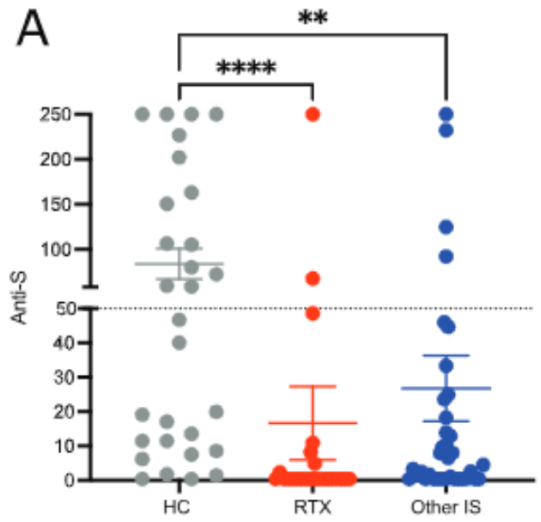
La réponse humorale…

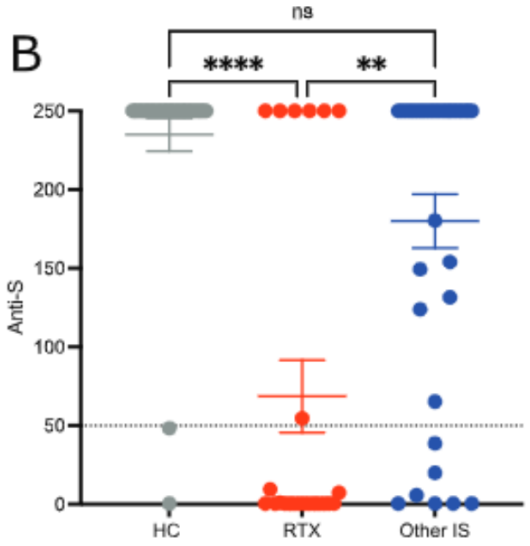
Arthritis & Rheumatology
Vol. 74, No. 6, June 2022, pp 927–933
DOI 10.1002/art.42058

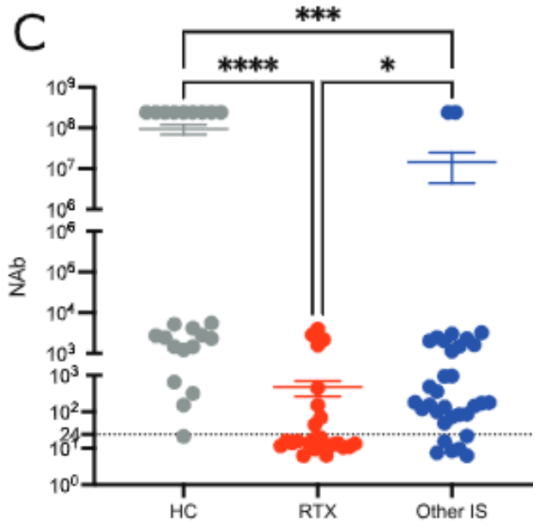
AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

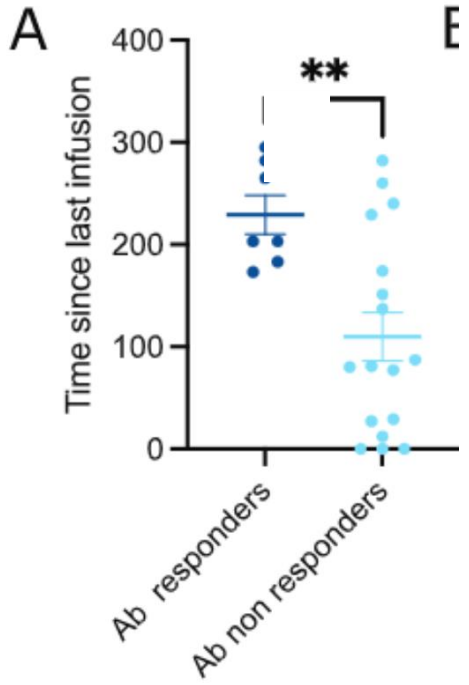
Rituximab Impairs B Cell Response But Not T Cell Response to COVID-19 Vaccine in Autoimmune Diseases

