Les vaccins de demain

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Inserm CIC 1408- Axe Vaccinologie, I-Reivac, Covireivac

Team GIMAP, CIRI, Inserm, U1111, CNRS, UMR530

Chaire Prévention, Vaccination, Contrôle de l'Infection PRESAGE

Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

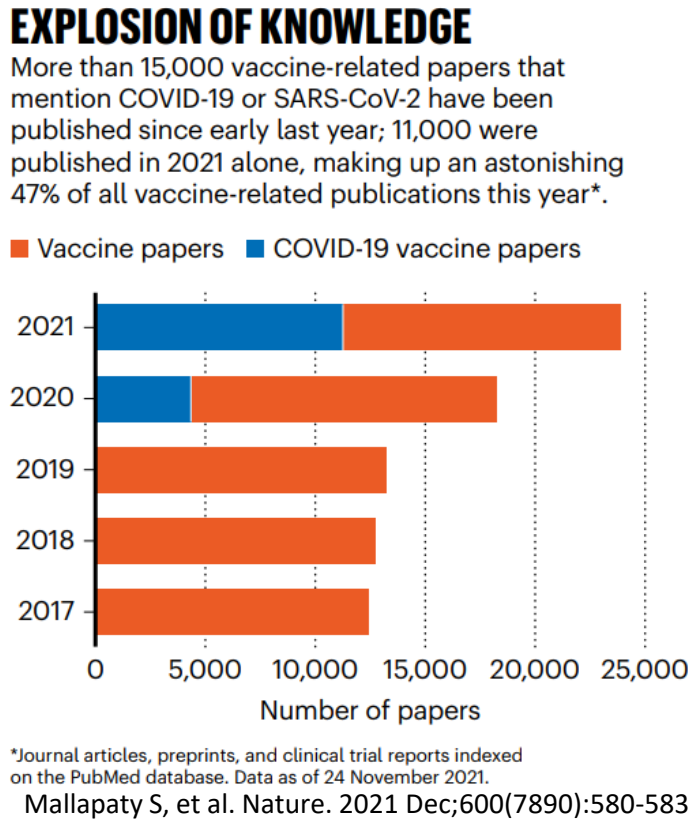
- Consultant ou membre d'un conseil scientifique: **PAS de rémunération à titre personnel** (Pfizer, Janssen, Sanofi Pasteur) — ☑ OUI ☐ NON
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents **PAS de rémunération à titre personnel** — ☑ OUI ☐ NON
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations — ☐ OUI ☑ NON
- Investigateur principal d'une recherche ou d'une étude clinique **(CIC)** (Sanofi Pasteur, GSK, Pfizer, MSD, Janssen, Moderna) — ☑ OUI ☐ NON

Membre du copil du I-REIVAC

Petit préambule

- Intérêt des vaccins, n'est plus à démontrer
- Populations changent, risques changent, émergences…bref toujours de nouveaux besoins!
- **Prévenir vaudra toujours mieux que guérir**

- Vaccination de masse
- Vaccination personnalisée
- La crise COVID est un catalyseur dvpt vaccinal!

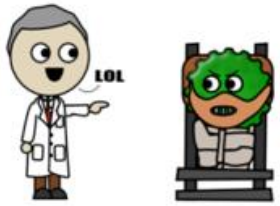


Mallapaty S, et al. Nature. 2021 Dec;600(7890):580-583

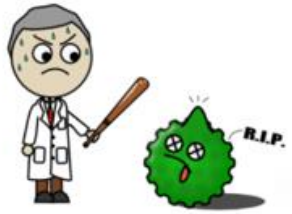
Demain (et déjà aujourd'hui):

le boom des plateformes, des adjuvants et des voies d'administration

Vaccin vivant atténué



Vaccin inactivé ("tué")



Entiers
Agent infectieux dans sa totalité

Sous-unitaires
Fragment de l'agent infectieux

Type of vaccine		Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)		Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism		Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid		Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle		Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle	Pathogen antigen; Gram-negative bacterial outer membrane	Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate	Polysaccharide; Carrier protein	*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)

Pollard AJ et al., https://doi.org/10.1038/s41577-020-00479-

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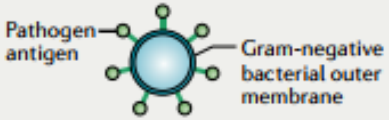
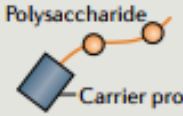
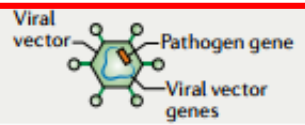
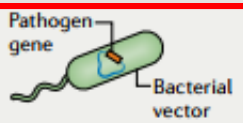
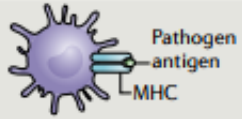
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate		*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored		Ebola	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored		Experimental	–
Antigen-presenting cell		Experimental	–

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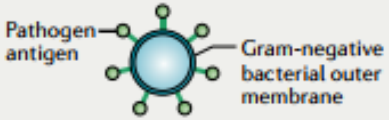
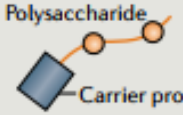
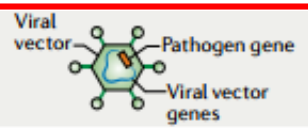
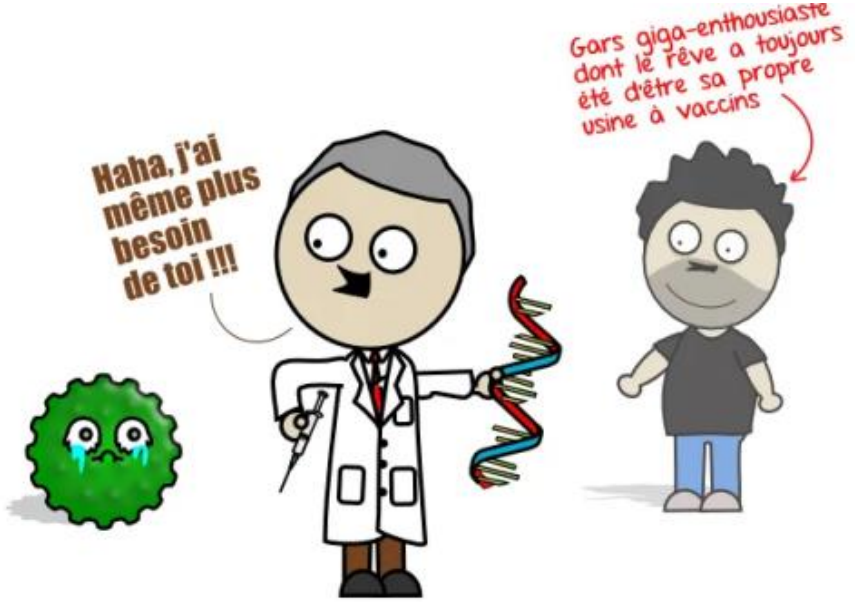
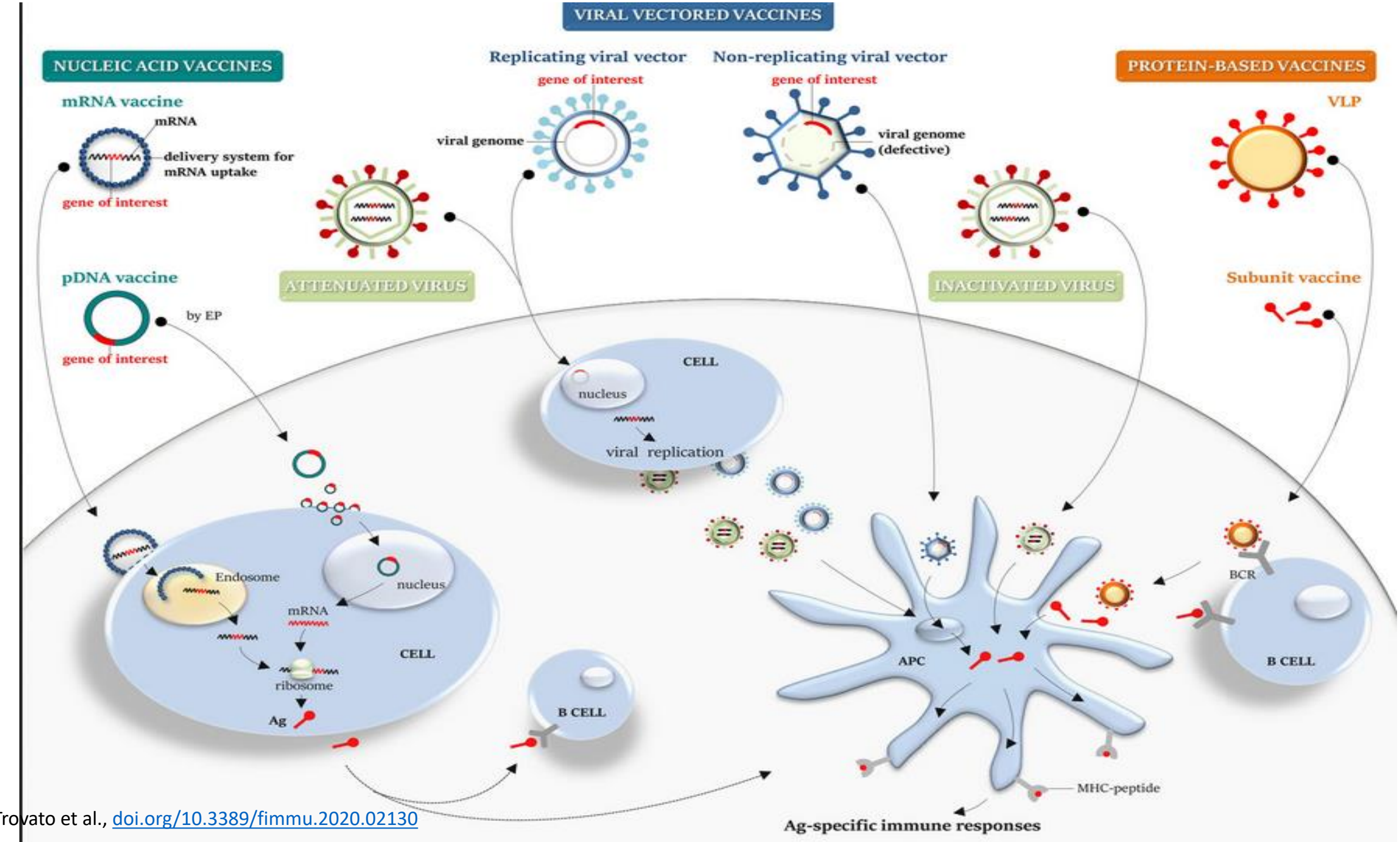
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate		*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored		Ebola	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)



Pollard AJ et al., https://doi.org/10.1038/s41577-020-00479-
https://lepharmachien.com/



M. Trovato et al., doi.org/10.3389/fimmu.2020.02130

mRNA vaccines

Moderna
Pfizer & BioNTech
CureVac

saRNA vaccine

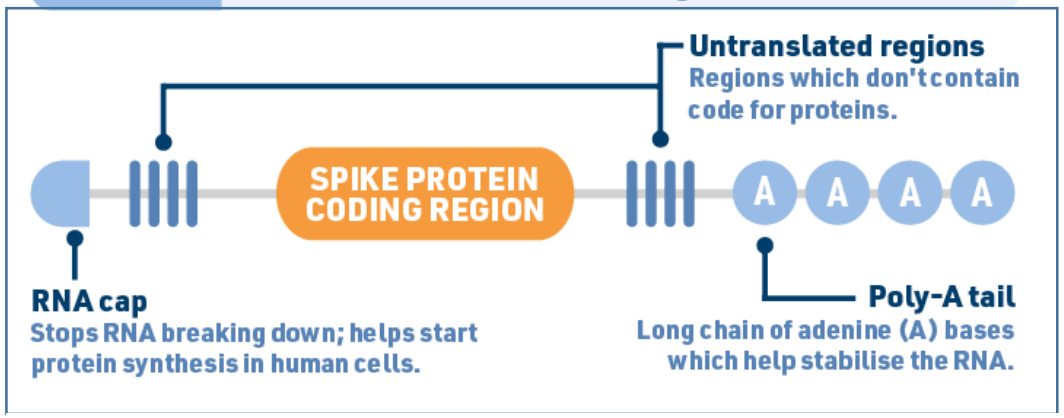
Imperial College
Arcturus

mRNA AND saRNA: WHAT'S THE DIFFERENCE?

