◆ DOVER, DELAWARE ◆ 2023 IMMUNIZATION SUMMIT ◆ DECEMBER 7, 2023 ◆

Emerging Vaccine Pipeline

The Immunization Coalition of Delaware

in partnership with the Delaware Division of Public Health

Jennifer Vodzak, MD

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Division of Infectious Diseases
Nemours Children's Hospital, Wilmington, DE

Disclosures

- ***I do not have any disclosures or conflicts of interests.***
- ***For today's presentation, companies that produce vaccines may be mentioned due to the nature of discussing vaccine products in the pipeline. Company and/or brand names will be used sparingly and when appropriate, for educational purposes only, and will be presented objectively as source references, without bias toward or against any particular product or company.***

Presentation Note

- Material presented is as up-to-date as possible in preparation for today's presentation.
- Information changes rapidly and new data need to be assessed and incorporated regularly.
- Medical science and clinical practice must adapt in agile ways to recommend and implement the best information and safest practices known at any given time.

Learning Objectives

1) Identify infectious disease targets for vaccines in the pipeline
2) Recognize various mechanisms of immune modulation that guide vaccine development
3) Describe research efforts in novel vaccine delivery methods

Pediatric providers have strong knowledge of current childhood vaccines since such products are a critical part of medical care for children.

However, knowledge regarding vaccine innovation and products in development may be more limited.

Clinical Practice

Understanding advancements in immune-based therapeutics, disease prevention, and vaccine delivery methods helps providers to appropriately counsel patients and families on current and new vaccine product options to provide the best care.

General Vaccination Concepts

"The main **principle of vaccination** is the proactive induction of a protective immune response by mimicking the natural interaction of an infectious pathogen (bacteria, viruses, etc.) with the human immune system."

Zepp F. (2016) Principles of Vaccination. In: Thomas S. (eds) Vaccine Design. Methods in Molecular Biology, vol 1403. Humana Press, New York, NY

- ✓ **Several different vaccine end points or goals can be targeted to determine if vaccine is effective**
  - **These are different for every infectious agent and every vaccine**
  - **The approach(es) for determining these goals follow consistent processes within many agencies to ensure standards and safety**

3 general use goals

1) **Protect an individual**
2) **Protect a population**
3) **Control an outbreak**

4 outcome-based goals

1) **Prevent mortality**
2) **Prevent severe illness/complications**
3) **Prevent disease**
4) **Prevent transmission**

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? Prevent people from dying

↓ Overall mortality
↓ Age-dependent mortality
↓ Population mortality

? Prevent disease (people getting sick)

↓ Severe disease (symptoms)
↓ Moderate disease (symptoms)
↓ Any disease (symptoms)

? Prevent complications and long-term issues from infection

↓ ICU care/high level support
↓ Hospitalizations
↓ Complications from disease

? Prevent pathogen transmission

↓ Horizontal transmission
(community spread, person-to-person)
↓ Vertical transmission
(mother to baby during pregnancy or delivery)

Developing new vaccine products

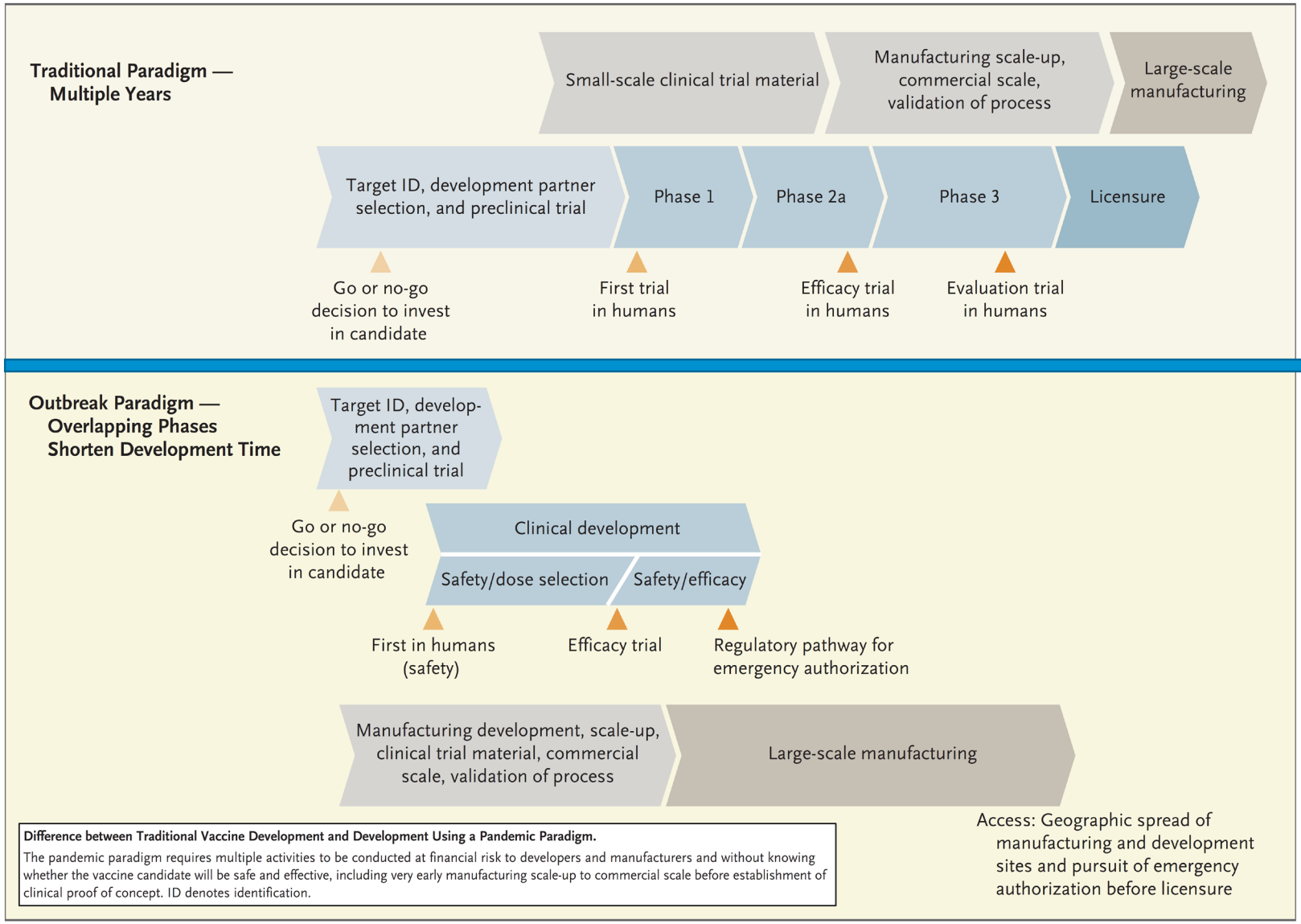
We need knowledge of…

1) **Human immune response to a pathogen**
   (expected & aberrant)
2) **Animal model that predicts human protection/response**
3) **Clear immunologic correlates of protection**
   (lab-based, measurable)
4) **Large trials with long-term follow-up**
   (at least 3 years preferred)
5) **Funding priorities**
   (public and/or private)

Perspective The NEW ENGLAND JOURNAL of MEDICINE

Developing Covid-19 Vaccines at Pandemic Speed

Nicole Lurie, M.D., M.S.P.H., Melanie Saville, M.D., Richard Hatchett, M.D., and Jane Halton, A.O., P.S.M.



Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm.
The pandemic paradigm requires multiple activities to be conducted at financial risk to developers and manufacturers and without knowing whether the vaccine candidate will be safe and effective, including very early manufacturing scale-up to commercial scale before establishment of clinical proof of concept. ID denotes identification.

Unprecedented speed

~~Typ opment 8-1 ars~~

Accelerated course

High risk groups
Benefit >> Risk ?

Broad application
minimum 12-18 mos

https://www.nejm.org/doi/full/10.1056/NEJMp2005630

Vaccine Strategy, Planning and Funding – U.S.

VACCINES

National Strategic Plan

for the United States | **2021–2025**

Federal Implementation Plan

for the United States | 2021–2025

VISION

The United States will be a place where vaccine-preventable diseases are eliminated through safe and effective vaccination over the lifespan.

Goal 1: Foster innovation in vaccine development and related technologies.
Goal 2: Maintain the highest possible levels of vaccine safety.
Goal 3: Increase knowledge of and confidence in routinely recommended vaccines.
Goal 4: Increase access to and use of all routinely recommended vaccines.
Goal 5: Protect the health of the nation by supporting global immunization efforts.

www.hhs.gov/vaccines/vaccines-national-strategic-plan/index.html

Vaccine Strategy, Planning and Funding – U.S.

Verbiage from www.hhs.gov/vaccines/vaccines-national-strategic-plan/index.html

Improved understanding of the pathogen-host interaction and the human immune system have led to innovations in the following areas:

- ✓ **Vaccine design** (e.g., advances in nucleic acid vaccine development)
- ✓ **Novel antigen delivery platforms**
  (e.g., liposomes, nanoparticles, and novel protein expression systems such as plant-based systems)
- ✓ **Promising vaccine delivery mechanisms** (e.g., microneedle patch)

Other advances include

- Structure-based vaccine design
- Machine-learning to identify and design antigens
- Novel adjuvants
- Alternative routes of vaccine administration (e.g., transdermal)

VACCINES
National Strategic Plan
for the United States | **2021–2025**

National Vaccine Advisory Committee (NVAC) – U.S.

www.hhs.gov/vaccines/nvac/index.html

NVAC Innovation in Immunization Subcommittee

Charge from the Assistant Secretary for Health

Develop report with recommendations outlining vaccine innovation agenda

- Describes vaccine innovation priorities
- Describe actions for advancing the development of new and existing vaccines
- Optimize public health and reduce disease burden in the United States

The final report should be ready for vote by the February 2024 NVAC meeting.

NVAC should create a working group

- Select NVAC members, Federal and non-federal stakeholders, Ex-officio and liaison members of NVAC and additional experts not on NVAC

The charge states that NVAC should write a report that includes:

- ❑ **Review of both conventional and promising novel approaches for vaccine discovery and development** as well as recommendations for actionable, high-impact activities that HHS and federal partners can take to advance clinical trial design, regulatory requirements, manufacturing processes, funding mechanisms, and business models; including ways we can leverage emerging technologies, processes, and workflows and suggestions for innovative collaborations.
- ❑ **Evidence-based approach for identifying and prioritizing vaccine candidates and immunization technologies** including their criteria for prioritization. NVAC should take the potential impact on disease burden, population health outcomes, health equity, economic impact, national health priorities, and scientific feasibility into account in the development of the approach.
- ❑ **List of vaccination innovation priorities,** including target antigens, molecular platforms, and immunization delivery technologies.
- ❑ **Forward-looking approach to introduce vaccines for special patient populations and neglected diseases** to portray their value and importance.
- ❑ **Scientific agenda outlining a framework of research direction** and identifies scientific needs and gaps that should be addressed by end of 2028.

Vaccine Strategy, Planning and Funding – Global

Resources, Funding, Collaboration, Innovation

Gavi The Vaccine Alliance — www.gavi.org/

Bill & Melinda Gates Foundation — www.gatesfoundation.org/our-work/programs/global-health/vaccine-development-and-surveillance

World Health Organization — www.who.int/health-topics/vaccines-and-immunization#tab=tab_1

PATH — www.path.org/ www.path.org/resources/path-2022-annual-report/

unicef — www.unicef.org/innovation/vaccine-microarray-patches-vmaps

BARDA — https://medicalcountermeasures.gov/barda/

wellcome — https://wellcome.org/

iavi Translating science into global health impact — www.iavi.org/our-science/pipeline

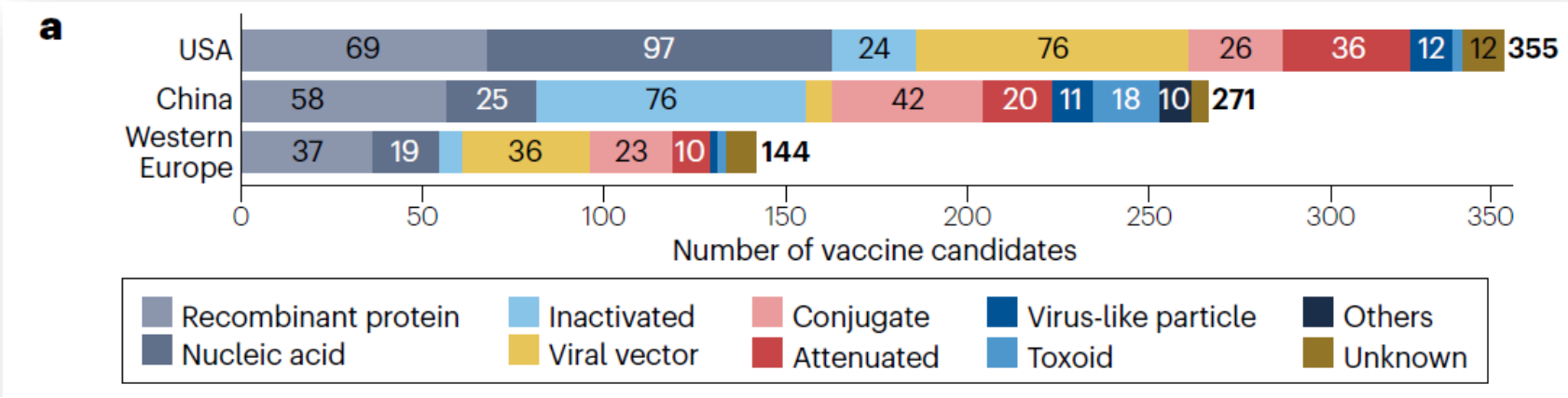
CEPI — https://cepi.net/

Sampling of organizations working toward reducing the burden of infectious diseases worldwide

…and many more!