Samuel Bitoun,[1] Julien Henry,[2] Delphine Desjardins,[3] Christelle Vauloup-Fellous,[4] Nicolas Dib,[2] Rakiba Belkhir,[2] Lina Mouna,[4] Candie Joly,[3] Marie Bitu,[3] Bineta Ly,[3] Juliette Pascaud,[3] Raphaèle Seror,[1] Anne-Marie Roque Afonso,[4] Roger Le Grand,[3] and Xavier Mariette[1]









La réponse humorale… ne fait pas tout

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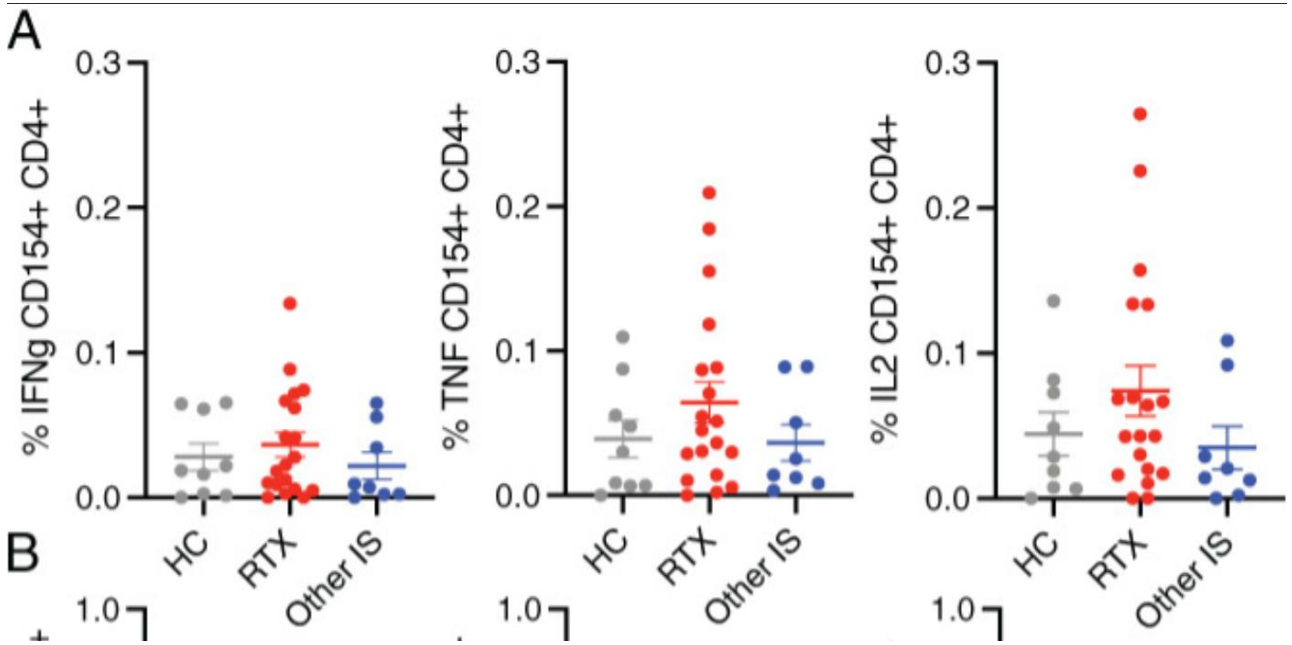
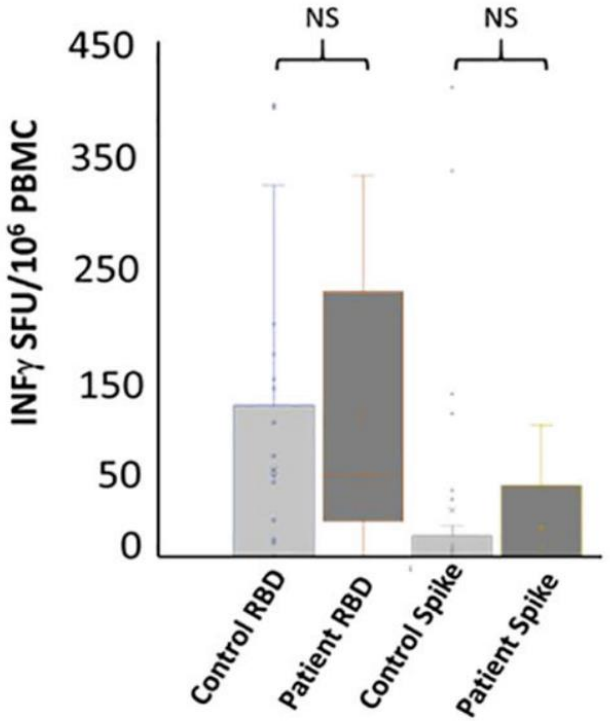