The structures of mRNA and saRNA are similar but have a key difference, as the diagrams below show.

mRNA

mRNA stands for messenger ribonucleic acid



Pas d'adjuvants

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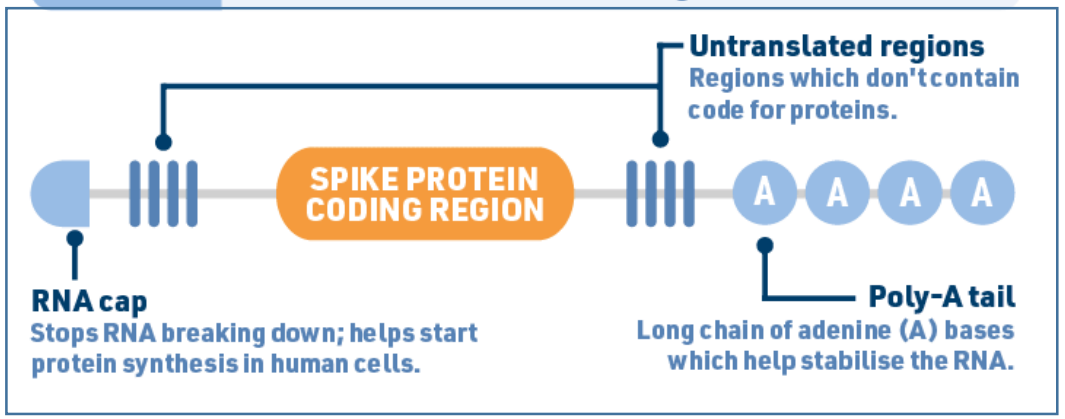
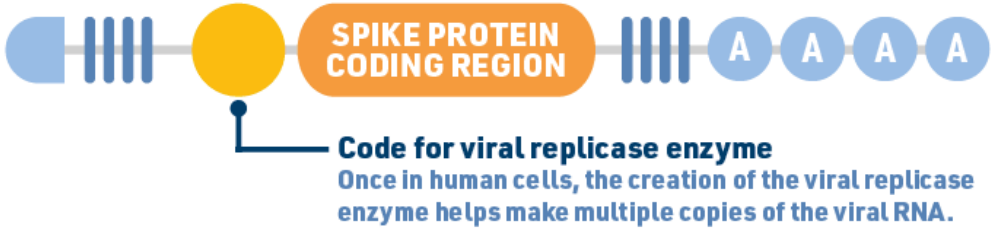


saRNA

saRNA stands for self-amplifying ribonucleic acid



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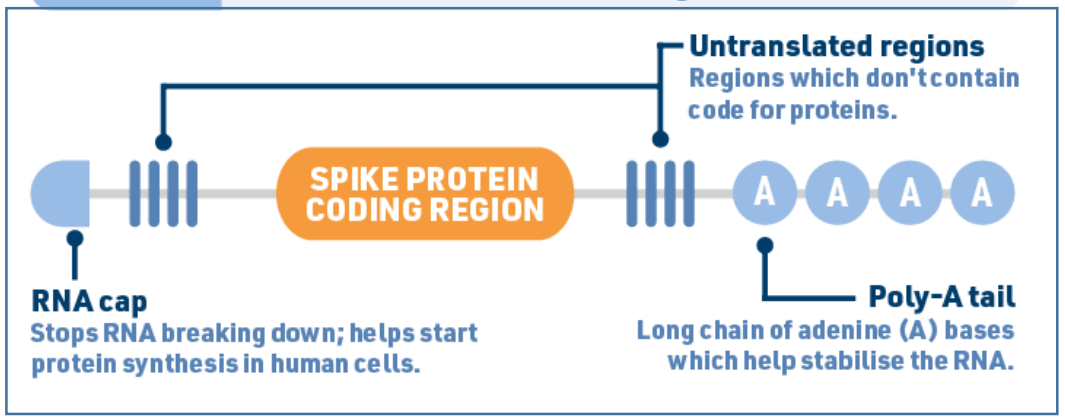

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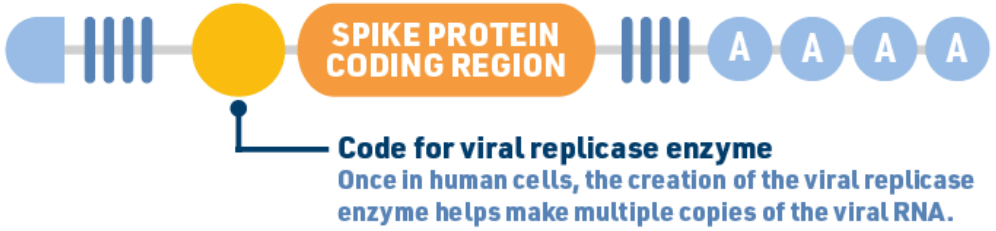


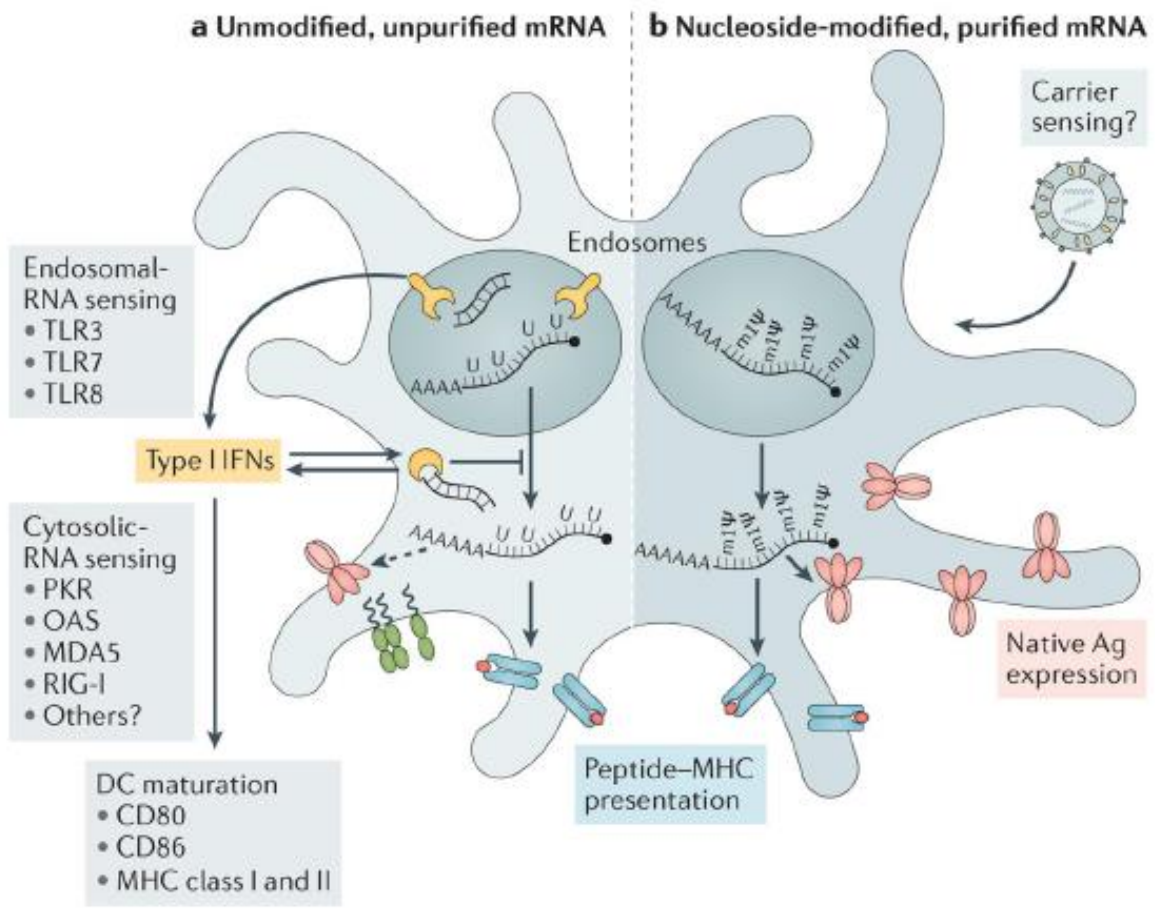
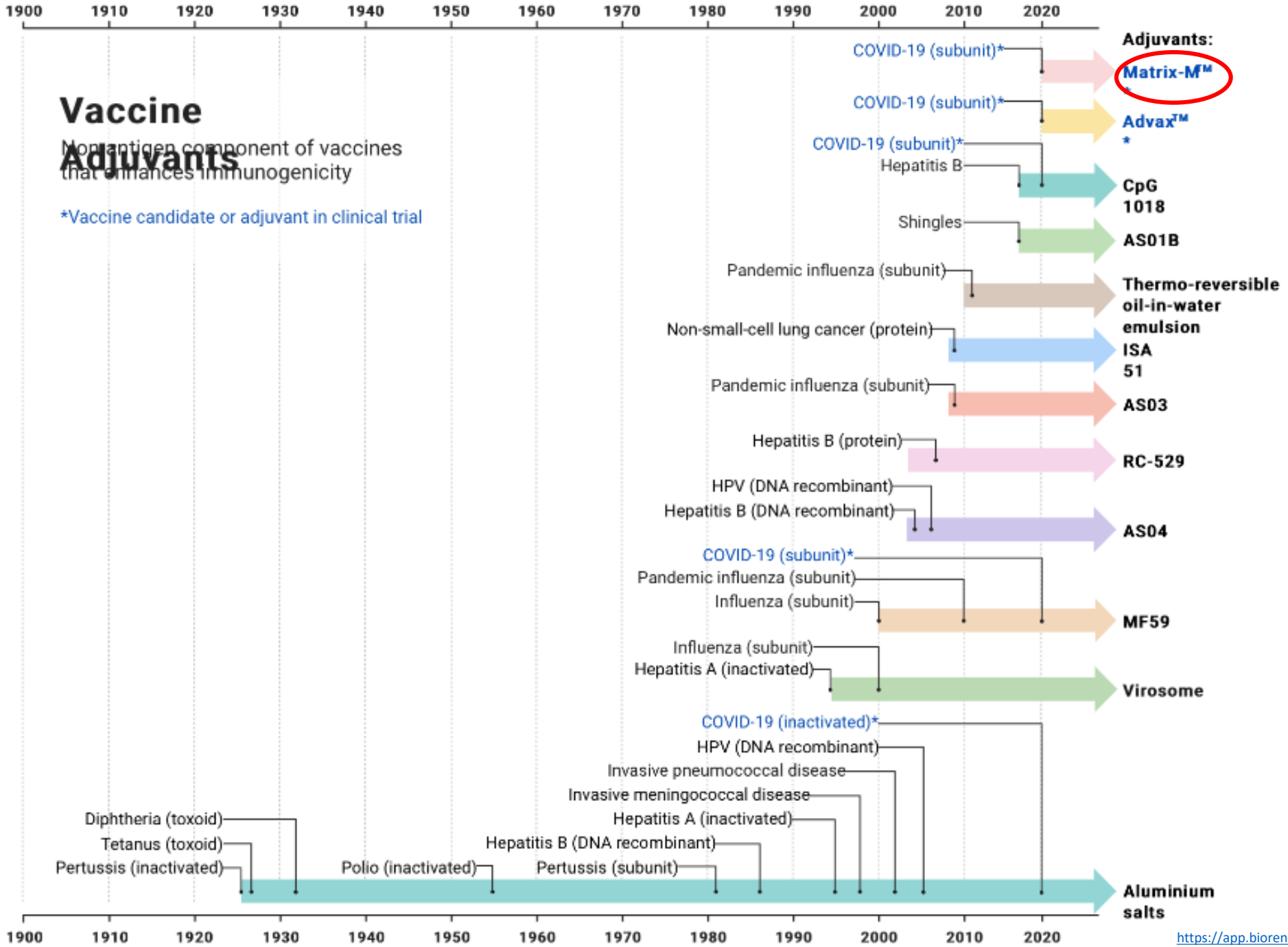


Figure 1. Innate immune sensing of mRNA vaccines

Pas d'adjuvants

Pardi N et al., Nat Rev Drug Discov. 2018 Apr;17(4):261-279

Vaccines	Advantages	Disadvantages
Viral vectored vaccines	Stimulation of innate immune response; induction of T and B cell immune response.	induction of anti-vector immunity: cell based manufacturing
RNA vaccines	Non-infectious, non-integrating, natural degradation, egg and cell free, rapid and scalable production; stimulation of innate immune response; induction of T and B cell immune response.	Concerns with instability and low immunogenicity.



https://app.biorender.com/biorender-templates/figures/5d3f084c4d6c910004dc43fe

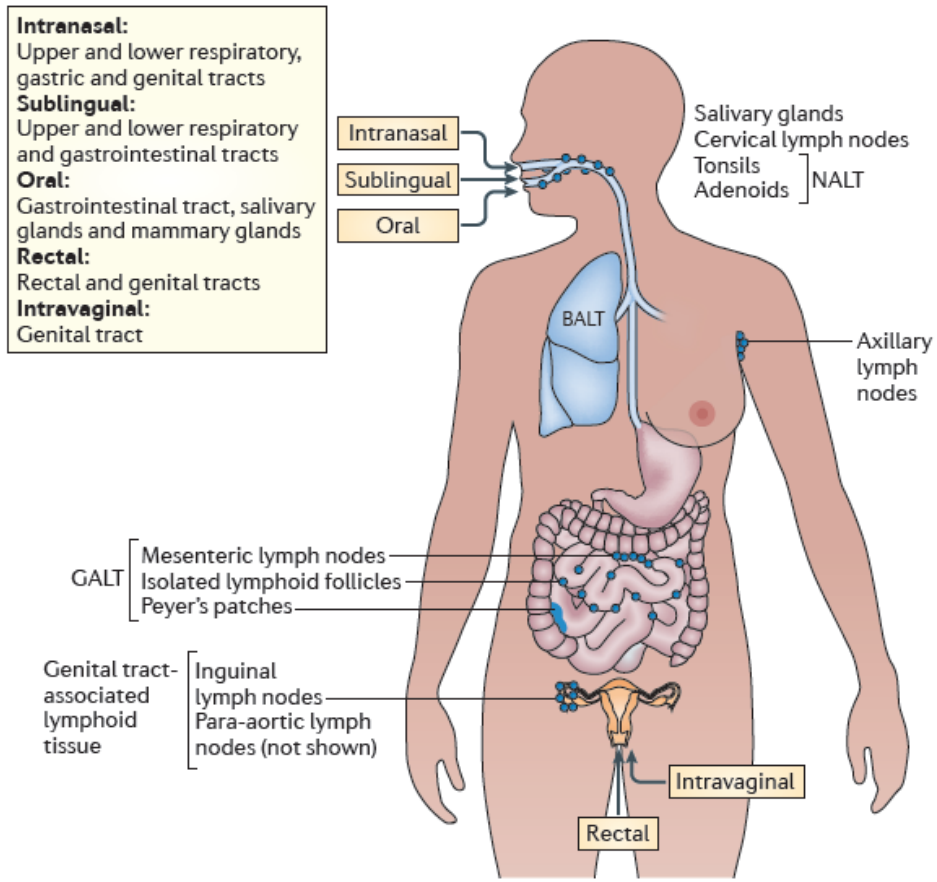
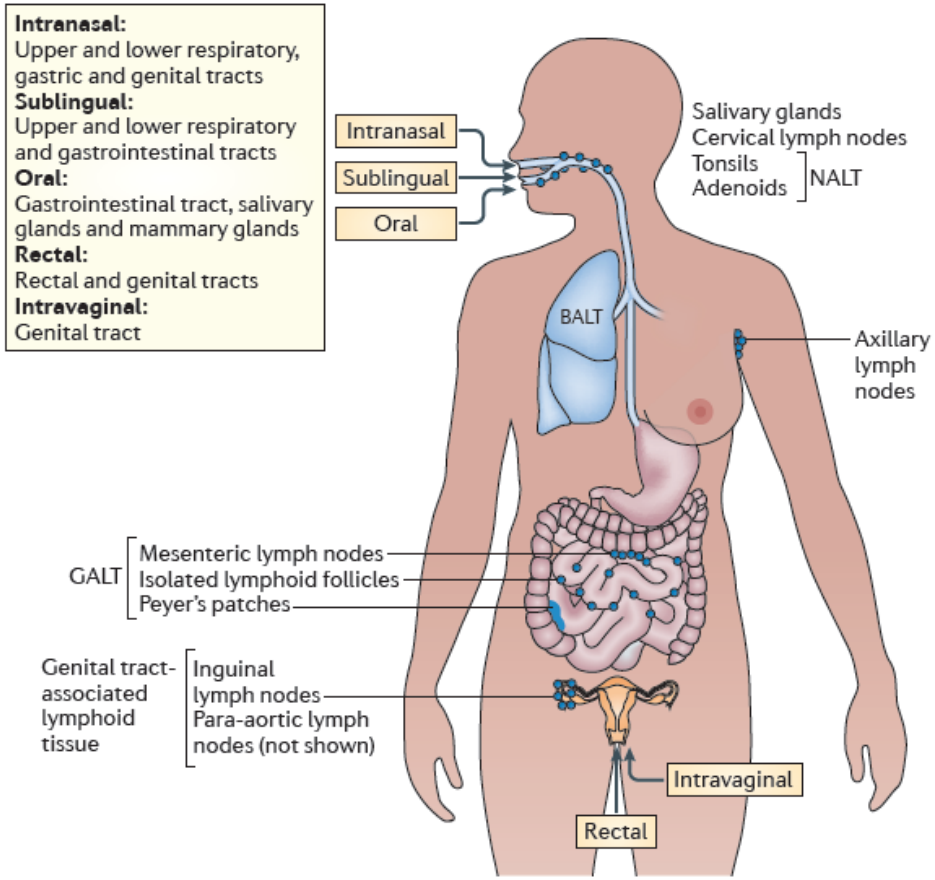