Fig. 2 | Distribution of vaccine candidates by geographic location and type of developer

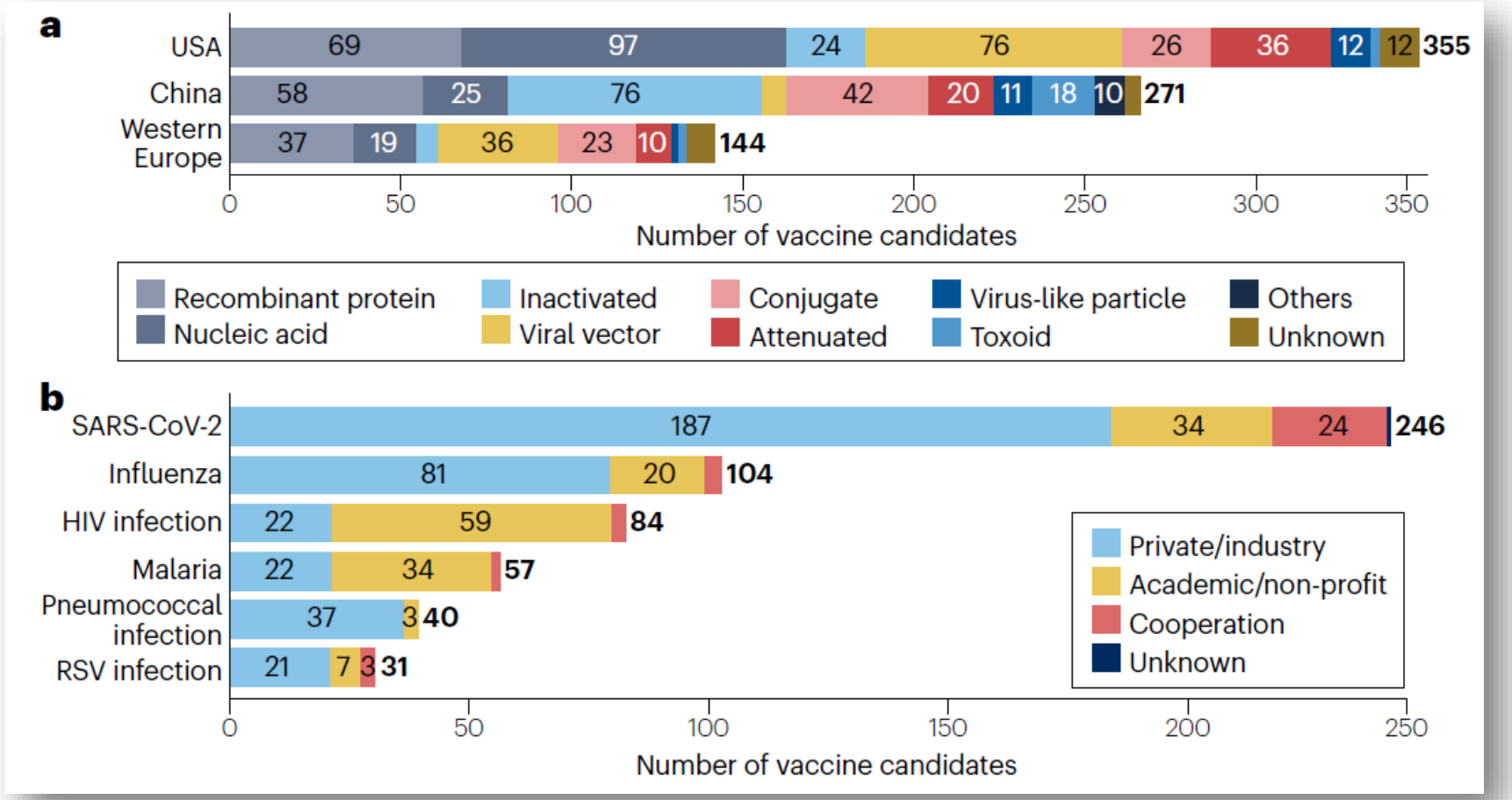
www.nature.com/articles/d41573-023-00119-4



a) Vaccine candidates with developers from the USA, China and western Europe, categorized by technical platform

Fig. 2 | Distribution of vaccine candidates by geographic location and type of developer

www.nature.com/articles/d41573-023-00119-4



a) Vaccine candidates with developers from the USA, China and western Europe, categorized by technical platform

b) Candidates for the top six diseases for vaccine development, by type of developer.

- 68% of candidates being developed independently or collaboratively by private companies/industry
- 25% being developed by academic or other non-profit organizations

Infectious disease targets for vaccines in the pipeline

Pathogen targets for vaccine product development

NEW

Borrelia burgdorferi (Lyme disease)
CMV (specific populations)
HIV

EBV
HSV
Gonorrhea

Zika virus

Norovirus
C. difficile

Group A Strep
Group B Strep

Chikungunya

Shigella
Salmonella paratyphi

IMPROVE on existing

Influenza - Universal
RSV (active and passive immunity)
SARS-CoV-2

Measles
HPV

Tuberculosis
Malaria

Ebola
Salmonella typhi

…and many more in early studies…

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NEW

- ✓ ***Borrelia burgdorferi*** (Lyme disease)
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RSV (active and passive immunity)
SARS-CoV-2

Measles
HPV

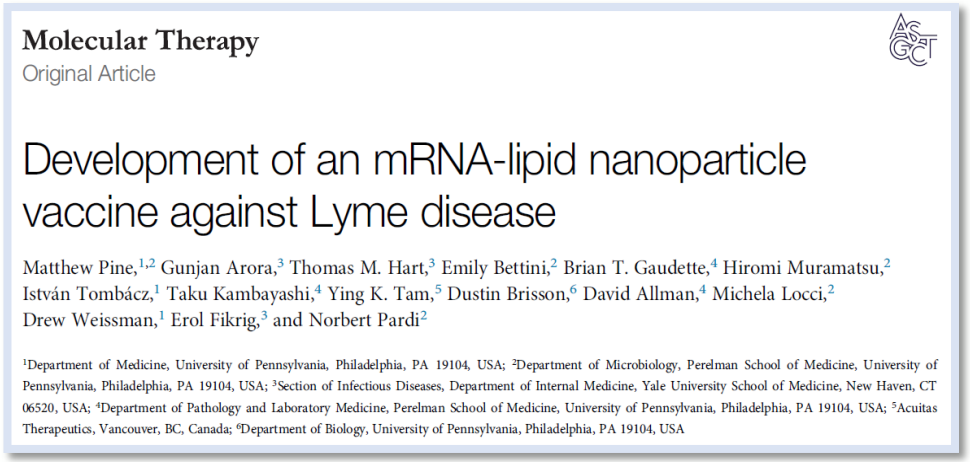
✓ **Tuberculosis**
Malaria

Ebola
Salmonella typhi

…and many more in early studies…

Lyme Disease → *Borrelia burgdorferi*

Penn Medicine



Molecular Therapy
Original Article

Development of an mRNA-lipid nanoparticle vaccine against Lyme disease

Matthew Pine,[1,2] Gunjan Arora,[3] Thomas M. Hart,[3] Emily Bettini,[2] Brian T. Gaudette,[4] Hiromi Muramatsu,[2] István Tombácz,[1] Taku Kambayashi,[4] Ying K. Tam,[5] Dustin Brisson,[6] David Allman,[4] Michela Locci,[2] Drew Weissman,[1] Erol Fikrig,[3] and Norbert Pardi[2]

[1]Department of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA; [2]Department of Microbiology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA; [3]Section of Infectious Diseases, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520, USA; [4]Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104, USA; [5]Acuitas Therapeutics, Vancouver, BC, Canada; [6]Department of Biology, University of Pennsylvania, Philadelphia, PA 19104, USA

Moderna

Pipeline: two novel mRNA vaccine candidates against Borrelia species (Lyme disease)

mRNA-1982

monovalent vaccine targeting prevalent US serotype

mRNA-1975

multivalent, includes 7 RNAs targeting 7 European serotypes

Europe - Phase 1/2 study, 800 subjects
Anticipate results informing immunogenicity in 2024

Pfizer and Valneva partnership

- July 2017: Fast Track designation by US FDA (Valneva)
- April 2020: Collaboration agreement between Valneva and Pfizer to co-develop VLA15 (updated June 2022)

VLA15-221 Phase 2 study showed a strong anamnestic antibody response for all serotypes in pediatric (5 to 11 years of age) and adolescent participants (12 to 17 years of age), as well as in adults (18 to 65 years of age), one month after administration of a booster dose (month 19).

"Safety and tolerability profile of VLA15 after a booster dose was consistent with previous studies as the vaccine candidate was **well-tolerated in all age groups** regardless of the primary vaccination schedule."