The immune response to Covid-19 mRNA vaccination among Lymphoma patients receiving anti-CD20 treatment

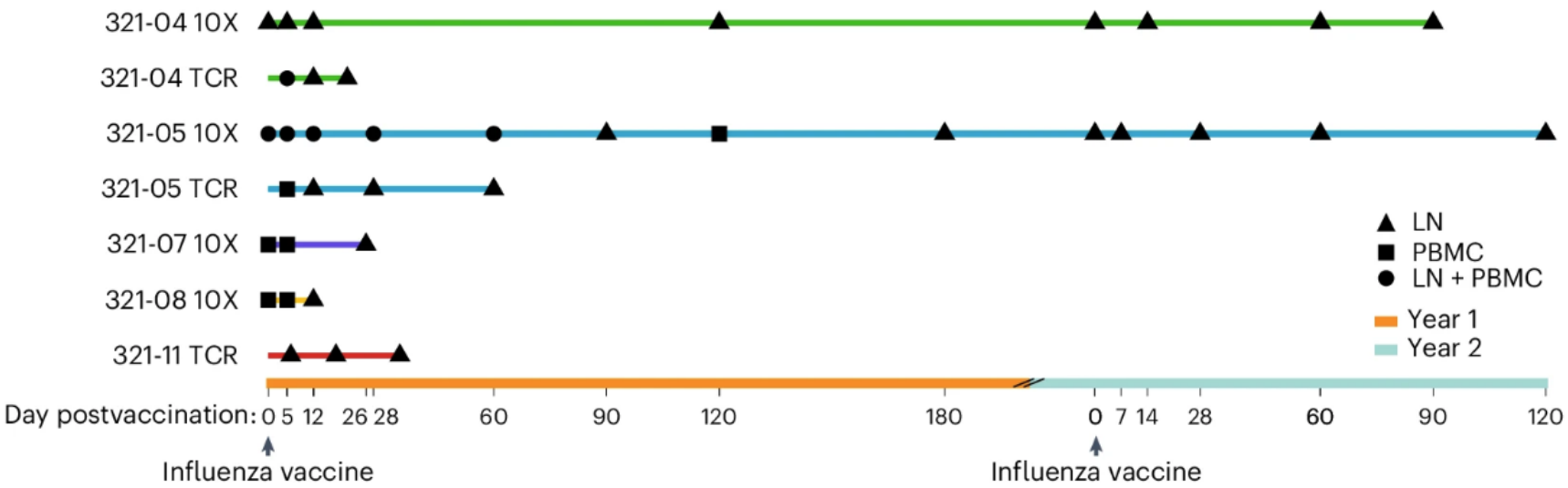


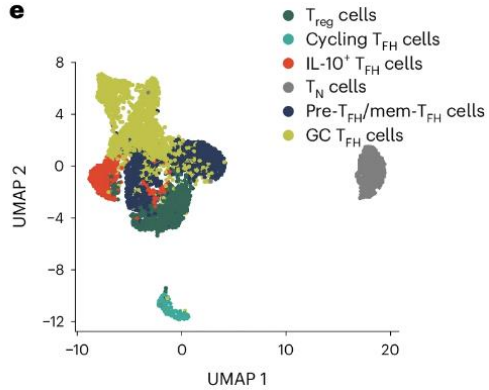
nature immunology

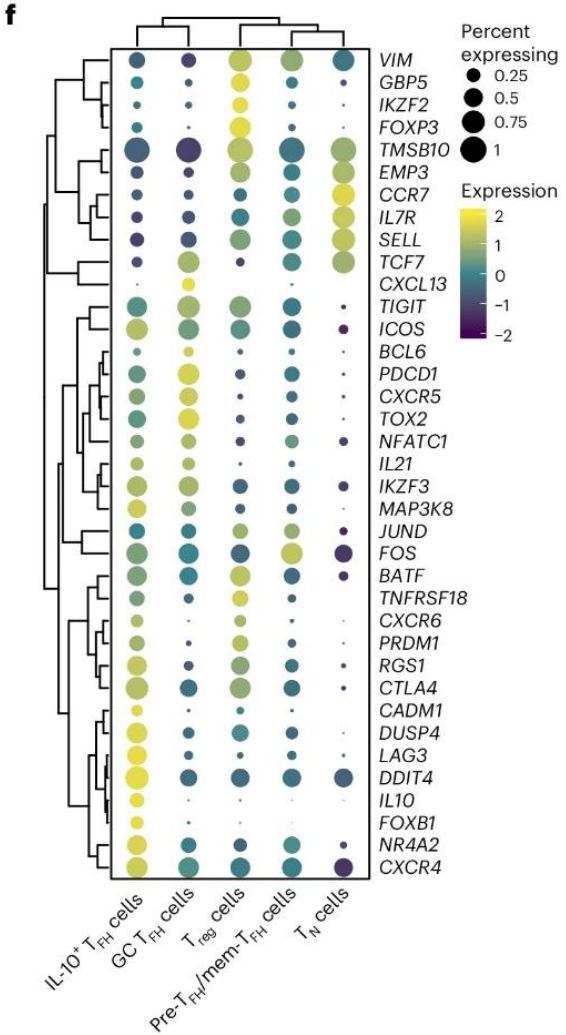