Figure 1 | **Mucosal immunization routes and compartmentalization of effector functions.** Within the mucosa-associated lymphoid tissue (MALT), subcompartments can be identified, such as the nasopharynx-associated lymphoid tissue (NALT), bronchus-associated lymphoid tissue (BALT), gut-associated lymphoid tissue (GALT) and genital tract-associated lymphoid tissue. Certain immunization routes are more effective at stimulating immunity within specific, most often closely located, subcompartments of the MALT. Intranasal vaccination is preferred for targeting the respiratory, gastric and genital tracts; oral vaccination is effective for immunity in the gut and for the induction of mammary gland antibodies (which are secreted in milk); rectal immunization is best for the induction of colon and rectal immunity and to some extent genital tract immunity; and intravaginal vaccination is the most effective for antibody and T cell immunity in the genital tract.



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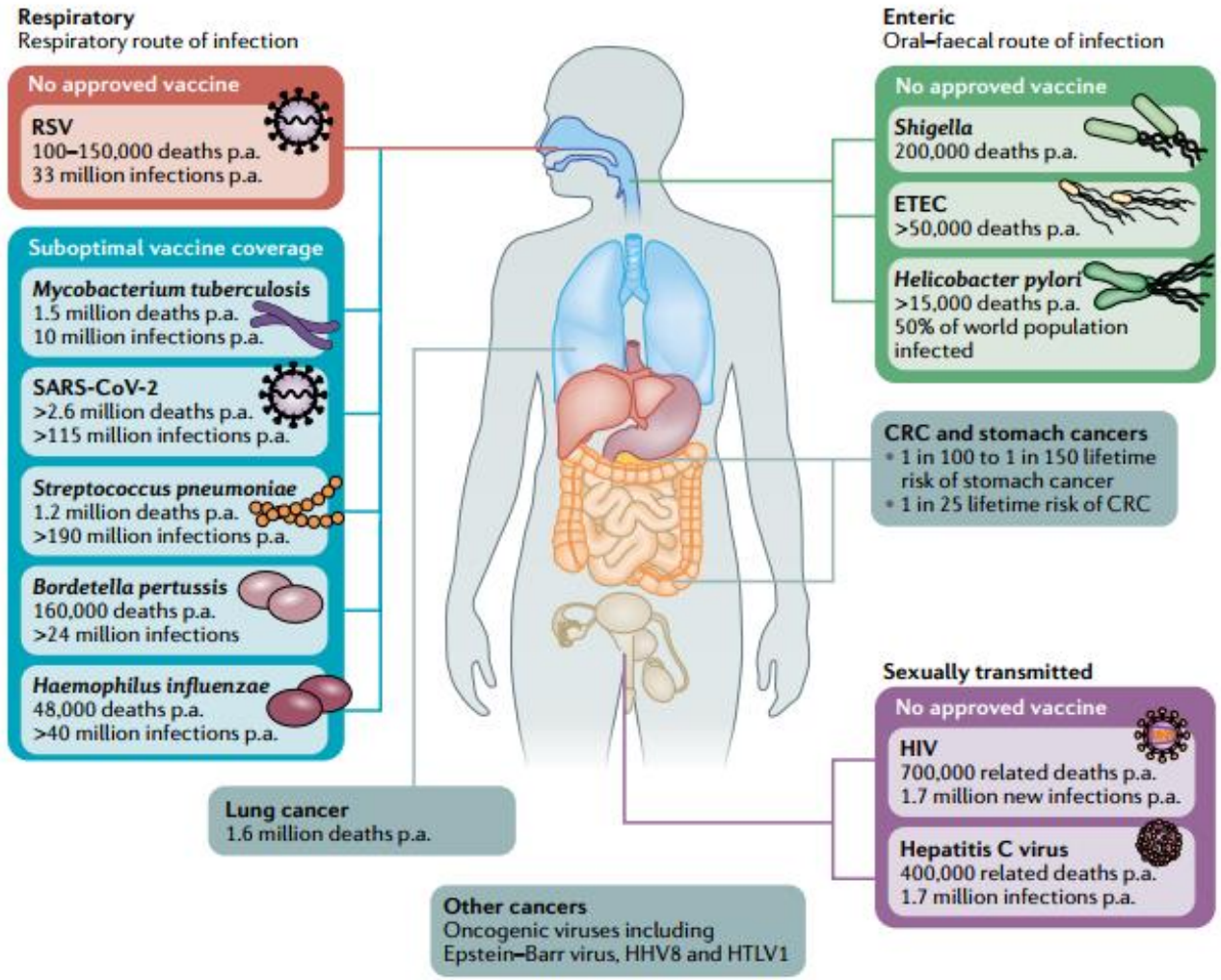

Fig. 1 | **Burden of mucosal diseases with unmet vaccine needs.** Respiratory, enteric and sexually transmitted infections

https://doi.org/10.1038/s41577-021-00583-2

Demain: des vaccins meilleurs

Vaccin anti-pneumococcique

Invasive pneumococcal disease incidence in children and adults in France during the pneumococcal conjugate vaccine era: an interrupted time-series analysis of data from a 17-year national prospective surveillance study

Naïm Ouldali, Emmanuelle Varon, Corinne Levy, François Angoulvant, Scarlett Georges, Marie-Cécile Ploy, Marie Kempf, Julie Cremniter, Robert Cohen, Daniel Levy Bruhl, Kostas Danis**

Lancet Infect Dis 2020; 21: 137–47

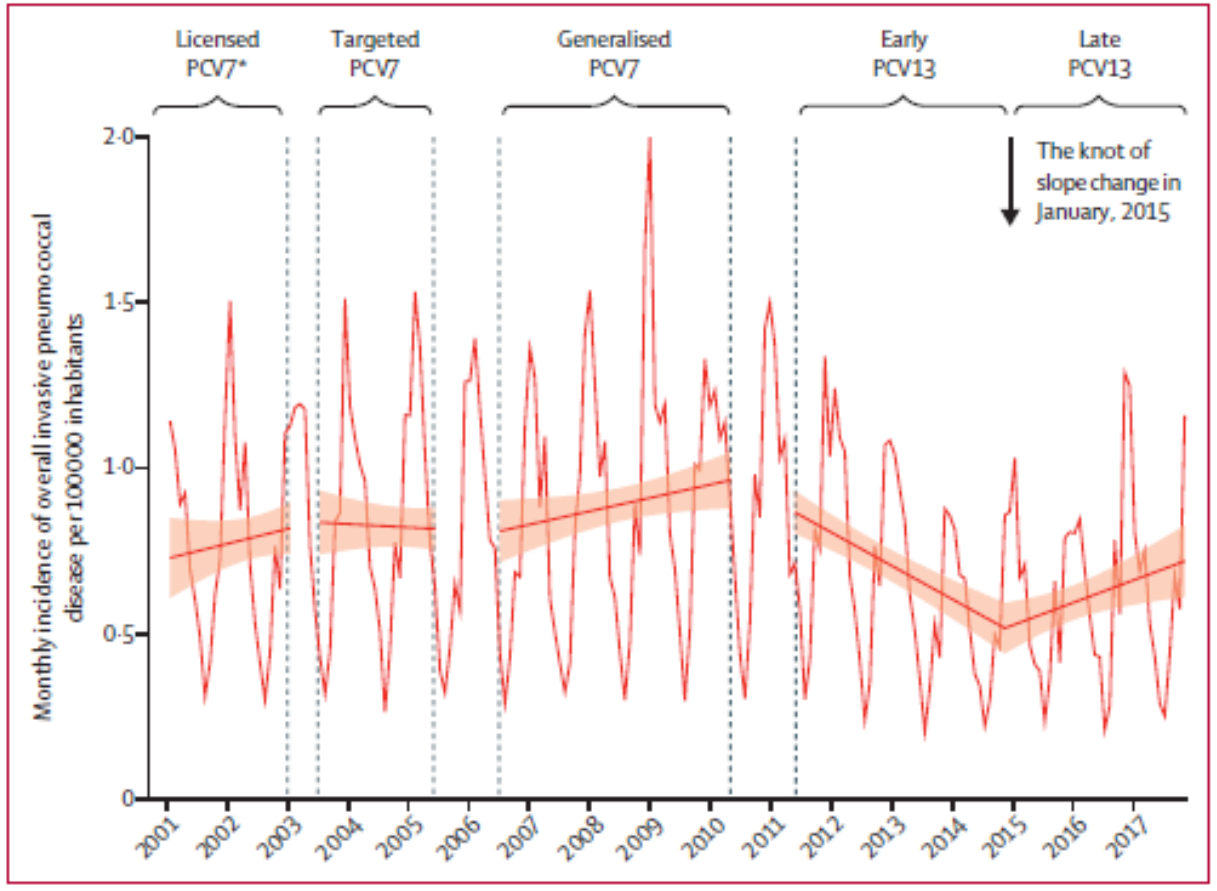

Figure 1: **Time-series analysis of invasive pneumococcal disease incidence over 17 years**
This figure represents data from 75 903 invasive pneumococcal disease cases. The bold slope lines were estimated by the segmented regression model; the red shading shows the 95% CI. The dotted vertical lines demarcate transition periods during which a new vaccine was implemented or changes to vaccination policy occurred. PCV=pneumococcal conjugate vaccine. Licensed PCV7=period from January, 2001, to December, 2002. Targeted PCV7=period from June, 2003, to May, 2005. Generalised PCV7=period from June, 2006, to May, 2010. Early PCV13=period from June, 2011, to December, 2014. Late PCV13=period from January, 2015, to December, 2017. *Licensed but not reimbursed PCV7 (vaccine coverage <10%).

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- Echappement/glissement sérotypes non contenus dans le PCV13
- Certains contenus dans le PPV23 mais pas tous, notamment 24F
- Schéma vaccinal de l'enfant ne contient pas le PPV23

	Licensed PCV7 period (January, 2001–December, 2002)	Targeted PCV7 period (June, 2003–May, 2005)	Generalised PCV7 period (June, 2006–May, 2010)	Early PCV13 period (June, 2011–December, 2014)	Late PCV13 period (January, 2015–December, 2017)
Children <2 years					
PCV7 serotypes (n=868)	67·9%	49·6%	9·8%	4·5%	5·8%
Serotypes specific to PCV13 plus serotype 6C (n=1187)	19·4%	31·6%	59·7%	15·1%	9·3%
Serotype 19A	9·3%	14·3%	29·1%	6·8%	3·7%
Serotype 3	3·2%	3·6%	4·2%	3·0%	4·7%
Main non-PCV13 serotypes (n=922)*	5·3%	10·4%	17·3%	55·2%	58·3%
Serotype 24F	1·5%	2·5%	5·7%	20·4%	24·4%
Serotype 15B/C *	1·8%	2·8%	3·1%	8·3%	8·1%
Serotype 10A *	0·4%	1·1%	2·4%	6·6%	6·4%
Serotype 12F *	0·2%	0·0%	1·7%	9·0%	4·8%
Serotype 22F *	0·2%	0·5%	1·9%	4·3%	4·8%
Serotype 8 *	0·6%	0·4%	0·7%	1·0%	4·0%
Serotype 15A	0·4%	2·0%	1·5%	4·7%	3·1%
Serotype 9N	0·2%	1·1%	0·4%	1·0%	2·9%
Adults ≥65 years					
PCV7 serotypes (n=2033)	50·8%	46·8%	23·2%	8·6%	6·6%
Serotypes specific to PCV13 plus serotype 6C (n=2601)	23·6%	27·8%	42·3%	36·9%	26·7%
Serotype 19A	8·7%	7·5%	14·6%	12·4%	7·4%
Serotype 3	8·2%	10·5%	10·1%	10·8%	14·3%
Main non-PCV13 serotypes (n=1977)	11·0%	11·8%	18·8%	30·3%	37·5%
Serotype 22F *	1·9%	3·5%	4·7%	6·8%	8·1%
Serotype 8 *	2·6%	1·6%	2·1%	2·3%	6·9%
Serotype 9N	1·7%	1·8%	2·4%	3·0%	5·3%
Serotype 12F *	0·2%	0·3%	2·1%	6·5%	4·8%
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Serotype 24F	1·4%	1·7%	2·7%	2·4%	2·7%
Serotype 15B/C *	0·5%	1·3%	0·9%	1·7%	2·4%

* Sérotype contenu dans le PPV 23

Vaccin anti-pneumococcique

vaccines

MDPI

Review

Development of Next Generation *Streptococcus pneumoniae* Vaccines Conferring Broad Protection

Malihe Masomian [1], Zuleeza Ahmad [1], Lai Ti Gew [2] and Chit Laa Poh [1,*]

1 Centre for Virus and Vaccine Research, School of Science and Technology, Sunway University, Kuala Lumpur, Selangor 47500, Malaysia; malihem@sunway.edu.my (M.M.); zuleezaa@sunway.edu.my (Z.A.)
2 Department of Biological Sciences, School of Science and Technology, Sunway University, Kuala Lumpur, Selangor 47500, Malaysia; janeg@sunway.edu.my
* Correspondence: pohcl@sunway.edu.my; Tel.: +60-3-7491-8622 (ext. 7338); Fax: +60-3-5635-8633