"**No vaccine-related serious adverse events** (SAEs) and **no safety concerns** were observed by an independent Data Safety Monitoring Board (DSMB)."

www.pfizer.com/news/announcements/valneva-and-pfizer-report-positive-pediatric-and-adolescent-phase-2-booster

Lyme Disease → *Borrelia burgdorferi*

VLA15 (Pfizer/Valneva) – **Phase III trials**

Investigational multivalent protein subunit vaccine - Targets outer surface protein A (OspA) of *B. burgdorferi*

- OspA: surface protein expressed by *B. burgdorferi* when present in a tick; blocking OspA limits transmission
- Vaccine covers 6 most common OspA serotypes (*B. burgdorferi sensu lato* species prevalent N. America, Europe)
- Alum-adjuvanted formulation; administered intramuscularly

An Efficacy, Safety, Tolerability, Immunogenicity, and Lot-Consistency Clinical Trial of a 6-Valent OspA-Based Lyme Disease Vaccine (VLA15) (VALOR)

ClinicalTrials.gov ID: NCT05477524
Sponsor: Pfizer Last Update Posted: 2023-11-28

https://clinicaltrials.gov/study/NCT05477524

Phase 3 trial
3-dose primary vaccination series at about 0, 2, and 5 to 9 months and then receive a booster dose about 12 months later.

…primary series completed before peak Lyme disease season followed by a booster dose just prior to beginning of second Lyme disease season.

Safety Study of a Vaccine to Help Protect Against Lyme Disease in Healthy Children

ClinicalTrials.gov ID: NCT05634811
Sponsor: Pfizer Last Update Posted: 2023-10-25

Initiated Dec 2022, estimated completion mid-2025

Phase 3, randomized, placebo-controlled, observer-blinded trial to evaluate the safety of a **6-VALENT OspA-BASED LYME DISEASE VACCINE (VLA15)** in healthy children 5 through 17 years of age

Anticipate 2026…

Lyme Disease → *Borrelia burgdorferi*

Pre-exposure antibody prophylaxis
(passive immunity - LymePrep)
to prevent Lyme Disease in endemic regions

MassBiologics at UMass Chan Medical School
www.jci.org/articles/view/144843/pdf

A Phase 1 Study in Healthy Subjects to Evaluate the Safety and Pharmacokinetics of a Human Monoclonal Antibody (2217LS) Against Borrelia Burgdorferi (B. Burgdorferi) Outer Surface Protein A (OspA)

ClinicalTrials.gov ID: NCT04863287
Sponsor: MassBiologics Last Update Posted: 2022-09-16

https://clinicaltrials.gov/study/NCT04863287

Purpose of study

1) Learn about safety and tolerability of subcutaneous (SC) injection of 2217LS when administered to healthy volunteers
2) Find out how much 2217LS is in the blood of healthy volunteers after receiving 2217LS SC

Competition to accelerate development of Lyme disease diagnostics

U.S. Department of Health and Human Services (HHS) and the Steven & Alexandra Cohen Foundation

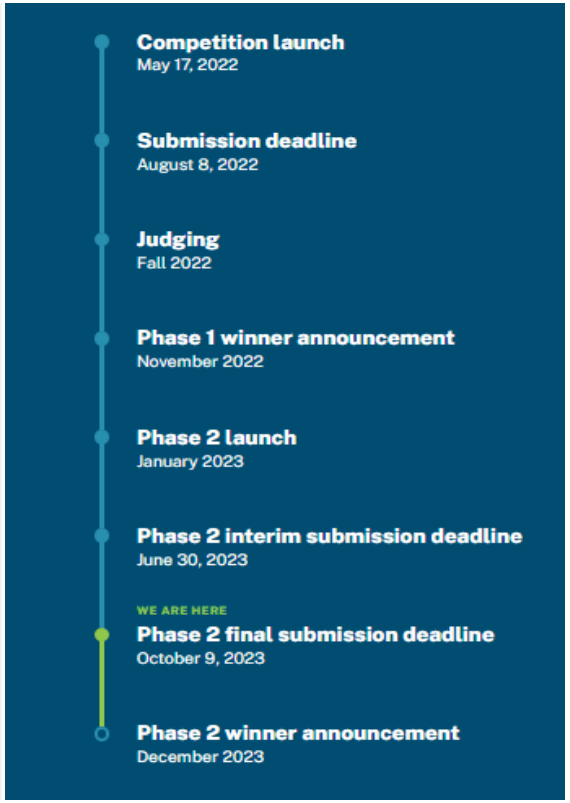
LymeX Diagnostics Prize timeline

Phase 1 was open to all eligible entrants to submit concept papers and plans for development. In Phase 2, 10 teams are participating in a virtual accelerator to help them refine their concepts.

VIEW DETAILED TIMELINE

Ultimate Goal
To nurture development of next-generation diagnostics toward Food and Drug Administration review.

Potential for awarding up to $10 million in prizes across all potential phases
subject to availability of funds



www.lymexdiagnosticsprize.com/

Cytomegalovirus (CMV) Vaccines

CONCLUSIONS

…there are numerous candidate CMV vaccines in development, both those targeted to prevent congenital infection and those targeted to prevent posttransplant infections.

The Journal of Infectious Diseases

SUPPLEMENT ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

The Status of Vaccine Development Against the Human Cytomegalovirus

Stanley A. Plotkin,[1] Dai Wang,[2] Abdel Oualim,[3] Don J. Diamond,[4] Camille N. Kotton,[5] Sally Mossman,[6] Andrea Carfi,[7] David Anderson,[8] and Philip R. Dormitzer[9]

[1]Department of Pediatrics, University of Pennsylvania, Vaxconsult, Doylestown, Pennsylvania, USA, [2]Merck & Co., Kenilworth, New Jersey, USA, [3]Sanofi-Pasteur, Swiftwater, Pennsylvania, USA, [4]City of Hope National Medical Center, Duarte, California, USA, [5]Massachusetts General Hospital, Boston, Massachusetts, USA, [6]GlaxoSmithKline Vaccines, Rockville, Maryland, USA, [7]Moderna Therapeutics, Cambridge, Massachusetts, USA, [8]VBI Vaccines, Cambridge, Massachusetts, USA, [9]Pfizer Vaccines, Pearl River, New York, USA

J Infect Dis. **2020** Mar 5;221(Suppl 1):S113-S122

https://academic.oup.com/jid/article/221/Supplement_1/S113/5781893

…early evidence from Phase II trials that vaccination can prevent acquisition of CMV by seronegative women exposed to CMV in nature, and there is solid evidence that CMV disease in seronegative solid organ recipients and in hematogenous stem cell recipients can be prevented.

There are as yet no Phase III data, but numerous candidate vaccines are moving forward, including several aimed at the goal of preventing congenital CMV disease.