Resource

https://doi.org/10.1038/s41590-024-01926-6

Influenza vaccination stimulates maturation of the human T follicular helper cell response







Shattgen, Nature Imunol, 2024

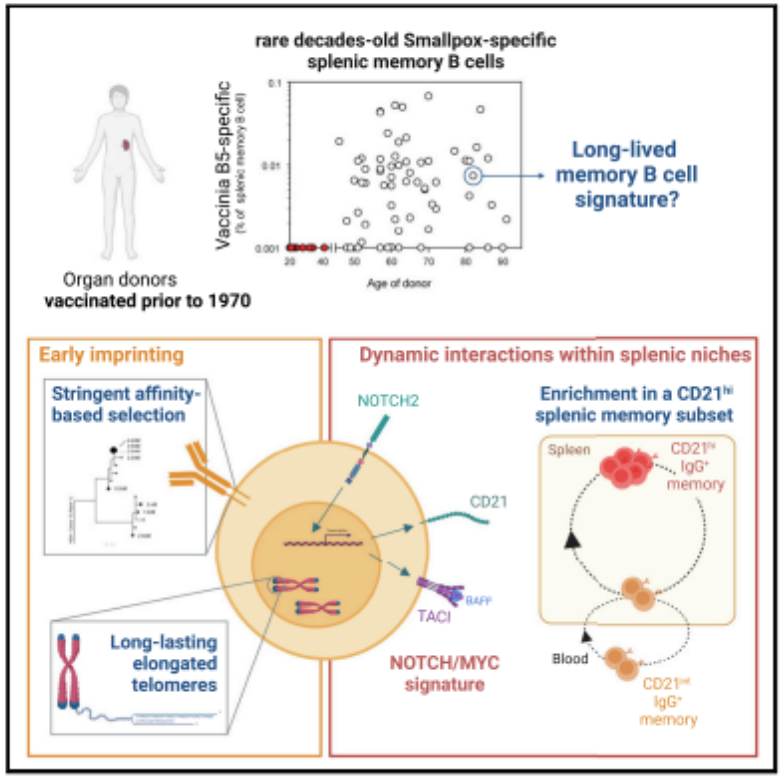
Des B mémoires épargnés ?