Vaccines 2020, 8, 132; doi:10.3390/vaccines8010132

- PCV 15 (V114) Merck phase 3 (serotypes PCV13 + 22F et 33F)
- PCV 20 Pfizer (phase 3)
- *S. pneumoniae* killed whole-cell vaccine (WCV) (phase 2)
- PnuBioVax (*S. pneumoniae* serotype 4 TIGR4) (phase 1)
- PPrV (recombinant proteins, PcpA, PhtD, and PlyD1) Sanofi Pasteur (phase 2 en association avec PHiD-CV)

Vaccin anti-pneumococcique

Clinical Infectious Diseases
MAJOR ARTICLE
Clin Inf Dis 2021

Safety, Tolerability, and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine (PCV20) in Adults 60 to 64 Years of Age

Donald Hurley,[1] Carl Griffin,[2] Mariano Young Jr,[3] Daniel A. Scott,[3] Michael W. Pride,[4] Ingrid L. Scully,[4] John Ginis,[3] Joseph Severs,[4] Kathrin U. Jansen,[4] William C. Gruber,[4] and Wendy Watson[3]

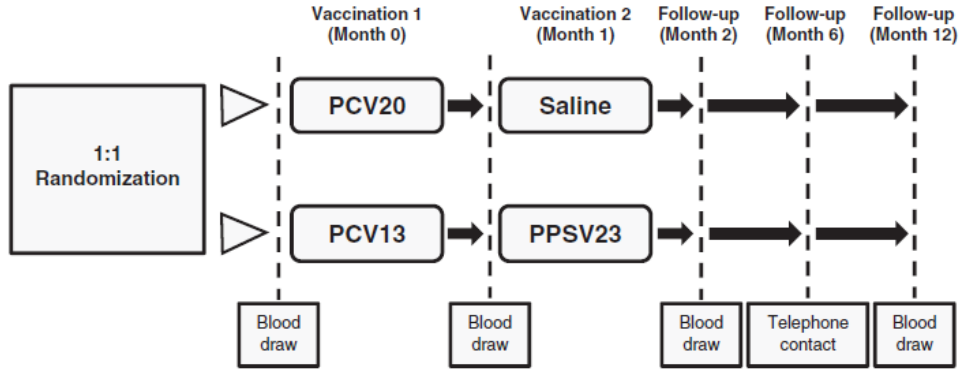
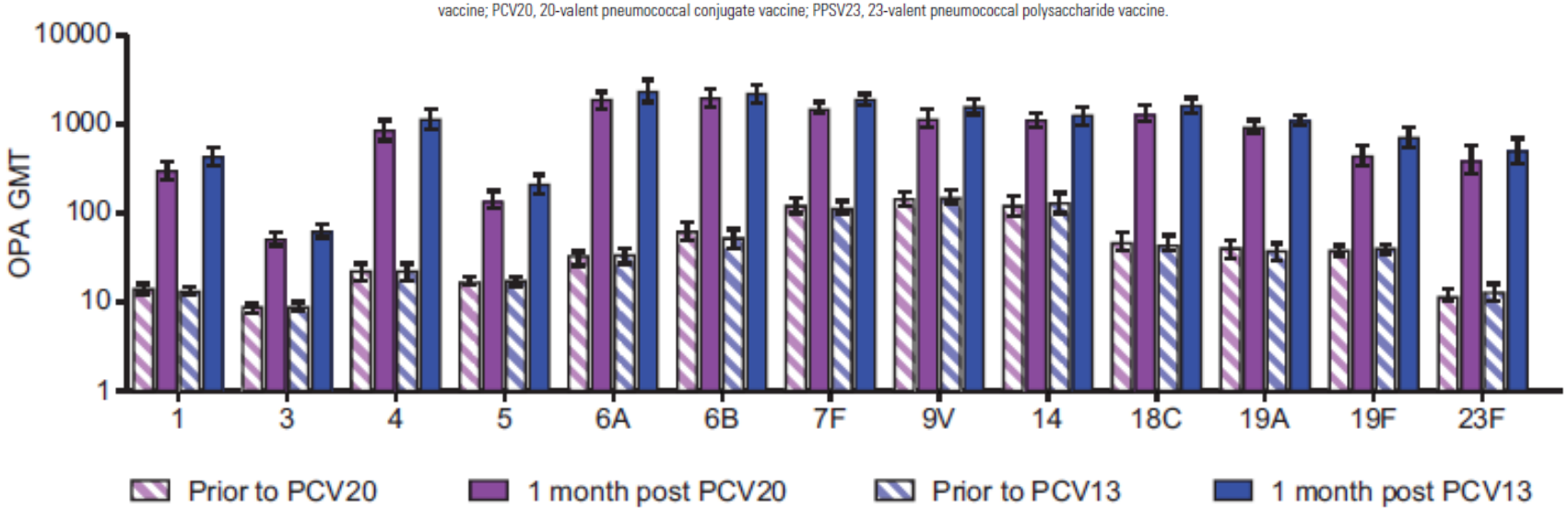


Figure 1. Study design. Immune responses measured at 12 months following vaccination 1 are not reported here. Abbreviations: PCV13, 13-valent pneumococcal conjugate vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine.

PCV 20=PCV 13+ nouveaux serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F)

PPV23 sert de contrôle pour l' immunogénicité des 7 serotypes additionnels du PCV20 (8, 10A, 11A, 12F, 15B, 22F, 33F).



GMFRs in Functional Antibody From Baseline 1 Month After Vaccination

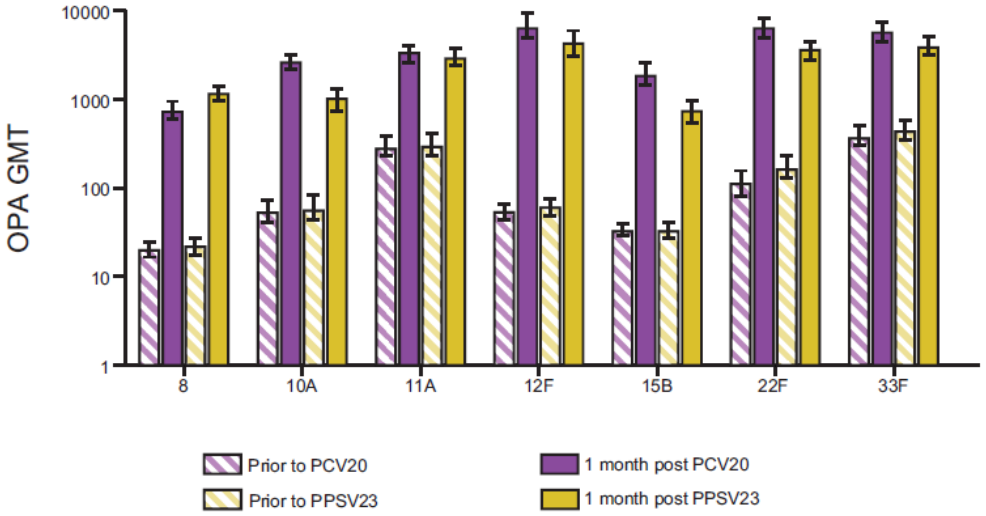
Serotype	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
PCV20	21.1	6.1	37.1	8.2	57.4	29.0	12.3	7.7	8.3	26.4	22.6	11.5	32.9
PCV13	33.5	7.1	51.0	11.6	68.6	38.8	15.8	10.1	9.6	35.2	30.9	18.4	39.8

Vaccin anti-pneumococcique

Clinical Infectious Diseases
MAJOR ARTICLE

Safety, Tolerability, and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine (PCV20) in Adults 60 to 64 Years of Age

Donald Hurley,[1] Carl Griffin,[2] Mariano Young Jr,[3] Daniel A. Scott,[3] Michael W. Pride,[4] Ingrid L. Scully,[4] John Ginis,[3] Joseph Severs,[4] Kathrin U. Jansen,[4] William C. Gruber,[4] and Wendy Watson[3]



GMFRs in Functional Antibody From Baseline 1 Month After Vaccination

Serotype	8	10A	11A	12F	15B	22F	33F
PCV20	36.7	47.5	11.0	112.2	56.7	54.4	14.0
PPSV23	56.4	17.0	9.7	76.1	20.8	20.0	9.0

Ne couvre toujours pas le 24F
Autorisé par la FDA, EMA

Table 2. Summary of Adverse Events (Safety Population)

	PCV20/Saline (n = 221[a]/213[b])		PCV13/PPSV23 (n = 222[a]/214[b])	
Time Point Type of AE	n (%)	(95% CI)	n (%)	(95% CI)
Following PCV20 or PCV13 administration through 1 month of follow-up				
Any AE	27 (12.2)	(8.2, 17.3)	29 (13.1)	(8.9, 18.2)
Severe AE	3 (1.4)	(.3, 3.9)	3 (1.4)	(.3, 3.9)
SAE	0	(.0, 1.7)	1 (0.5)	(.0, 2.5)
NDCMC	2 (0.9)	(.1, 3.2)	1 (0.5)	(.0, 2.5)
Following saline or PPSV23 administration through 1 month of follow-up				
Any AE	15 (7.0)	(4.0, 11.3)	40 (18.7)	(13.7, 24.6)
Severe AE	1 (0.5)	(.0, 2.6)	6 (2.8)	(1.0, 6.0)
SAE	0	(.0, 1.7)	4 (1.9)	(.5, 4.7)
NDCMC	2 (0.9)	(.1, 3.4)	4 (1.9)	(.5, 4.7)
From 1 month following saline or PPSV23 administration through 12 months of follow-up				
SAE	9 (4.2)	(2.0, 7.9)	7 (3.3)	(1.3, 6.6)
NDCMC	9 (4.2)	(2.0, 7.9)	3 (1.4)	(.3, 4.0)
Throughout the study				
SAE	9 (4.1)	(1.9, 7.6)	11 (5.0)	2.5, 8.7
NDCMC	13 (5.9)	(3.2, 9.8)	8 (3.6)	(1.6, 7.0)

Vaccin contre la tuberculose

- La tuberculose reste dans le monde une des principales causes de mortalité infectieuse: 1,4 millions de décès dont 210 000 PVVIH en 2019
- ≈ 1,7 milliards de personnes infectées, 5-15% évolueront vers une tuberculose maladie: ID, âge avancé…
- BCG: CI chez ID, durée de l'immunité variable (10-20 ans, max 60), meilleure efficacité si IDR négative, efficacité modérée (0-77%!)
- Besoin de nouveaux vaccins

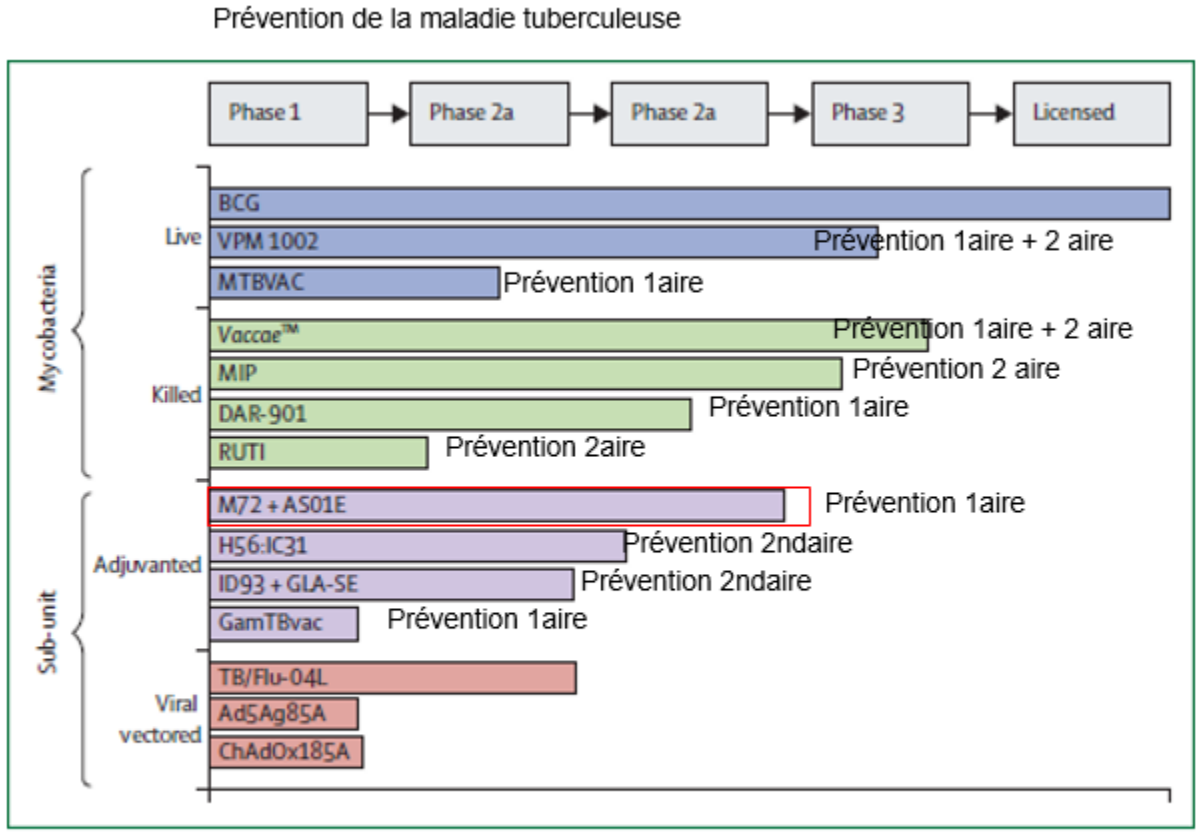


Figure: **Tuberculosis vaccine candidates in clinical development**
The indicated clinical development stages of vaccine candidates are based on an extrapolation from data in ClinicalTrials.gov.