Cytomegalovirus (CMV) → Specific populations

A Phase 3, Randomized, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1647 Cytomegalovirus (CMV) Vaccine in Healthy Participants 16 to 40 Years of Age

ClinicalTrials.gov ID: NCT05085366
Sponsor: ModernaTX, Inc.
Last Update Posted: 2023-11-21

https://clinicaltrials.gov/study/NCT05085366

CMVictory Trial

The main purpose of this study is to evaluate:

- Efficacy of mRNA 1647 vaccine in CMV-seronegative female participants
- Safety and reactogenicity of mRNA-1647 vaccine in all participants

Initiated October 2021, estimated completion mid-2026

"It is exciting that for the first time in the 50 years of CMV vaccine development we have a phase 3 trial underway"

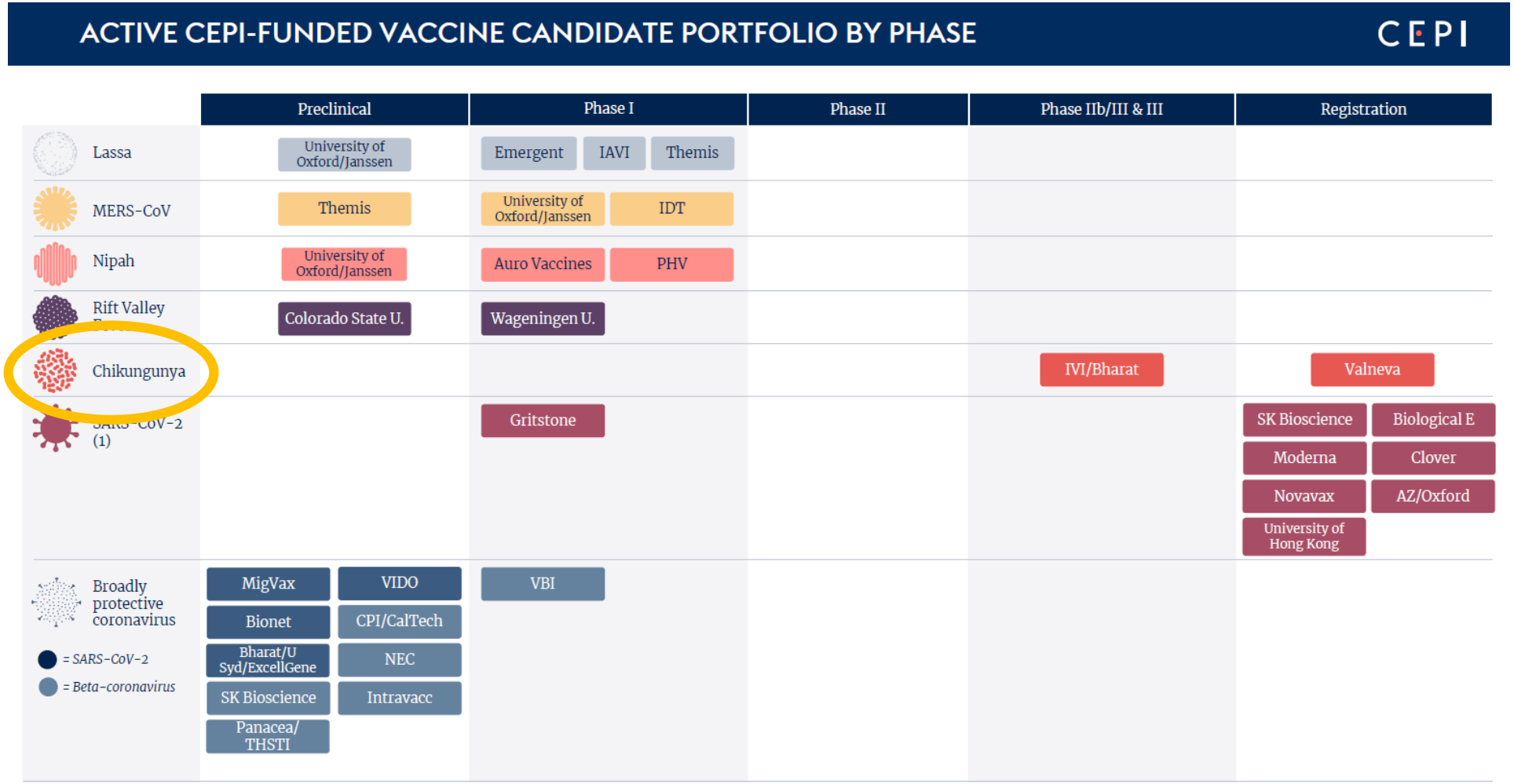
Sallie Permar, MD, PhD
NewYork-Presbyterian/Weill Cornell Medical

in recent interview with
Managed Healthcare Executive

www.managedhealthcareexecutive.com/view/cytomegalovirus-update-for-the-first-time-a-phase-3-vaccine-trial-idweek-2023

CEPI → Coalition for Epidemic Preparedness Innovations - Global

"Innovative global partnership between public, private, philanthropic, and civil society organisations"



(1) CEPI has also funded booster studies of SARS-CoV-2 vaccines developed by Medigen and Vaxxinity

Chikungunya Virus (CHIKV)

www.thelancet.com Vol 401 June 24, 2023

www.thelancet.com/journals/lancet/article/PIIS0140-6736(23)00641-4/fulltext

Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial

Martina Schneider, Marivic Narciso-Abraham, Sandra Hadl, Robert McMahon, Sebastian Toepfer, Ulrike Fuchs, Romana Hochreiter, Annegret Bitzer, Karin Kosulin, Julian Larcher-Senn, Robert Mader, Katrin Dubischar, Oliver Zoihsl, Juan-Carlos Jaramillo, Susanne Eder-Lingelbach, Vera Buerger, Nina Wressnigg

VLA1553 is a live-attenuated vaccine

for active immunization and prevention of disease caused by chikungunya virus

March 2022: Phase 3 data reported in 4,115 adults aged 18 years and above showing a 98.9% seroresponse rate at 28 days with single vaccination

June 2023: Results published in Lancet
The Lancet subsequently published these results in June 2023.

Final lot-to-lot consistency results were published in May 2022, twelve-month persistence data in December 2022, and adolescent data in November 2023.

Follow-up study underway to monitor 5-year immune response data (NCT04838444).

News!

November 2023

VLA1553 received U.S. FDA approval

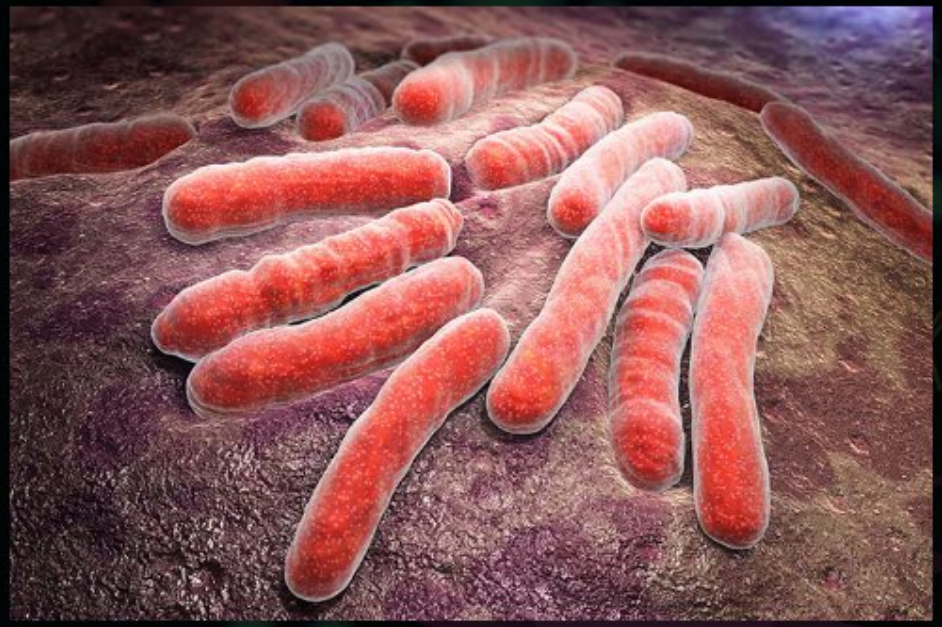
under brand name IXCHIQ® (Valneva)

Indicated for prevention of disease caused by CHIKV in individuals **18 years of age and older who are at increased risk of exposure to CHIKV.**

Continued approval in US is contingent upon verification of clinical benefit in confirmatory studies.