Article

Immunity

Human anti-smallpox long-lived memory B cells are defined by dynamic interactions in the splenic niche and long-lasting germinal center imprinting

Graphical abstract



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In brief

Immune memory in humans has been shown to extend well beyond decades. Chappert et al. provide an extensive functional characterization of human splenic smallpox/vaccinia protein B5-specific MBCs, generated more than four decades ago, to decipher the distinct selection and survival mechanisms associated with MBCs longevity.

Article

Human germinal centres engage memory and naive B cells after influenza vaccination

https://doi.org/10.1038/s41586-020-2711-0

Received: 2 March 2020

Accepted: 20 August 2020

Published online: 31 August 2020

Jackson S. Turner[1,11], Julian Q. Zhou[2,11], Julianna Han[3,11], Aaron J. Schmitz[1], Amena A. Rizk[1], Wafaa B. Alsoussi[1], Tingting Lei[1], Mostafa Amor[1], Katherine M. McIntire[1], Philip Meade[4,5], Shirin Strohmeier[4], Rafael I. Brent[1], Sara T. Richey[3], Alem Haile[6], Yuhe R. Yang[3], Michael K. Klebert[6], Teresa Suessen[7], Sharlene Teefey[7], Rachel M. Presti[8], Florian Krammer[4], Steven H. Kleinstein[2,9], Andrew B. Ward[3] & Ali H. Ellebedy[1,10]✉

JEM Journal of Experimental Medicine

ARTICLE

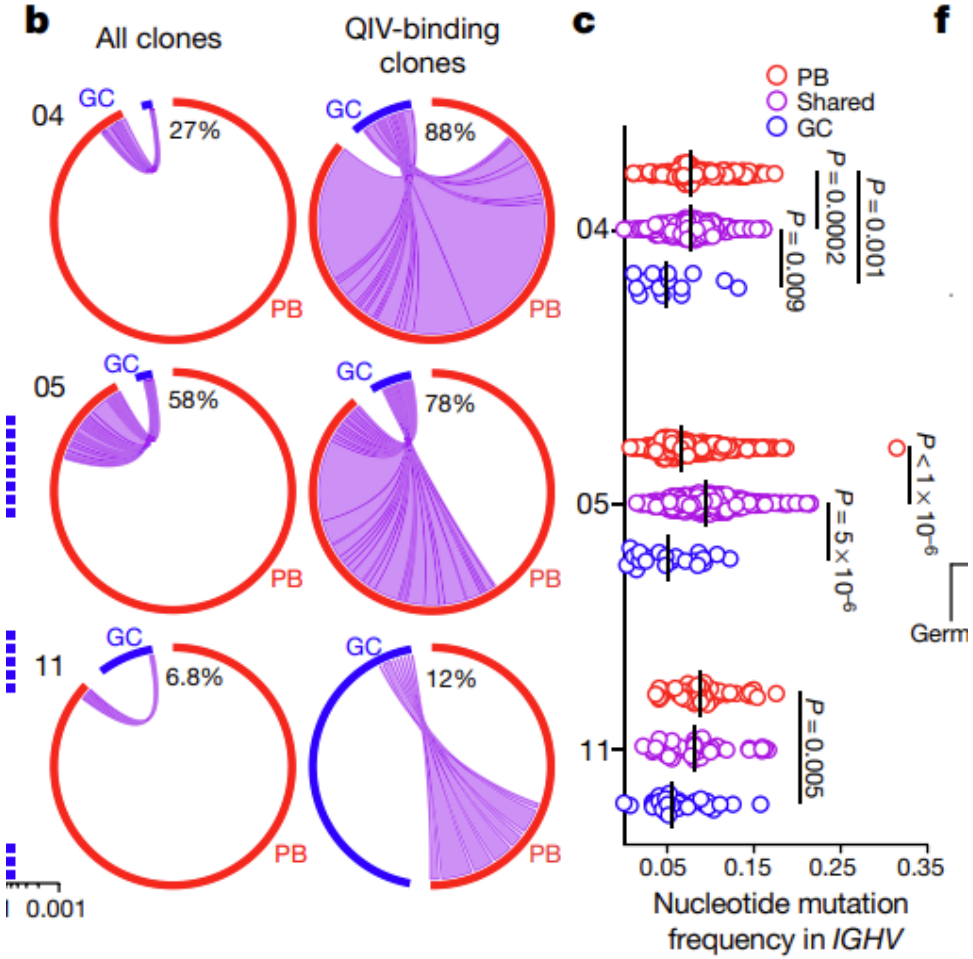
Maturation of germinal center B cells after influenza virus vaccination in humans