Rapport sur la tuberculose dans le monde 2020 : résumé d'orientation OMS, http://apps.who.int/iris
Schrager LK, et al., Lancet Infect Dis. 2020 Mar;20(3):e28-e37.
Brazier b et al., Seminars in Immunopathology (2020) 42:315–331
https://www.clinicaltrials.gov

Vaccin contre la tuberculose

The NEW ENGLAND JOURNAL of MEDICINE
N Engl J Med 2019; **381:** 2429-2439

ORIGINAL ARTICLE

Final Analysis of a Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

D.R. Tait, M. Hatherill, O. Van Der Meeren, A.M. Ginsberg, E. Van Brakel, B. Salaun, T.J. Scriba, E.J. Akite, H.M. Ayles, A. Bollaerts, M.-A. Demoitié, A. Diacon, T.G. Evans, P. Gillard, E. Hellström, J.C. Innes, M. Lempicki, M. Malahleha, N. Martinson, D. Mesia Vela, M. Muyoyeta, V. Nduba, T.G. Pascal, M. Tameris, F. Thienemann, R.J. Wilkinson, and F. Roman

- M72: protéine de fusion derivée de 2 Ag Mt
- 08/2014 à 11/ 2015, inclusion adultes 18 -50 ans IGRA+, VIH -, Sans evidence de tuberculose maladie
- Kenya, Afrique du Sud et Zambie.
- Endpoint= Tuberculose maladie: PCR+, culture crachats
- 3575 participants ont été randomisés 1:1, 3573 ont reçu au moins une dose de M72/AS01E ou de placebo, et 3330 ont reçu les 2 doses.
- 2 doses à 1 mois d'intervalle, suivi 3 ans

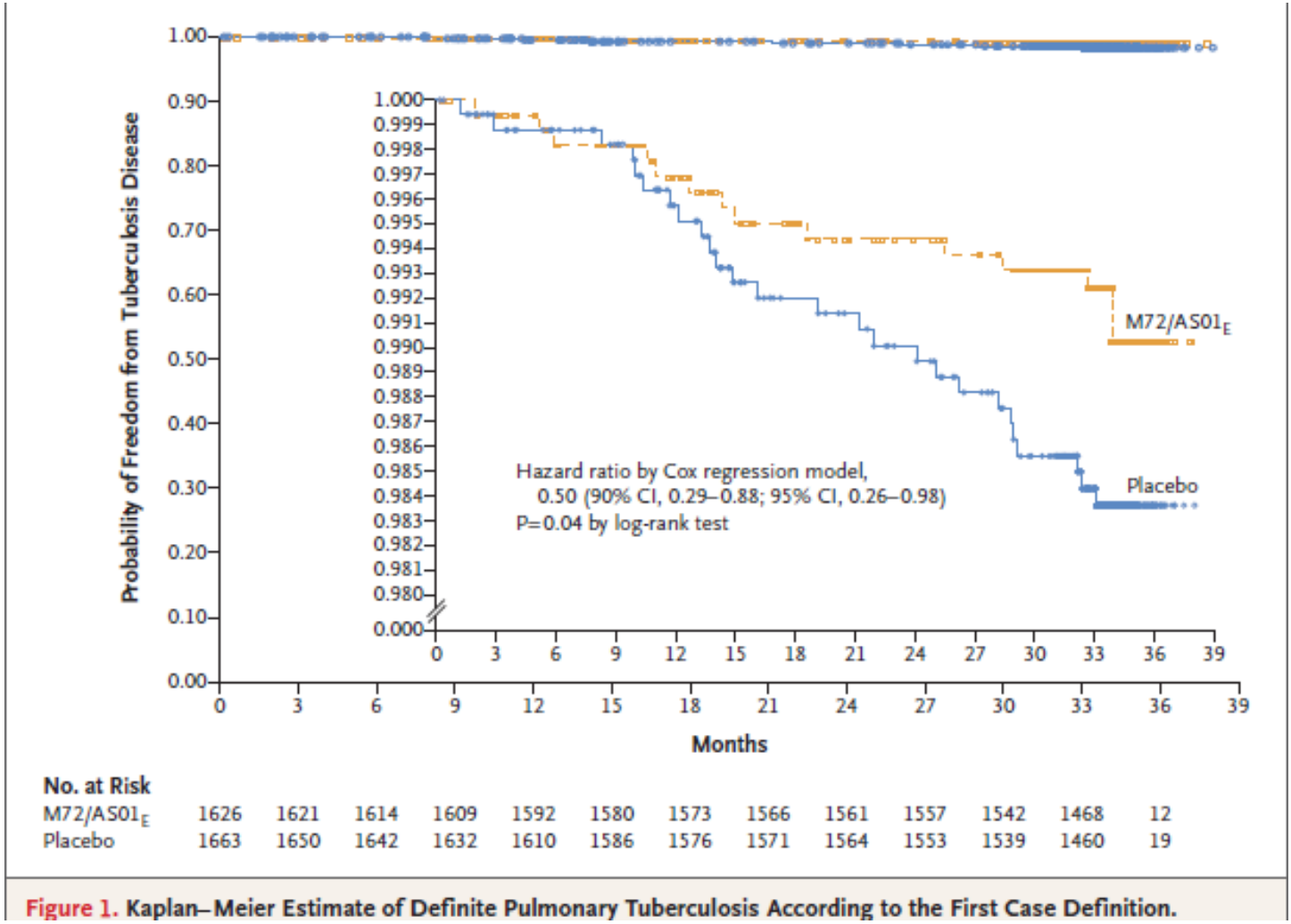


Figure 1. Kaplan–Meier Estimate of Definite Pulmonary Tuberculosis According to the First Case Definition.

Profil de sécurité tout à fait correct
Essai programmé chez les PVVIH (*NCT04556981)*

GSK→Gate medical research institute

Vaccin antigrippal

- Efficacité vaccinale des vaccins inactivés faible, variable selon les années, populations (10-60%)
- Amélioration via fortes doses, méthode d'administration, des adjuvants
- Durée protection courte
- Toujours souche dépendante+++

TABLE 1 Advantages and disadvantages of different influenza vaccines

Vaccine Type	Advantage	Disadvantage
Inactive vaccine	a) All age groups (except children under 6 months) with no contraindications can receive inactivated influenza vaccine b) Safe in pregnant women c) Use in immunocompromised patients	a) Soreness at the vaccination site,fever, headache, myalgia, or any physical unease happen mostly in children b) Allergy c) In rare case autoimmune disorders
Live attenuate	a) Safe in cystic fibrosis patients b) No systemic allergic reactions such as urticaria, angioedema, rhinitis, and eczema	a) Mild to moderate symptoms including runny nose, sneezing, nasal discomfort, fever and headache b) Is not recommended to be routinely used in pregnant women
Recombinant	a) High safety profile without involving infectious viruses b) Rapid, stable c) Induces humoral and cellular immune responses	a) Low immunogenicity b) Require appropriate adjuvants
DNA vaccine	a) Induce all three arms of adaptive immunity, CTLs, antibodies, and helper T cells b) Possible mucosal delivery and thus may stimulate innate immunity	a) Lower immunogenicity, low level of T-cell, and B-cell memory due to b) Integration of DNA vaccine genetic material into cellular or host DNA, c) Development of autoimmune disorders against host DNA
Universal vaccine	M2e: a) Induces M2e-specific humoral and cellular immune responses; b) Elicits broad cross-protection against divergent virus strains Epitope-base: a) They are considered to be safe, easy to produce, and stable. b) Can induce B-cell and T-cell in the same formulation	a) Single M2e molecule induces lower immune responses a) The main disadvantage of the epitope-based vaccine is that algorithms may fail to predict all the appropriate epitopes
CTL inducing vaccine	a) Target conserved influenza virus proteins and improve recovery and inhibit disease progression	a) Need to have an epitope that can be recognized by all major histocompatibility complex (MHC)
RNA vaccine	a) Safety b) Efficacy c) Higher potency (especially with self-amplifying RNA vaccines)	a) Possibility of adverse consequences like thrombus and/or edema b) Limited availability in cases of pandemic and endemic diseases.

Keshavarz M et al., Rev Med Virol. 2019;29:e2014.
Ostrowsky J et al., Current Opinion in Virology 2020, 40:28–36

Vaccin antigrippal

- Task force: développement vaccin antigrippal universel
- Cibles: HA stalk protein (stable), NA, matrix protein 2 (M2) et la nucleoprotein (NP).
- M2 et NP sont conservées au sein des souches humaines et aviaires

Universal influenza vaccine candidates in clinical development

Targeted response	Vaccine target	Vaccine platform	Phase	Candidate name	Development partners
B cell (antibody) responses to conserved regions of the virus	NA, HA gene suppression	LAIV	1	CodaVax	Codagenix, Inc. (US)
	HA	mRNA	1	Modified mRNA lipid nanoparticles	Moderna, Inc. (US)
	HA stalk	Ferritin-based nanoparticles	1	H1ssF_3928	NIAID Vaccine Research Center (US)
	HA stalk, HA head	Recombinant HA	3	Nano-Flu	Novavax (US)
	M2e	Recombinant subunit VLP	1	ACAM-FLU-A	Sanofi Pasteur (US)
	HA (H1)	Viral vector	2	VXA-A1.1	Vaxart, Inc. (US)
	M2e	Recombinant fusion protein	1	Vax102	VaxInnate Corp (US)
Cross-protective T cell responses against the virus' internal proteins	NP, M1, PB1, PB2	Synthetic peptide	1	FP-01.1	Altimmune (US) (Immune Targeting Systems Ltd)
	M2-deficient	LAIV	2	M2SR	Flugen, Inc. (US)
	NP, M1, M2	Synthetic peptide	2	FLU-v	Imutex Ltd (SEEK/hVIVO) (UK)
	NP, M1	Viral vector	1	MVA/ ChAdOx1-NP + M1	Jenner Institute/University of Oxford (UK)
	NP	Nanoparticles	2	OVX836	Osivax SAS (France)
	NP, M1	Viral vector	2	MVA-NP + M1	Vaccitech (UK)
B and T cell responses	HA (H1)	Viral vector	2	NasoVAX	Altimmune, Inc. (US)
	NP, M1, HA2	Recombinant peptide	3	Multimeric-001	BiondVax Pharmaceuticals (Israel); NIAID; Seventh Framework Program (EU)
	NP, M2e	Fusion protein	1	N8205	Dynavax (US)
	NP, M2e	DNA	1	VGX-3400	GeneOne Life Sciences, Inc. (South Korea)
	NA, cHA, HA head, HA stalk	Functional cHA	1	Chimeric HA (cHA)-based vaccines	Mount Sinai School of Medicine (US); GSK (US); PATH (US)
	NP, NA, HA	DNA	1	INO-4301	Inovio Pharmaceuticals (US)
	Recombinant HA (H1, H3, and 2 IBV HAs)	VLP	3	Quadrivalent VLP (QVLP)	Medicago, Inc. (Canada)
	M2e, HA2 stalk epitopes	Recombinant protein	1	Uniflu	VA Pharma LLC (Russia); Russian Federation Ministry of Health
	NS1-deficient	LAIV	1	deltaFLU	Vivaldi Biosciences (US); Icahn School of Medicine at Mount Sinai (US); AVIR Green Hills Biotechnology AG (Austria)

Source: CIDRAP, Universal Influenza Vaccine Technology Landscape; URL: http://www.cidrap.umn.edu/universal-influenza-vaccine-technology-landscape

Abbreviations: Chimeric HA (cHA); Hemagglutinin (HA); Influenza B virus (IBV); Live attenuated influenza virus vaccine (LAIV); Matrix Protein (M1); Membrane protein (M2); Membrane protein ion channel ectodomain (M2e); Neuraminidase (NA); Nonstructural protein (NS1); Nucleoprotein (NP); Viral RNA polymerases (PB1, PB2); Virus-like particle (VLP).

Ostrowsky J et al., Current Opinion in Virology 2020, 40:28–36
Gouma S et al., Annu Rev Virol. 2020 September 29; 7(1): 495–512

Comparison of the safety and immunogenicity of a novel Matrix-M-adjuvanted nanoparticle influenza vaccine with a quadrivalent seasonal influenza vaccine in older adults: a phase 3 randomised controlled trial

Vivek Shinde, Iksung Cho, Joyce S Plested, Sapeckshita Agrawal, Jamie Fiske, Rongman Cai, Haixia Zhou, Xuan Pham, Mingzhu Zhu, Shane Cloney-Clark, Nan Wang, Bin Zhou, Maggie Lewis, Patty Price-Abbott, Nita Patel, Michael J Massare, Gale Smith, Cheryl Keech, Louis Fries, Gregory M Glenn

novel recombinant, *Spodoptera frugiperda* (Sf9) insect cell or baculovirus system-derived, quadrivalent haemagglutinin nanoparticle influenza vaccine (qNIV), formulated with a saponin-based adjuvant, Matrix-M.

Compared to standard-dose quadrivalent inactivated influenza vaccine .