VLA1553 is also under accelerated assessment by the European Medicines Agency (EMA) and a standard regulatory review is underway with Health Canada.

Tuberculosis → no new approved vaccine in 102 years since BCG



Credit: Alexey Kotelnikov / Alamy Stock Photo

Milestone 5 1921

BCG: the first vaccine for tuberculosis

Tuberculosis has been an infectious scourge throughout human history. Working in France, Albert Calmette and Camille Guérin developed their eponymous live attenuated vaccine for tuberculosis (BCG) and used it for the first time to protect at-risk infants. Read More

By Zoltan Fehervari

www.nature.com/immersive/d42859-020-00005-8/index.html

Milestones | 28 September 2020

Nature Milestones in Vaccines

Tuberculosis – Vaccine Development & Challenges

Vaccine 38 (2020) 135–142

Contents lists available at ScienceDirect

Vaccine

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

Review

Preferred product characteristics for therapeutic vaccines to improve tuberculosis treatment outcomes: Key considerations from World Health Organization consultations

Johan Vekemans [a,*], Michael James Brennan [b], Mark Hatherill [c], Lewis Schrager [a], Bernard Fritzell [d], Kathryn Rutkowski [e], Beatrice De Vos [d], Matteo Zignol [a], Georges Thiry [d], Ann M. Ginsberg [e], Barry Walker [d]

[a] Word Health Organization, Geneva, Switzerland
[b] Independent
[c] South African Tuberculosis Vaccine Initiative, University of Cape Town, South Africa
[d] Tuberculosis Vaccine Initiative, Lelystad, the Netherlands
[e] International Aids Vaccine Initiative, NY, USA

vaccines

Vaccines 2023, 11, 1304 MDPI

Review

Next-Generation TB Vaccines: Progress, Challenges, and Prospects

Li Zhuang [1,2], Zhaoyang Ye [2], Linsheng Li [2], Ling Yang [2] and Wenping Gong [1,*]

Tuberculosis 126 (2021) 102040

Contents lists available at ScienceDirect

Tuberculosis

journal homepage: http://www.elsevier.com/locate/tube

The TB vaccine development pathway – An innovative approach to accelerating global TB vaccine development

Danielle Roordink [a,*], Ann Williams [a], Bernard Fritzell [a], Dominick J. Laddy [b], Emmanuelle Gerdil [a], Anne Marie Graffin [a], Dereck Tait [c], Leo van der Pol [a], Ilona van den Brink [a], Marit Holleman [a], Jelle Thole [a], Gerald Voss [a], Maria Lempicki [b], Georges Thiry [a]

[a] TuBerculosis Vaccine Initiative (TBVI), Lelystad, the Netherlands
[b] IAVI, New York, USA
[c] IAVI, Cape Town, South Africa

The TB Vaccine Accelerator Council: harnessing the power of vaccines to end the tuberculosis epidemic

Flickr - UN Photo/ Sophia Paris

Published Online
September 21, 2023
https://doi.org/10.1016/
S1473-3099(23)00589-3

"The council will work to boost the tuberculosis vaccine pipeline and facilitate the licensing and use of safe and effective tuberculosis vaccines, through partnership-based, innovative solutions to close crucial gaps in knowledge and financing."

Tuberculosis Vaccine Goals – one organization

RESEARCH GOALS

Accelerate development of new tools to prevent, diagnose and treat TB by identifying innovative product-development pathways and improving collaboration among actors in product development.

Vaccines

- ✓ Develop a **new TB vaccine by 2025.**
- ✓ Diversify and **broaden the pipeline of next-generation TB vaccine candidates** by expanding research on Mtb immunology and basic mycobacteriology and develop animal models that better reflect human infection and disease.
- ✓ Provide resources and support to **efficiently** move a diverse range of vaccine concepts from the laboratory to the clinic.
- ✓ Significantly **accelerate clinical development of vaccine candidates** and ensure sufficient financing, resources and capacity to advance multiple promising candidates through efficacy trials and licensure without delay.
- ✓ Conduct research on correlates of **vaccine-induced protection** during vaccine efficacy trials to inform vaccine design, expedite clinical trials of future vaccine candidates.
- ✓ Work with countries and affected communities to prepare for **successful licensure and roll-out** of new TB vaccines once licensed.

Stop TB Partnership
Working Group on New TB Vaccines

www.stoptb.org/global-plan-to-end-tb/global-plan-to-end-tb-2023-2030

Tuberculosis

as of September 2023

16 vaccine candidates

TB Vaccine Pipeline

Vaccine candidates under clinical development

There are 16 vaccine candidates in the pipeline as of September 2023, of which 11 are in active trials. The candidates are placed under the phase which corresponds to the most advanced ongoing or completed trial.

Platform

- Mycobacterial - Live attenuated
- Mycobacterial - Inactivated
- Viral vector
- Protein/Adjuvant
- DNA/RNA