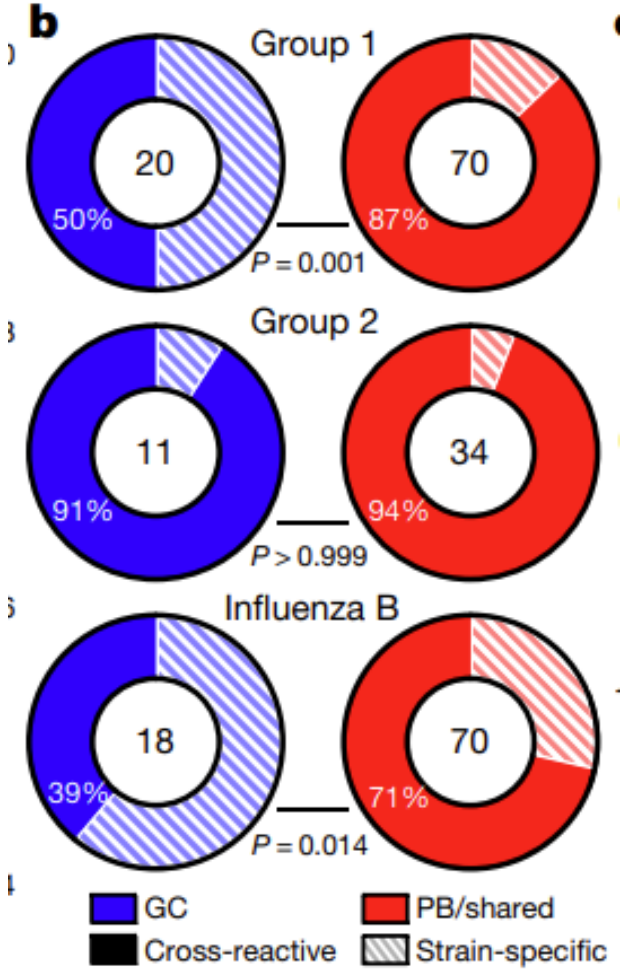
Katherine M. McIntire[1*], Hailong Meng[2*], Ting-Hui Lin[3*], Wooseob Kim[1,4], Nina E. Moore[3], Julianna Han[3], Meagan McMahon[5], Meng Wang[2,6], Sameer Kumar Malladi[1], Bassem M. Mohammed[1], Julian Q. Zhou[1], Aaron J. Schmitz[1], Kenneth B. Hoehn[2], Juan Manuel Carreño[5], Temima Yellin[5], Teresa Suessen[7], William D. Middleton[7], Sharlene A. Teefey[7], Rachel M. Presti[8,9,10], Florian Krammer[5,11,12], Jackson S. Turner[1], Andrew B. Ward[3], Ian A. Wilson[3**], Steven H. Kleinstein[2,13,6**], and Ali H. Ellebedy[1,9,10**]