65 years-old

	A/Brisbane (H1N1)		A/Kansas (H3N2)		B/Maryland (B/Victoria)		B/Phuket (B/Yamagata)	
	HAI (egg)	HAI (wtVLP)	HAI (egg)	HAI (wtVLP)	HAI (egg)	HAI (wtVLP)	HAI (egg)	HAI (wtVLP)
qNIV (n=1280)								
Day 0 GMT	26·2 (25·0–27·4)	31·7 (30·0–33·5)	55·1 (53·5–56·8)	27·3 (26·1–28·6)	70·7 (68·0–73·5)	29·8 (28·5–31·1)	69·1 (66·0–72·3)	45·8 (44·0–47·7)
Day 28 GMT	49·3 (46·7–51·9)	76·6 (72·4–81·1)	151·5 (143·3–160·2)	153·6 (143·9–163·9)	110·7 (106·1–115·6)	62·8 (59·8–66·0)	168·5 (160·2–177·2)	118·3 (113·0–123·8)
Day 28 GMFR	1·9 (1·8–2·0)	2·4 (2·3–2·5)	2·7 (2·6–2·9)	5·6 (5·3–6·0)	1·6 (1·5–1·6)	2·1 (2·0–2·2)	2·4 (2·3–2·5)	2·6 (2·5–2·7)
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001
Day 28 SCR, n (% [95% CI])	282 (22·0% [19·8–24·4])	419 (32·7% [30·2–35·4])	535 (41·8% [39·1–44·6])	894 (69·8% [67·2–72·3])	143 (11·2% [9·5–13·0])	321 (25·1% [22·7–27·5])	401 (31·3% [28·8–33·9])	453 (35·4% [32·8–38·1])
Day 28 SPR, n (% [95% CI])	884 (69·1% [66·4–71·6])	1055 (82·4% [80·2–84·5])	1265 (98·8% [98·1–99·3])	1182 (92·3% [90·7–93·7])	1269 (99·1% [98·5–99·6])	1039 (81·2% [78·9–83·3])	1267 (99·0% [98·3–99·5])	1240 (96·9% [95·8–97·8])
IIV4 (n=1286)								
Day 0 GMT	26·0 (24·9–27·1)	32·4 (30·7–34·2)	54·7 (53·1–56·3)	26·5 (25·4–27·7)	69·8 (67·2–72·5)	29·5 (28·3–30·8)	66·5 (63·6–69·6)	44·3 (42·7–46·1)
Day 28 GMT	45·0 (42·7–47·3)	62·7 (59·2–66·4)	126·8 (120·3–133·6)	90·7 (84·9–96·9)	106·3 (102·3–110·6)	47·2 (45·2–49·4)	133·9 (127·7–140·5)	78·4 (75·1–81·9)
Day 28 GMFR	1·7 (1·7–1·8)	1·9 (1·8–2·0)	2·3 (2·2–2·4)	3·4 (3·2–3·6)	1·5 (1·5–1·6)	1·6 (1·5–1·7)	2·0 (1·9–2·1)	1·8 (1·7–1·8)
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001
Day 28 SCR, n (% [95% CI])	219 (17·0% [15·0–19·2])	275 (21·4% [19·2–23·7])	443 (34·4% [31·8–37·1])	636 (49·5% [46·7–52·2])	137 (10·7% [9·0–12·5])	173 (13·5% [11·6–15·4])	294 (22·9% [20·6–25·3])	228 (17·7% [15·7–19·9])
Day 28 SPR, n (% [95% CI])	830 (64·5% [61·9–67·2])	985 (76·6% [74·2–78·9])	1264 (98·3% [97·4–98·9])	1045 (81·3% [79·0–83·4])	1269 (98·7% [97·9–99·2])	933 (72·6% [70·0–75·0])	1254 (97·5% [96·5–98·3])	1174 (91·3% [89·6–92·8])
qNIV vs IIV4								
Day 28 baseline-adjusted GMTR$_{\text{qNIV/IIV4}}$	1·09 (1·03–1·15)	1·24 (1·17–1·32)	1·19 (1·11–1·27)	1·66 (1·53–1·79)	1·03 (0·99–1·07)	1·32 (1·26–1·39)	1·23 (1·16–1·29)	1·47 (1·40–1·55)
p value	0·0027	<0·0001	<0·0001	<0·0001	0·15	<0·0001	<0·0001	<0·0001
Day 28 absolute SCR % difference	5·0% (1·9 to 8·1)	11·4% (7·9 to 14·7)	7·3% (3·6 to 11·1)	20·4% (16·6 to 24·1)	0·5% (−1·9 to 2·9)	11·6% (8·6 to 14·6)	8·5% (5·0 to 11·9)	17·7% (14·3 to 21·0)
p value	0·0017	<0·0001	<0·0001	<0·0001	0·72	<0·0001	<0·0001	<0·0001

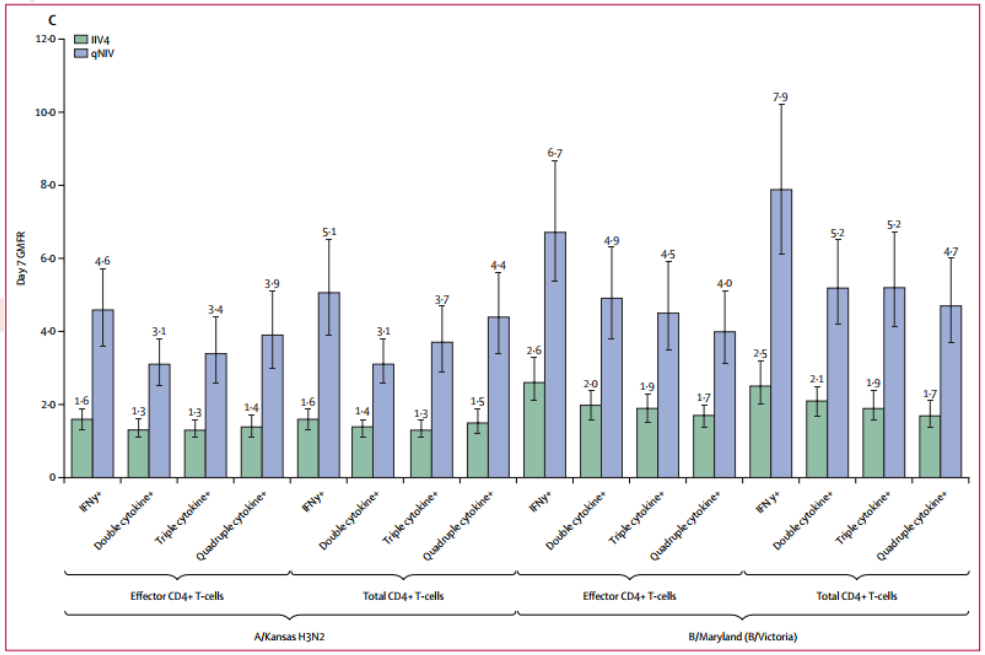


Figure 2: Cell-mediated immune responses with qNIV compared with IIV4

https://doi.org/10.1016/S1473-3099(21)00192-4

Demain: des vaccins nouveaux

Vaccin contre VIH

- En 2019, 38 millions de personnes vivent avec le VIH au niveau mondial, 1,7 millions de nouvelles infections
- Echec de nombreux essais vaccins depuis > 30 ans
- Echec recent de la phase 3 de l'essai HVTN702 (6ème essai clinique complet)

Recent efficacy trials and their related phase 1/2a trials.

Immunogen	NCT Trial number	Other names	Phase	Adjuvant	Completion Date*
Vector: ALVAC-HIV (vCP2438), Protein: bivalent subtype C gp120	NCT03284710	HVTN107	1/2a	Alum vs. MF59	Dec 2019
Vector: ALVAC-HIV (vCP2438), Protein: bivalent subtype C gp120	NCT03122223	HVTN120	1/2a	MF59 vs. $AS01_B$	Jul 2020
Vector: ALVAC-HIV (vCP2438), Protein: bivalent subtype C gp120	NCT02968849	HVTN702/Uhambo	2b/3	MF59	Aug 2021; prematurely terminated
Vector: Ad26.Mos4.HIV, Protein: subtype C gp140 and/or mosaic gp140	NCT02935686	ASCENT/HVTN118/ HPX2003	1/2a	Alum	Jan 2022
Vector: Ad26.Mos4.HIV, Protein: subtype C gp140	NCT03060629	HVTN705/Imbokodo	2	Alum	Jul 2022
Vector: Ad26.Mos4.HIV, Protein: bivalent subtype C gp140 and mosaic gp140	NCT03964415	HVTN706/Mosaico	3	Alum	Mar 2024

* Actual or predicted completion date.

Lee JH, et al., Semin Immunol. 2021 Jul 13:101470.

Vaccin contre VIH

- « Recombinant canarypox (ALVAC-vCP2438) containing HIV-1 gag (clade B LAI), pro (clade B LAI), env (gp120; clade ZM96.C), and gp41 (clade B LAI) transmembrane anchor », adjuvanté avec MF59
- Essai réalisé en Afrique du Sud
- > 5000 participants
- Proche de l'essai RV144, qui avait montré une efficacité modérée en 2009 en Thailande en utilisant « Recombinant canarypox (ALVAC; vCP1521) containing HIV-1 gag (clade B LAI), pro (clade B LAI), env (gp120 AE 92TH023), and gp41 (clade B LAI) transmembrane anchor » adjuvanté aluminium
- **Arrêt prématuré**

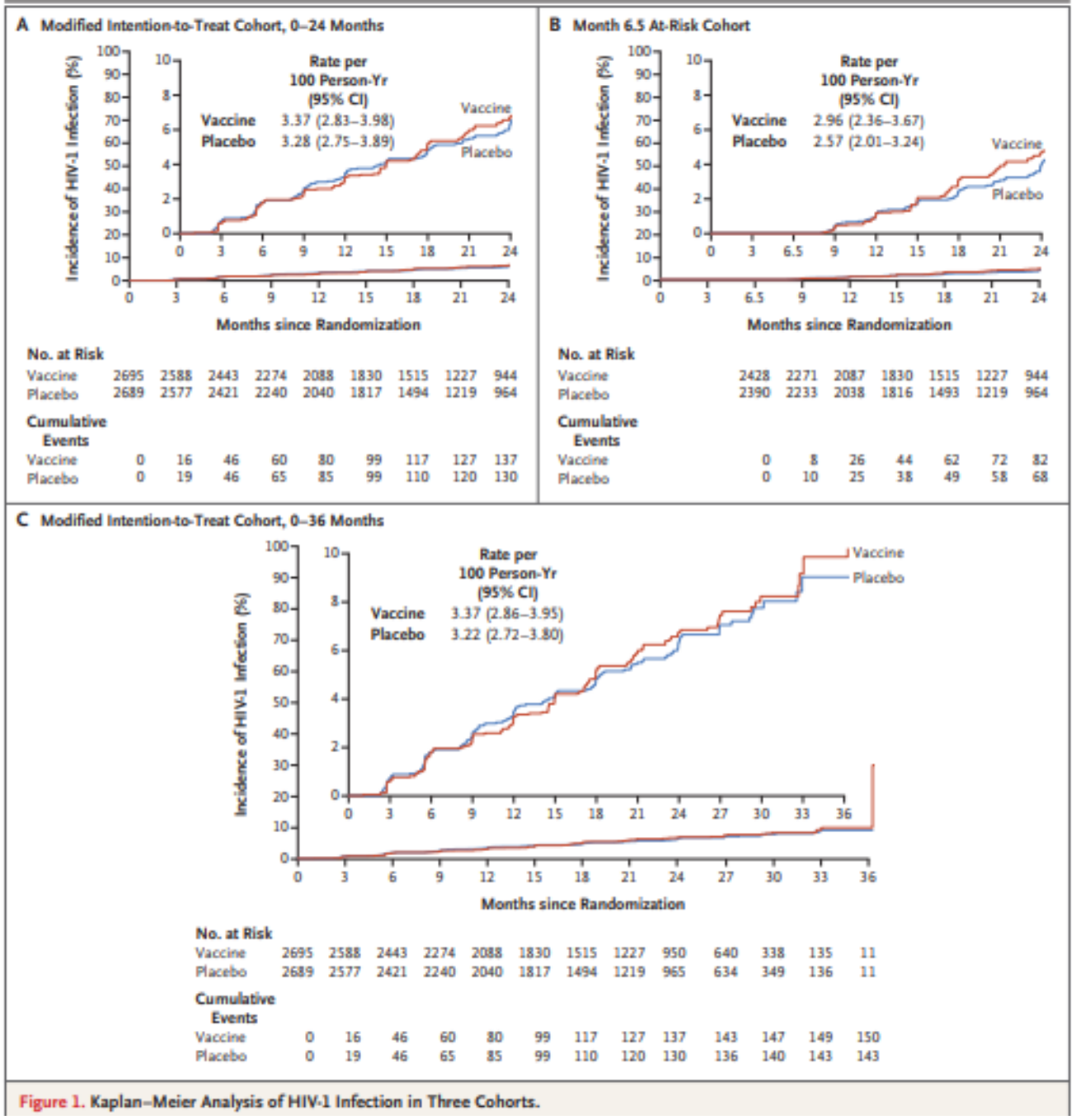


Figure 1. Kaplan–Meier Analysis of HIV-1 Infection in Three Cohorts.

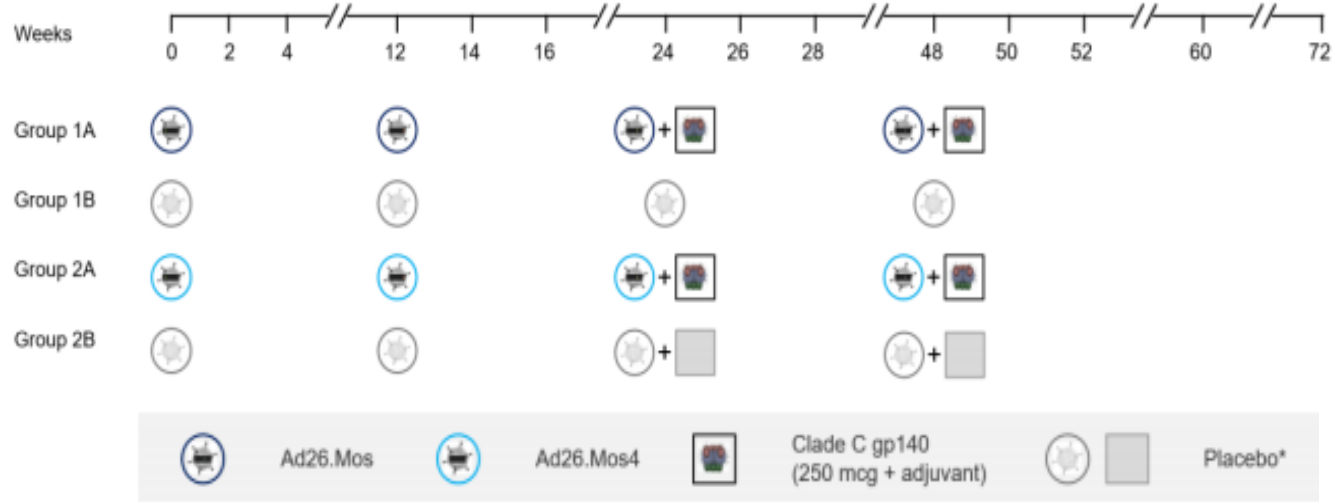
Bekker LG, et al.; N Engl J Med. 2021 Mar 25;384(12):1089-1100.
Zolla Pazner S et al., Lancet HIV 2021; 8: e449–52

Vaccin contre VIH

Safety and immunogenicity of two heterologous HIV vaccine regimens in healthy, HIV-uninfected adults (TRAVERSE): a randomised, parallel-group, placebo-controlled, double-blind, phase 1/2a study

Lancet HIV 2020; 7: e688–98

Lindsey R Baden, Daniel J Stieh*, Michal Sarnecki, Stephen R Walsh, Georgia D Tomaras, James G Kublin, M Juliana McElrath, Galit Alter, Guido Ferrari, David Montefiori, Philipp Mann, Steven Nijs, Katleen Callewaert, Paul Goepfert, Srilatha Edupuganti, Etienne Karita, Johannes P Langedijk, Frank Wegmann, Lawrence Corey, Maria G Pau, Dan H Barouch, Hanneke Schuitemaker, Frank Tomaka, and the Traverse/HVTN 117/HPX2004 Study Team*



- Etude aux USA et Rwanda, 201 patients randomisés, 198 vaccinés
- Vaccin tétravalent contient Ad26-encoded mosaic Env supplémentaire
- Vaccin tétravalent, bon profil de tolérance/ sécurité, idem trivalent
- Tétravalent induit une meilleure réponse immune que le trivalent (Elisa; Ac de liaison, ADCC, IFN gamma, réponse CD4, CD8)
- Arrêt de la Phase 2B (NCT03060629 en Afrique du Sud chez les femmes en 2021)

Johnson & Johnson and Global Partners Announce Results from Phase 2b Imbokodo HIV Vaccine Clinical Trial in Young Women in Sub-Saharan Africa

- Poursuite en Phase 2B (NCT03964415 USA, Europe MSM)

PV1/PrEPVacc

Status Ongoing

Phase IIb

Principal Investigator(s) Prof. Pontiano Kaleebu

Objective

This international, multi-centre, double-blind vaccine study is a three-arm prospective 1:1:1 randomisation comparing each of two experimental combination vaccine regimens i.e. DNA/AIDSVAX (weeks 0,4,24,48) and DNA/CN54gp140 (weeks 0,4) + MVA/CN54gp140 (weeks 24,48) with placebo control. There will be a concurrent open-label 1:1 randomisation to compare daily TAF/FTC (week 0-26) to daily TDF/FTC (weeks 0-26) as pre-exposure prophylaxis.