Trial staus

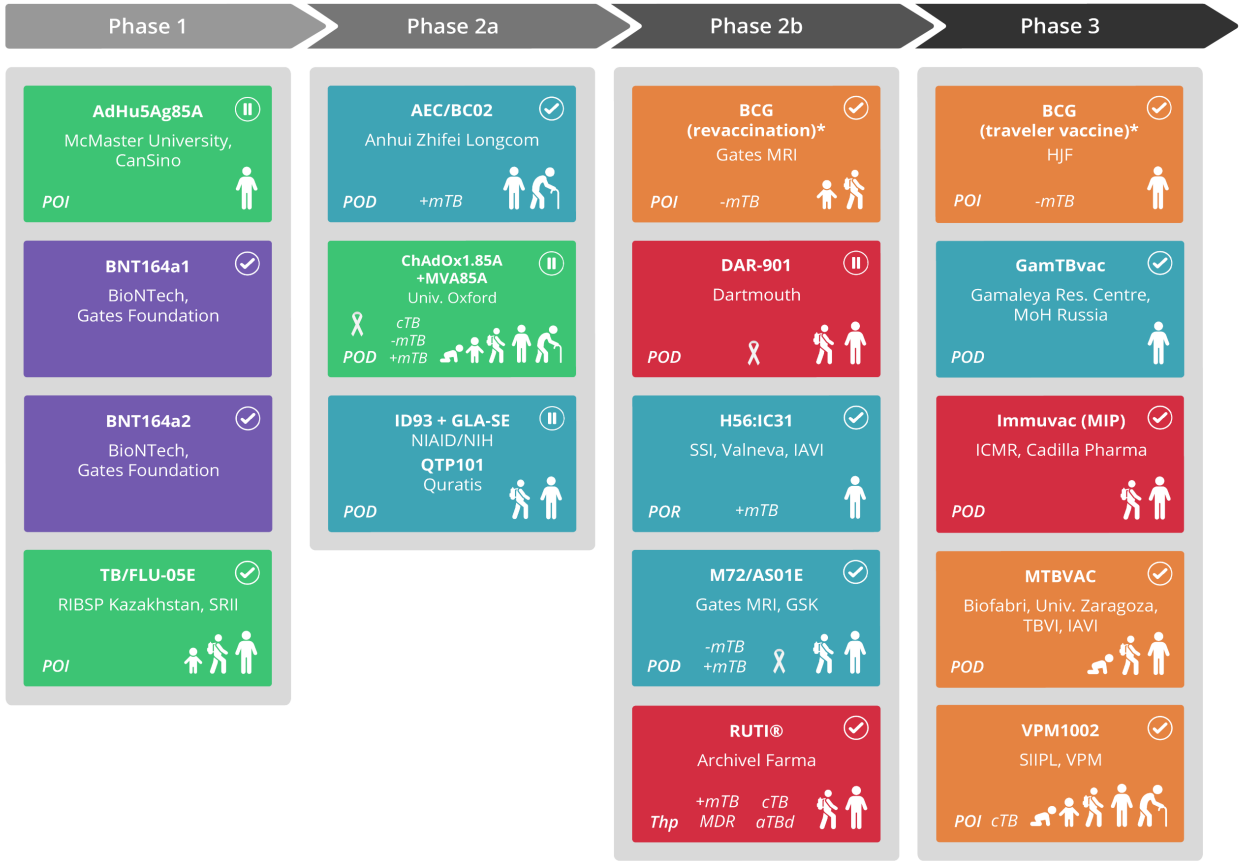
- Active trials
- No active trials

Candidate target population

- Elderly
- Adults
- Adolescents
- Children
- Infants
- People living with HIV
- -mTB — People without mTB infection
- +mTB — People with mTB infection
- aTBd — People with active TB disease
- MDR — People with MDR-TB
- cTB — People cured of active TB

Primary candidate indication

- *POI* — Prevention of Infection
- *POD* — Prevention of Disease
- *POR* — Prevention of Recurrence
- *Thp* — Therapeutic



**BCG appears twice in the pipeline to distinguish between the investigation of its use in BCG-naïve individuals (traveler vaccination) and in individuals who have previously been vaccinated with BCG (revaccination).*

Stop TB Partnership
Working Group on New TB Vaccines

Information reported by vaccine sponsors or found in clinical trial registries or other public sources.

For the full list of completed trials for each candidate, visit www.newtbvaccines.org/tb-vaccine-pipeline/

Last update: 28 September 2023

Tuberculosis

as of September 2023

12 candidates in 14 active trials

TB Vaccine Pipeline

Active clinical trials of TB vaccine candidates

There are 14 active clinical trials across 12 candidates as of September 2023.

Platform

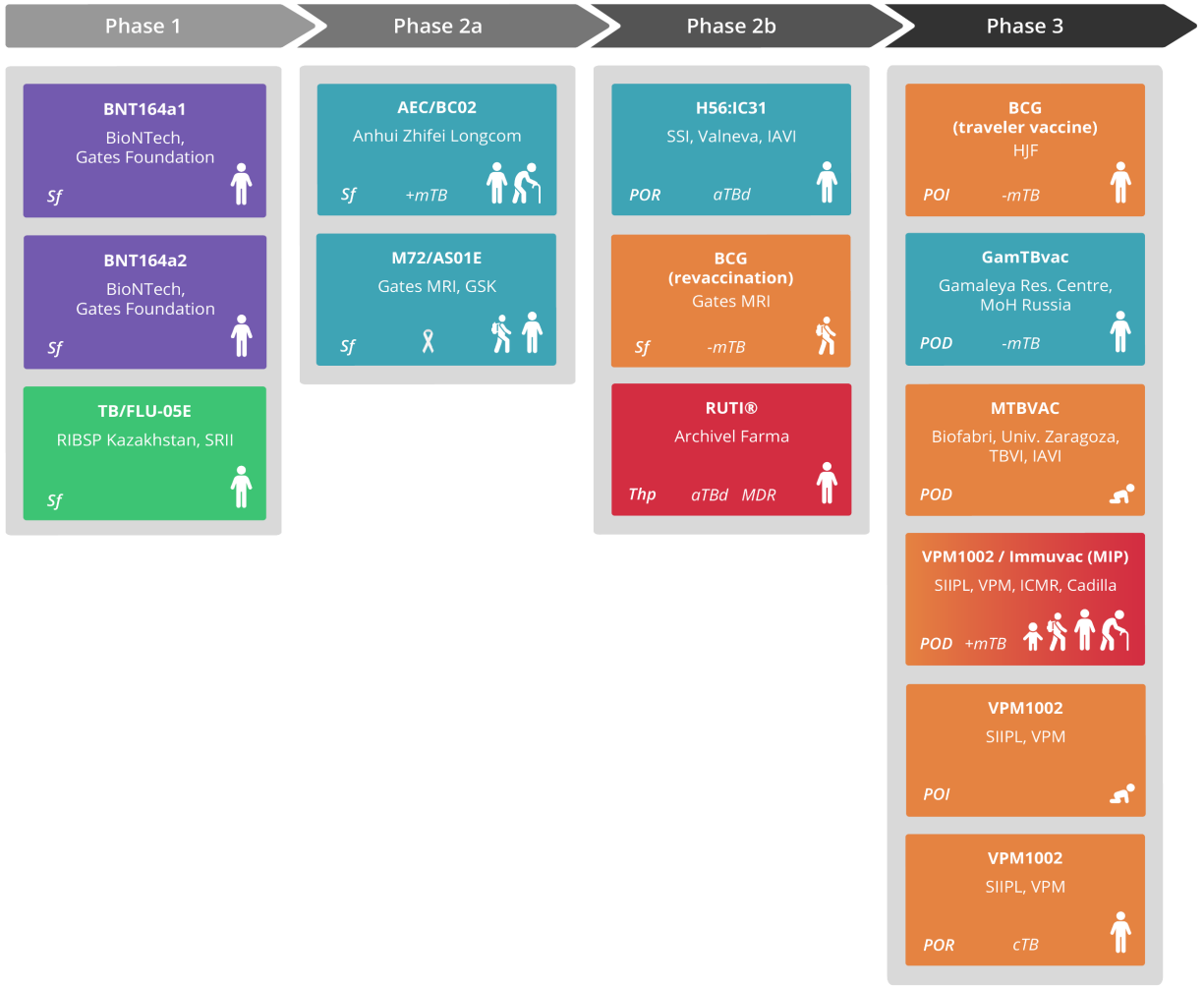
- Mycobacterial - Live attenuated
- Mycobacterial - Inactivated
- Viral vector
- Protein/Adjuvant
- DNA/RNA

Trial target population

- Elderly
- Adults
- Adolescents
- Children
- Infants
- People living with HIV
- -mTB — People without mTB infection
- +mTB — People with mTB infection
- aTBd — People with active TB disease
- MDR — People with MDR-TB
- cTB — People cured of active TB

Primary endpoint

- *Sf* — Safety
- *POI* — Prevention of Infection
- *POD* — Prevention of Disease
- *POR* — Prevention of Recurrence
- *Thp* — Therapeutic



Stop TB Partnership
Working Group on New TB Vaccines

Information reported by vaccine sponsors or found in clinical trial registries or other public sources.