Tuner, Nature, 2020

McIntire, JEM, 2024

Diversité de la réaction GC





Tuner, Nature, 2020
McIntire, JEM, 2024

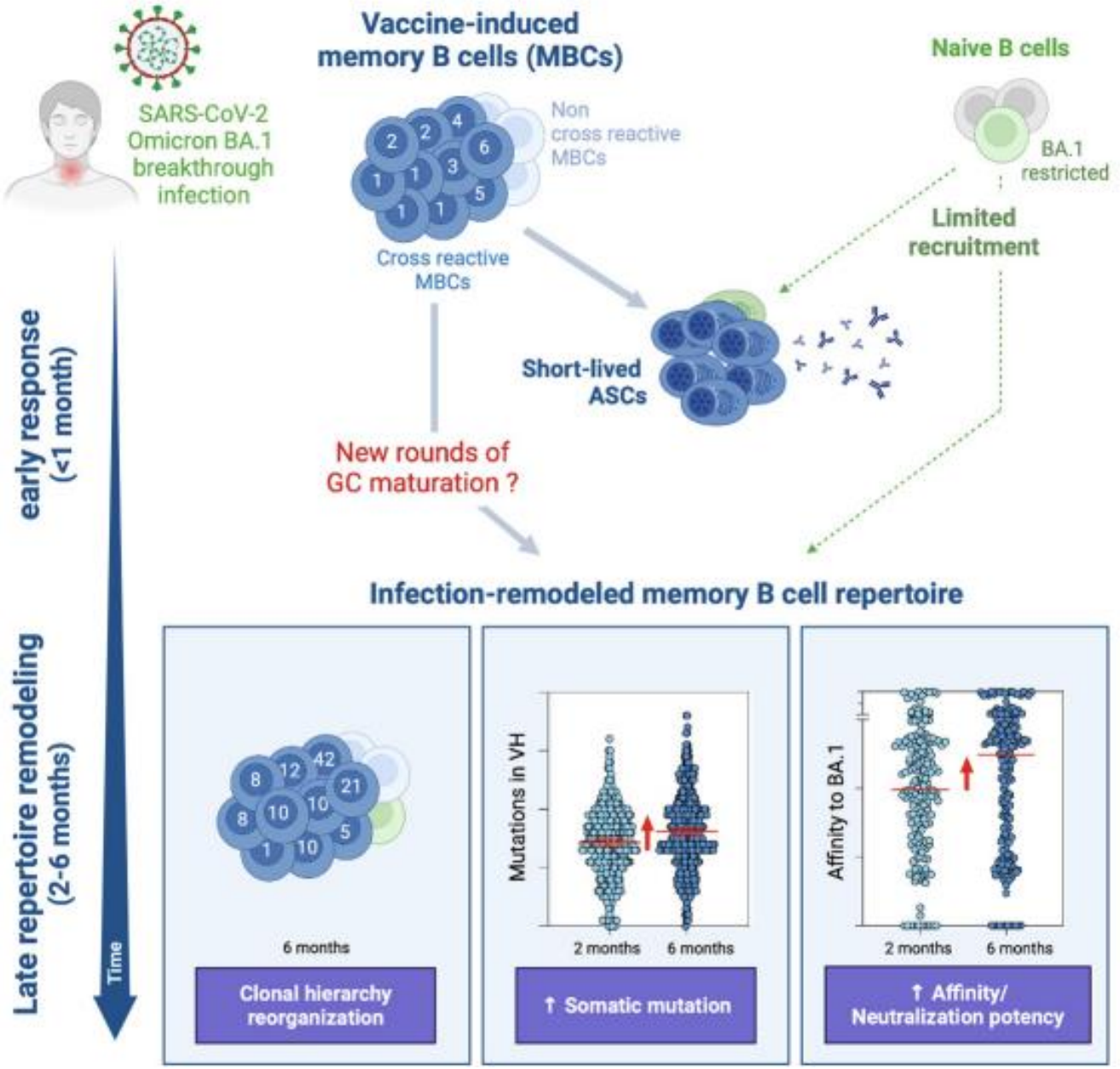
Diversité de la réaction GC

Immunity

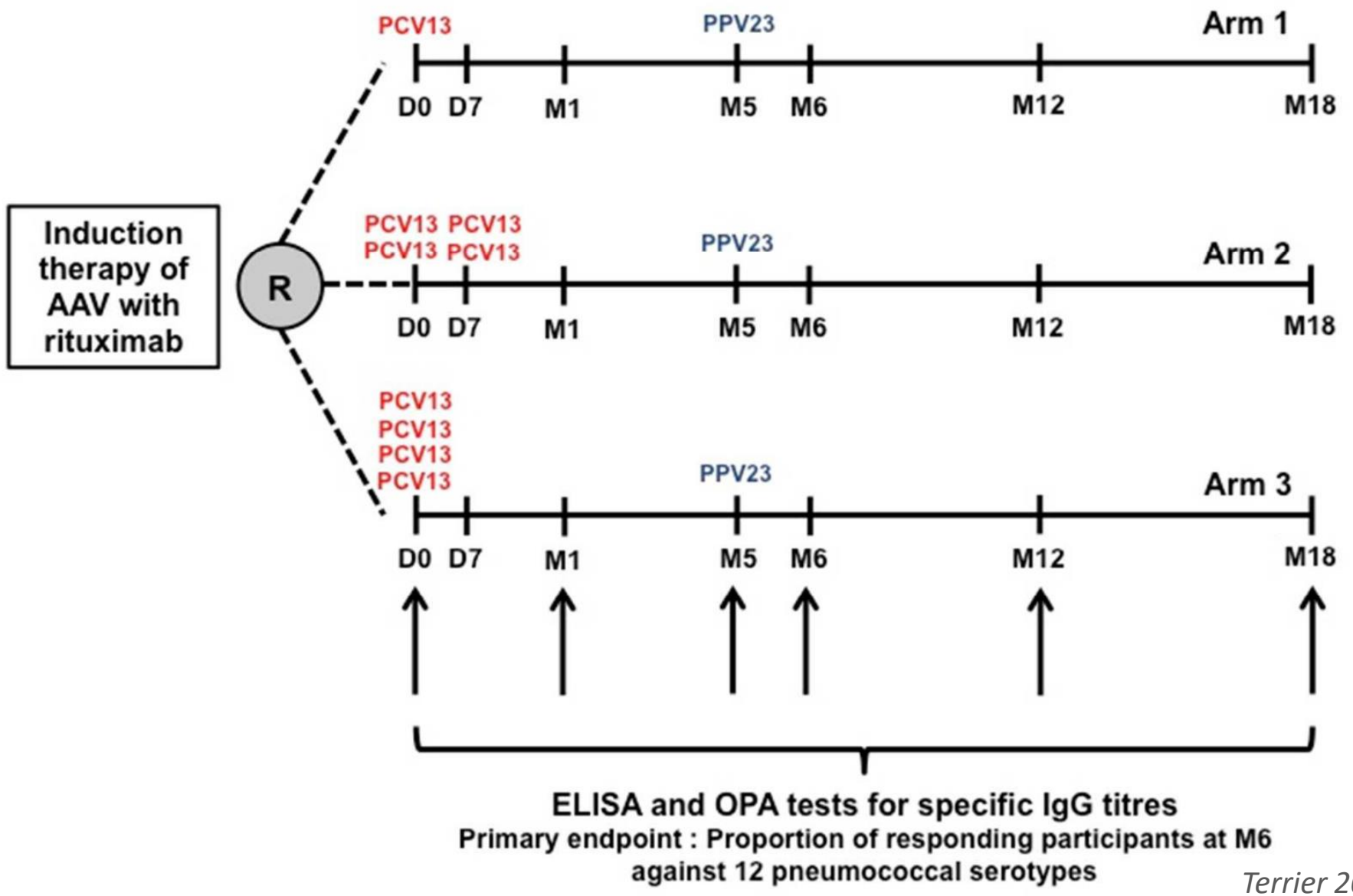
Article

SARS-CoV-2 Omicron BA.1 breakthrough infection drives late remodeling of the memory B cell repertoire in vaccinated individuals

Sokal, Immunity, 2023



Rituximab et temporalité



Terrier 2020, Rev Med Interne

Conclusion

Anticipation pas toujours possible

Adaptation aux traitements et à la maladie

Vaccination sûre

Pas d'anticorps vaccinaux ≠ pas d'intérêt

Meilleure immunogénicité :

- Suspension traitement?
- Doses surajoutées?

Importants bénéfices potentiels de nouveaux/futurs vaccins

- Shingrix et Ac anti IFNα-récepteurs..

Merci pour votre attention !