Last updated January 31, 2022

Prevention Option(s) HIV Vaccine PrEP

Observational Prospective Cohort

Study Design Placebo-controlled
Randomized
Double-blind

Arms and Assigned

JANUARY 2020 → MARCH 2023

Enrollment 1 668

Age Range 18 Years ↔ 40 Years

Population Men
Women

https://www.prepvacc.org/

Sites

MRC/UVRI Uganda Research Unit on AIDS
Masaka
Uganda

MRC HPRU
Durban
South Africa

MUHAS
Dar es Salaam
United Republic of Tanzania

MMRC
Mbeya
United Republic of Tanzania

INS/CISPOC
Maputo
Mozambique

March 8, 2022

First mRNA HIV Vaccine Clinical Trial Launches

Jennifer Abbasi

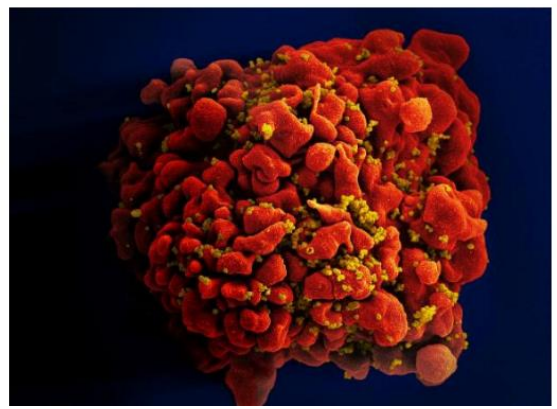
JAMA. 2022;327(10):909. doi:10.1001/jama.2022.2699

Moderna Inc is setting its sights on HIV. The biotech firm, along with nonprofit partner IAVI, the International AIDS Vaccine Initiative, announced in late January that researchers had administered the first doses of an investigational mRNA HIV vaccine to volunteers in a phase 1 clinical trial.

NIH launches clinical trial of three mRNA HIV vaccines

Phase 1 study is among first to examine mRNA technology for HIV.

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has launched a Phase 1 clinical trial evaluating three experimental HIV vaccines based on a messenger RNA (mRNA) platform—a technology used in several approved COVID-19 vaccines. NIAID is sponsoring the study, called HVTN 302, and the NIAID-funded HIV Vaccine Trials Network (HVTN), based at Fred Hutchinson Cancer Research Center in Seattle, is conducting the trial.



"Finding an HIV vaccine has proven to be a daunting scientific challenge," said Anthony S. Fauci, M.D. NIAID director. "With the success of safe and highly effective COVID-19 vaccines, we have an exciting opportunity to learn

Vaccin contre le Lyme

- Borréliose de Lyme: 300000 cas annuels aux USA, au moins 100000 en Europe
- « Ancêtres » vaccins ciblant OspA efficaces (1 vaccin recombinant + Al: FDA en 1998 mais trop peu utilisé/polémique, fin commercialisation en 2002) et le 2ème 1 vaccin recombinant sans Al pas de commercialisation
- Plusieurs approches dans les stratégies vaccinales:
  - Cibler *B. burgdoferi* dans le vecteur (OspA)
  - Cibler le spirochète chez l'hôte (protéines de surface, lipides paroi bactérienne, bactéries mutées vivantes)
  - Bloquer la transmission (vaccin ciblant les réservoirs et les vecteurs, génerant une immunité anti-tiques)

Gomes-Solecki M, et al., Clin Infect Dis. 2020 :10;70(8):1768-1773.
Steere AC, et al., N Engl J Med. 1998 Jul 23;339(4):209-15.
Sigal LH, et al., N Engl J Med. 1998 Jul 23;339(4):216-22.
Nigrovic LE, et al., Epidemiol Infect. 2007 Jan;135(1):1-8.

Vaccin contre le Lyme

- But= vaccin ciblant les espèces USA et Europe
- Arrêt du vaccin hexavalent Baxter bioscience, NCT01504347,
- Seuls vaccins en phase de développement chez l'Homme: vaccin recombinant hexavalent ciblant 6 sérotypes OspA, vaccin VLA15 recombinant +Aluminium
- Phase 2 Valneva, NCT03769194, NCT03970733
  - Pas de publication complète des résultats
  - Safety ok , taux d'AC élevés
  - Accord avec Pfizer pour la phase 3 pas encore débutée
- Fast track FDA phase 2
- Phase 3: Pfizer+Valneva

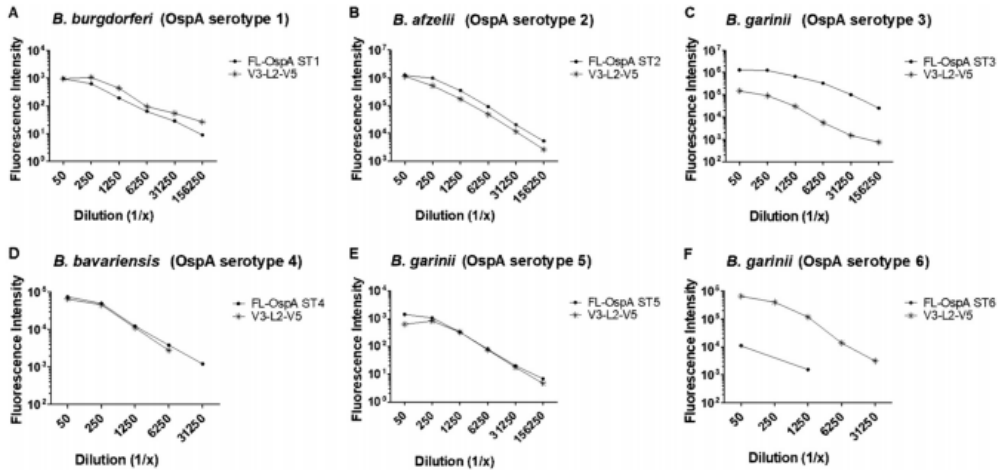


FIG 7 Antibodies generated by V3-L2-V5 versus the corresponding FL-OspA serotypes. The antibodies generated by V3-L2-V5 were tested by surface binding assay. The binding of vaccine-induced antibodies to OspA was compared to the binding of antibodies generated by FL-OspA of the corresponding serotypes (ST1 to ST6). The surface binding assay was carried out with *B. burgdorferi* OspA ST1 ZS7, *B. afzelii* OspA ST2 Pra10, *B. garinii* OspA ST3 PFr, *B. bavariensis* OspA ST4 PFin, *B. garinii* OspA ST5 PHei, and OspA ST6 KL11. The results are represented as fluorescence intensity.

Wressnigg N, et al., Clin Vaccine Immunol. 2014 Nov;21(11):1490-9
Nayak A, et al., Infect Immun. 2020 Mar 23;88(4):e00917-19
https://clinicaltrials.gov/ct2/show/results/NCT03769194?term=VLA15&cond=Lyme&draw=2&rank=3

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SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

INFECTIOUS DISEASES

mRNA vaccination induces tick resistance and prevents transmission of the Lyme disease agent

Andaleeb Sajid[1]†, Jaqueline Matias[1]†, Gunjan Arora[1]†, Cheyne Kurokawa[1], Kathleen DePonte[1], Xiaotian Tang[1], Geoffrey Lynn[1], Ming-Jie Wu[1], Utpal Pal[2,3], Norma Olivares Strank[1], Norbert Pardi[4], Sukanya Narasimhan[1], Drew Weissman[4], Erol Fikrig[1]*

Ability of lipid nanoparticle–containing nucleoside-modified mRNAs encoding 19 *I. scapularis* salivary proteins (19ISP) to enhance the recognition of a tick bite and diminish *I. scapularis* engorgement on a host and thereby prevent *B. burgdorferi* infection.

Guinea pigs were immunized with a 19ISP mRNA vaccine and subsequently challenged with *I. scapularis*. Animals administered 19ISP developed **erythema at the bite site** shortly after ticks began to attach, and these **ticks fed poorly, marked by early detachment and decreased engorgement weights**. 19ISP immunization also **impeded *B. burgdorferi* transmission in the guinea pigs**. The effective induction of local redness early after *I. scapularis* attachment and the inability of the ticks to take a normal blood meal suggest that 19ISP may be used either alone or in conjunction with traditional pathogen-based vaccines for the prevention of Lyme disease, and potentially other tick-borne infections

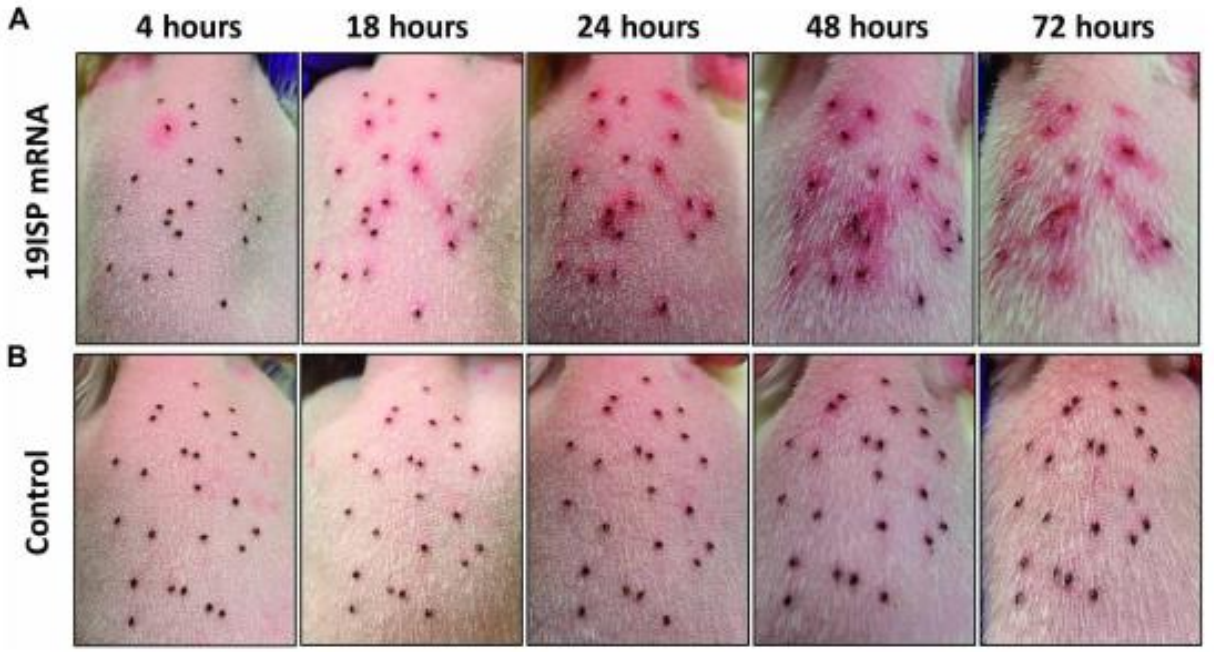

Fig. 2. Tick challenge of 19ISP mRNA-LNP immunized guinea pigs induces erythema. Guinea pigs were immunized with 19ISP or control (IL-21) mRNA, and 25 *I. scapularis* nymphs were allowed to engorge on their shaved backs. All animals were monitored for the development of erythema as a cardinal initial sign of acquired tick resistance over a period of 6 days or until all ticks detached. The images show representative (**A**) 19ISP-immunized or (**B**) control animals at the indicated time points.

Vaccin contre le VRS

- Vrai problème chez le nourrisson: 3,2 millions d'hospitalisations dans le monde en 2015, 118000 décès, 50% < 6mois
- Femmes enceintes
- Adultes: personnes âgées, immunodéprimés: formes graves, 4-10% mortalité
- Histoire vaccinale compliquée

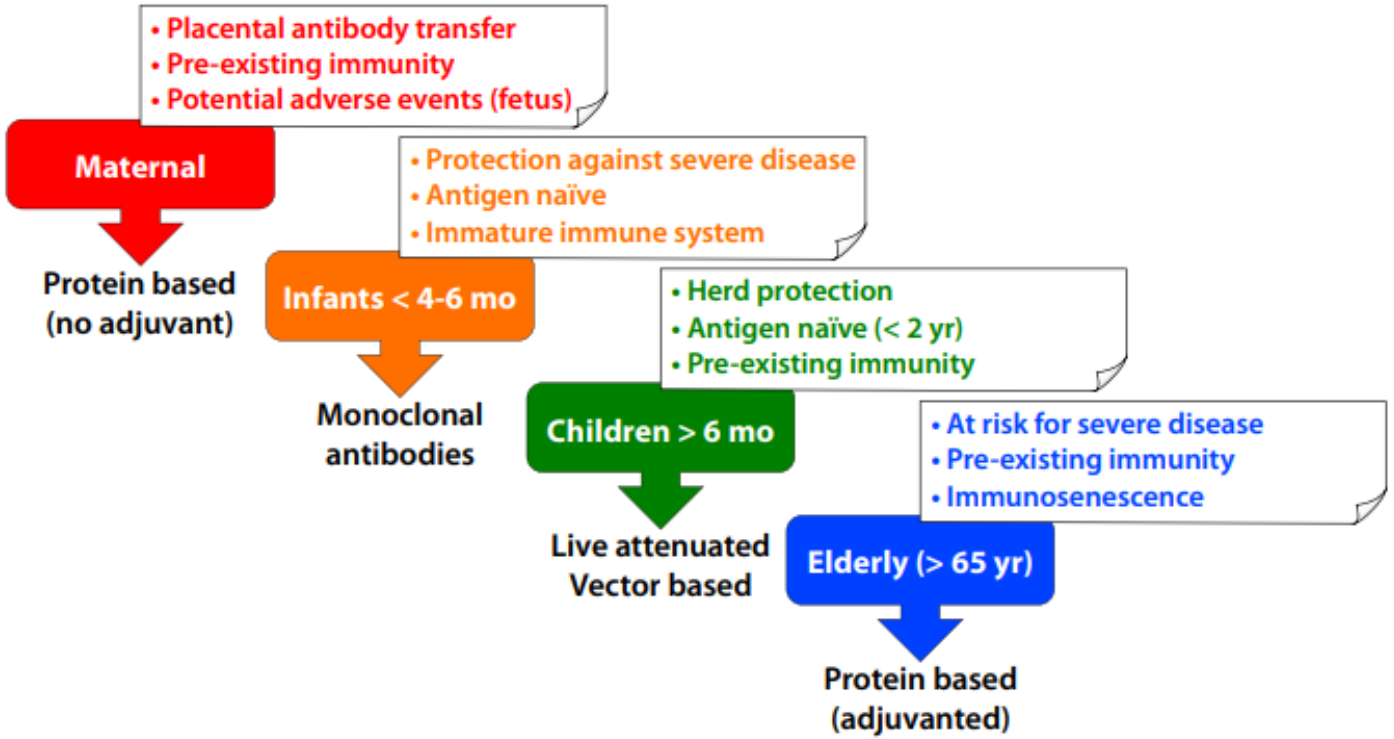

Figure 3. Target populations and respiratory syncytial virus vaccine types. There are different vaccine strategies according to the main target populations. The 4 main target populations are color coded. The nuances and characteristics of each target population are included in the adjacent balloon and the preferred vaccine strategy underneath each target population.

Mejias A, et al., Ann Allergy Asthma Immunol. 2020 Jul;125(1):36-46.

Vaccin contre le VRS

Pas encore complètement certain

RSV Vaccines in Clinical Development

Vaccine type (manufacturer)	Viral target	Target population	Administration route	Clinical development	Advantages	Challenges
PROTEIN VACCINES						
Particle based						
RSV F nanoparticle (Novavax, Gaithersburg, Maryland)	Prefusogenic	Maternal, elderly, pediatric	Systemic	Phase 3, phase 2, phase 1	Safe, immunogenic	Post-F based? Risk of ERD, antibody durability
Subunit						
DS-Cav1 (NIH/NIAID, Bethesda, Maryland)	Pre-F	Maternal and elderly	Systemic	Phase 1	Induce high-affinity neutralizing antibody, facilitate cross-priming, safe	Factors that affect transplacental transfer, instability of pre-F, antibody durability, no protection for premature infants
GSK RSV F (GlaxoSmithKline, Brentford, United Kingdom)	Pre-F	Maternal and elderly	Systemic	Phase 1		
DPX-RSV (Immunovaccine, Dartmouth, Canada, and VIB, Flander, Belgium)	SH	Elderly	Systemic	Phase 1		
RSV-F (Janssen, Beerse, Belgium)	Pre-F	Elderly	Systemic	Phase 1		
RSV-F (Pfizer, New York, New York)	Pre-F	Maternal and elderly	Systemic	Phase 2		
RSV-G (Advaccine Biotech, Beijing, China)	G	Pediatric and elderly	Systemic	Phase 1		
LIVE VACCINES						
Vector based						
AdV26 RSV (Janssen)	Pre-F	Pediatric and elderly	Systemic	Phase 2	Not attenuated, low risk of ERD, no interference with maternal antibodies	Potential for developing antivector immunity
ChAdV155-RSV (GlaxoSmithKline)	Pre-F, N, M2-1	Pediatric	Systemic	Phase 2		
VXA-RSV (AdV5) (Vaxart, South San Francisco, California)	Post-F	Elderly	Mucosal and systemic	Phase 1		
MVA-BN RSV (Bavarian Nordic, Kvistgaard, Denmark)	Post-F, GA/GB, N, M2	Elderly	Systemic	Phase 2		
Live-attenuated/chimeric						
rBCG/N-hRSV (Universidad de Chile, Santiago, Chile)	N	Newborn	Systemic	Phase 1	Predominant T_H1 immune responses	
RSV/ΔG (Intravac)	Lacks G	Pediatric	Mucosal	Phase 1	Low risk of ERD, intranasal delivery, replication in presence of maternal antibody, broad stimulation of immune responses	Balance of attenuation/ immunogenicity, reverse to wild type, stability for mass production
RSV ΔNS2 Δ1313/1314L	Pre-F/post-F	Pediatric	Mucosal and systemic	Phase 1		
RSV 276						
RSV 6120/ΔNS2/1030_S (Sanofi Pasteur, Lyon, France, and NIH)						
SeV/RSV (St Jude Hospital, Atlanta, Georgia)	F	Pediatric	Mucosal	Phase 1		

Abbreviations: Adv, adenovirus; ERD, enhanced RSV disease; F, fusion; G, attachment; MVA, modified vaccinia Ankara virus; ND, not disclosed; NIAID, National Institute of Allergy and Infectious Diseases; NIH, National Institutes of Health; post-F, postfusion; pre-F, prefusion; RSV, respiratory syncytial virus; SeV, Sendai virus; SH, small hydrophobic.

Mejias A, et al., Ann Allergy Asthma Immunol. 2020 Jul;125(1):36-46.
Madhi SA, et al.,N Engl J Med. 2020 Jul 30;383(5):426-439.

Vaccin contre *E. coli* uropathogènes

TABLE 1 | Non-antibiotic therapeutic options for the treatment of urinary tract infections.

Therapeutic options	References	Mechanism	Benefits	Drawbacks
Vaccine				
Targeting adhesion	(O'Hanley et al., 1985; De Ree and Van den Bosch, 1987; Riegman et al., 1988; Wizemann et al., 1999; Langermann et al., 2000; Roberts et al., 2004; Poggio et al., 2006; Habibi et al., 2016)	• Block the liaison adhesin-host cell receptor (pili vaccine) • Reduction of adhesion and protection against cystitis (FimH vaccine)	• Decrease the bacterial colonization • Protection of the bladder and the kidneys	• Heterogeneity of the proteins of the bacterial membrane
Targeting capsule	(Kaijser et al., 1983; Roberts et al., 1993; Kumar et al., 2005; Stenutz et al., 2006)		• Promising animal model results	• No human studies • Great heterogeneity in antigen used making creation of a vaccine with broad protection difficult
Targeting toxins	(O'Hanley et al., 1991; Ellis and Kuehn, 2010)	• Reduction of renal injury	• Decrease virulence	• No long-term protection
Targeting iron metabolism	(Alteri et al., 2009; Brumbaugh et al., 2013)	• Effective immunologic reaction against specific molecules	• Protection of the bladder and the kidneys • Reduce UTI recurrence	• Cannot target all UPEC strains (heterogeneity of the targets)

Loubet P, et al.,Front Microbiol. 2020 Jul 3;11:1509.

Vaccin contre *E. coli* uropathogènes

Table 1 – Available vaccines, administration methods, and vaccine content

Vaccine	Method of administration	Bacterial content
UroVaxom (OM-89)	One oral tablet to be taken once a day for 3 mo ± booster tablet for the first 10 d of months 6–9	6 mg of lyophilised bacterial lysates derived from 18 *E. coli* strains
Uromune	Two doses of 100 µl each (10^8 bacteria/puff) daily sublingually, for a duration of 3 mo	*E. coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Enterococcus faecalis*
Solco-Urovac	Vaginal suppository given weekly for the first 3 wk, then a booster monthly for 3 mo Intramuscular injection, initially weekly for 3 wk, with a booster at 6 mo	10 Uropathogenic strains of bacteria including 6 *E. coli* strains, *K. pneumoniae*, *Proteus mirabilis*, *Proteus morganii*, and *E. faecalis*
ExPEC4V	Single intramuscular injection of 0.5 ml	Genetically detoxified form of exotoxin A from *Pseudomonas aeruginosa* linked to four serotype surface polysaccharide antigens of *E. coli* (O1A, O2, O6A, O25B)

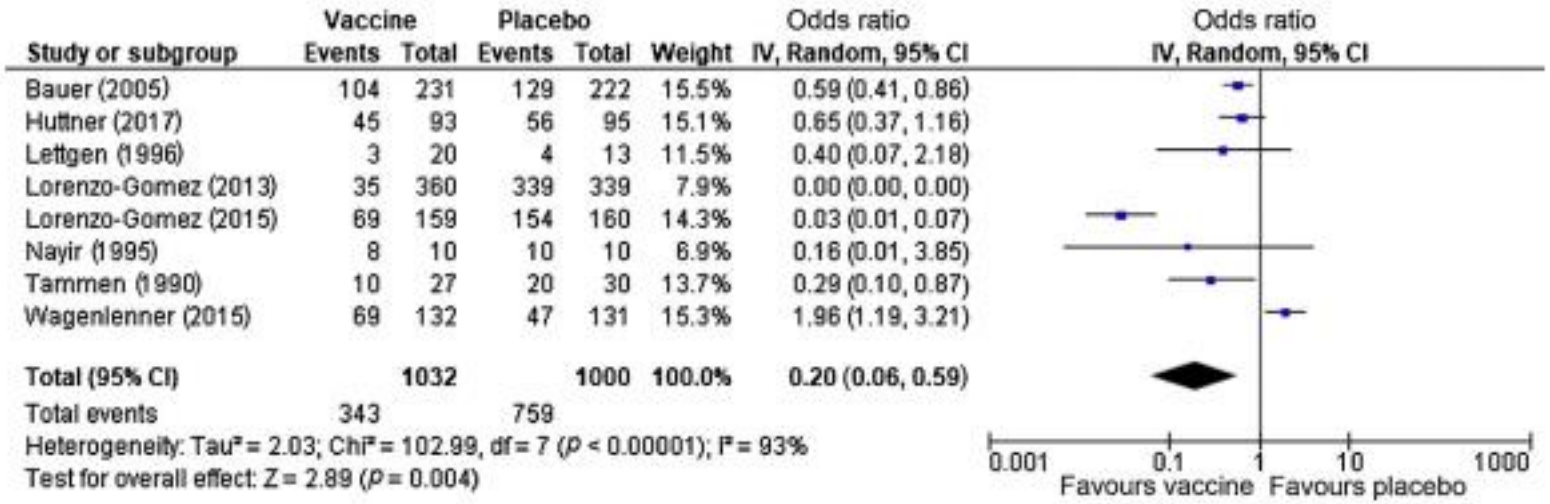

Fig. 5 – Long-term efficacy of vaccines. CI = confidence interval; IV = inverse variance.

Prattley S, et al,Eur Urol Focus. 2020 May 15;6(3):593-604.

Vaccin contre *Staphylococcus aureus*

frontiers in Immunology

REVIEW
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Staphylococcus aureus Vaccine Research and Development: The Past, Present and Future, Including Novel Therapeutic Strategies

Jonah Clegg[1,2], Elisabetta Soldaini[1], Rachel M. McLoughlin[2], Stephen Rittenhouse[3], Fabio Bagnoli[1] and Sanjay Phogat[1]*

TABLE 1 | *Staphylococcus aureus* vaccines currently enrolled in clinical trials.

Company	Vaccine	Phase	Clinical trial number	Study population	Literature
GSK	SA-5Ag: Adjuvanted	I: Recruiting	NCT04420221	18 – 50 year olds at risk of recurrent skin infections	
Novadigm Therapeutics	NDV-3A: Als-3 (*C. albicans* cross reactive cell wall protein) + Alum	II: Ongoing	NCT03455309	Military Personnel	(136, 137)
Olymvax	rFSAV: Hla, SpA, SEB, IsdB, MntC + Alum	II: Ongoing	CTR20181788, NCT03966040		(138)
Pfizer	SA4Ag: CP5-dptx, CP8-dptx, ClfA, MntC	IIb: Failure	NCT02388165	Patients undergoing spinal surgery	(20, 139–141)
Integrated Biotherapeutics	i. Stebvax: SEB + alum ii. IBT-V02: SEB, SEA, TSST-1, LukS, LukF, LukAB, Hla + alum	I: Completed I: Scheduled	NCT00974935	18 – 40 year olds	(142)

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Safety, immunogenicity, and efficacy of NDV-3A against *Staphylococcus aureus* colonization: A phase 2 vaccine trial among US Army Infantry trainees

Eugene V. Millar [a,b,*], Jason W. Bennett [c], Burc Barin [d], Patrick M. Carey [e], Natasha N. Law [a,b,e], Caroline E. English [a,b], Michael M. Schwartz [f], Terrence Cochrane [f], Michael W. Ellis [g], David R. Tribble [a], M. Timothy Cooke [f], John P. Hennessey [f]

US Army Infantry trainees (Fort Benning, GA) in a phase 2, randomized, double blind, placebo-controlled trial of NDV-3A, a vaccine containing a recombinant adhesin/invasion protein of Candida albicans that has structural similarity to the S. aureus protein clumping factor A. Study participants received one intramuscular dose of NDV-3A or placebo (adjuvant alone) within 72 h of arrival on base. Longitudinal nasal and oral (throat) swabs were collected throughout the 14-week Infantry training cycle. Safety, immunogenicity, and efficacy of NDV-3A against S. aureus nasal / oral acquisition were the endpoints.

Table 5

Vaccine Efficacy Against *S. aureus* Colonization Detected by Positive Nasal, Oral, and Nasal/Oral Culture by 56 Days Post Vaccination – Baseline *S. aureus* Nasal/Oral Colonization Negative Subjects.

Endpoint at 56 days post-vaccination	Vaccine Efficacy[a] (95% CI)	p-value[b]
Positive nasal culture	12.1% (-31.6%, 41.3%)	0.31
Positive oral culture	2.4% (-50.9%, 36.9%)	0.52
Positive nasal/oral culture	6.2% (-37.6%, 36.1%)	0.43

Le plus attendu…..

Le vaccin contre la connerie: toujours pas au point

http://ministereduchomage.fr

https://nostalgia.blog4ever.com