For the full list of completed trials for each candidate, visit www.newtbvaccines.org/tb-vaccine-pipeline/

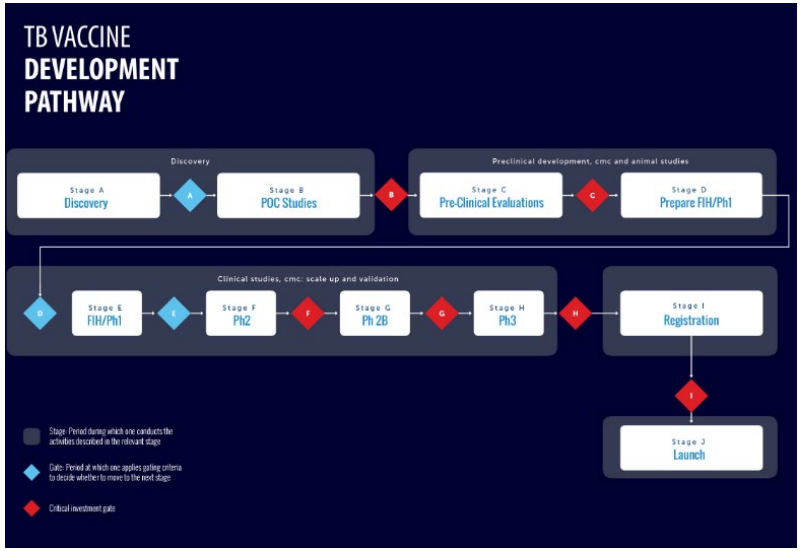
Last update: 28 September 2023

Tuberculosis

From the website:

TBVI is continuously working on supporting the development of new vaccine candidates. Vaccine developers are kindly invited to share an update if needed by contacting TBVI.

www.tbvi.eu/what-we-do/pipeline-of-vaccines/



www.tbvacpathway.org/

Last update October 2022

	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3
Infants & neonates	BCG-ZMP1 University Zurich, TBVI				VPM1002 SII, Max Planck, VPM, TBVI MTBVAC Biofabri, Unizar, TBVI
Adolescents & Adults	H107 SSI, TBVI BCG, ChadOx/MVA PPE15-85A Univ. of Oxford, TBVI CMV-6Ag Aeras, Vir Biotech, OHSU CysVac2/Ad University Sydney, TBVI BCG-ZMP1 University Zurich, TBVI	Ad5 Ag85A McMaster, CanSino ChadOx1.85A MVA 85A Aerosol / IM Univ. of Oxford, TBVI TB/Flu04L RIBSP	MTBVAC Biofabri TBVI UNIZAR IAVI ID93/GLA-SE (QTP101) Quratis AEC/BC02 Anhui Zhifei Longcom	M72 + ASO1 GSK, GMRI DAR-901 Dartmouth University, Aeras H56:IC31 SSI, Valneva, Aeras BCG Revaccination Gates MRI	VPM1002 SII, Max Planck, VPM MIP Cadila Pharma GamTBVac MoH Russia
Therapeutic	MVA Multiphasic vac. Transgene H107 SSI	ID93/GLA-SE ACTG, HVTN H56:IC31 SSI, Valneva TB/Flu01L RIBSP	RUTI Archivel Pharma	Ruti Archivel Pharma	VPM1002 SII, Max Planck, VPM

Live · Wholecell · Subunit · Vector · TBVI involved

TBVI TuBerculosis Vaccine Initiative

Shigella

Herrera CM, et al. **From Kiyoshi Shiga to Present-Day Shigella Vaccines: A Historical Narrative Review**. Vaccines. 2022; 10(5):645

www.mdpi.com/2076-393X/10/5/645

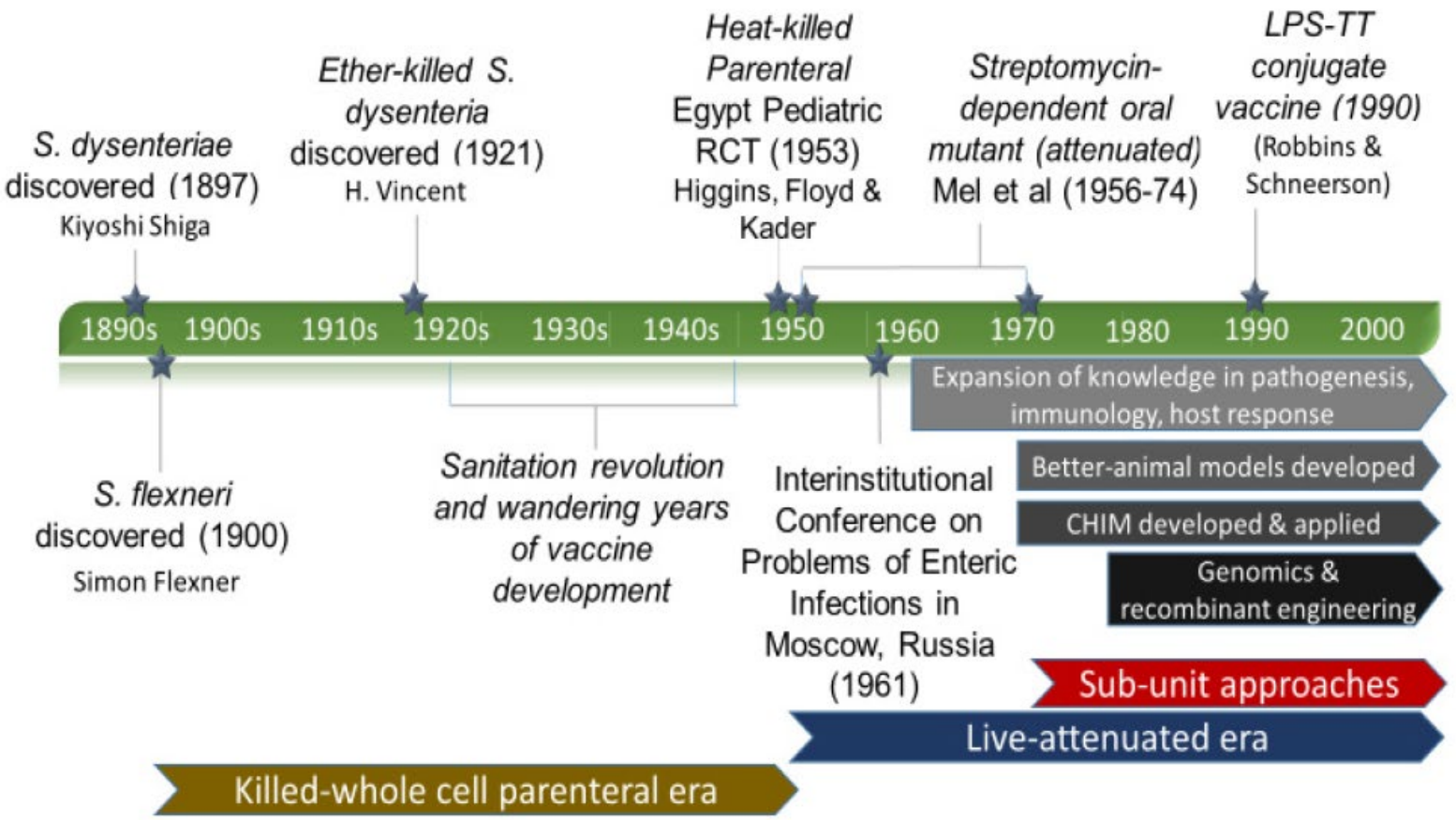


Figure 2. Shigella Vaccine Development History—major achievements and influences (LPS-lipopolysaccharide, TT-tetanus toxoid).

Nearly 100 years later…

Several promising candidates:

- ✓ **O-antigen conjugate vaccines are most advanced candidates**
- ✓ **Live attenuated and subunit vaccines are also in clinical trials**

Shigella → Innovation in disease mitigation

Novel Treatment…Not a vaccine…

First-in-human Phase 1/2a study – to assess clinical safety and efficacy of ShigActive™ in healthy adults with experimental Shigella challenge

A Phase 1/2a Double-Blind, Randomized, Placebo-Controlled Trial to Assess the Safety and Efficacy of Oral Administration of the Bacteriophage Preparation, ShigActive™, in a Human Experimental Model of Shigellosis With Shigella Flexneri 2a Strain

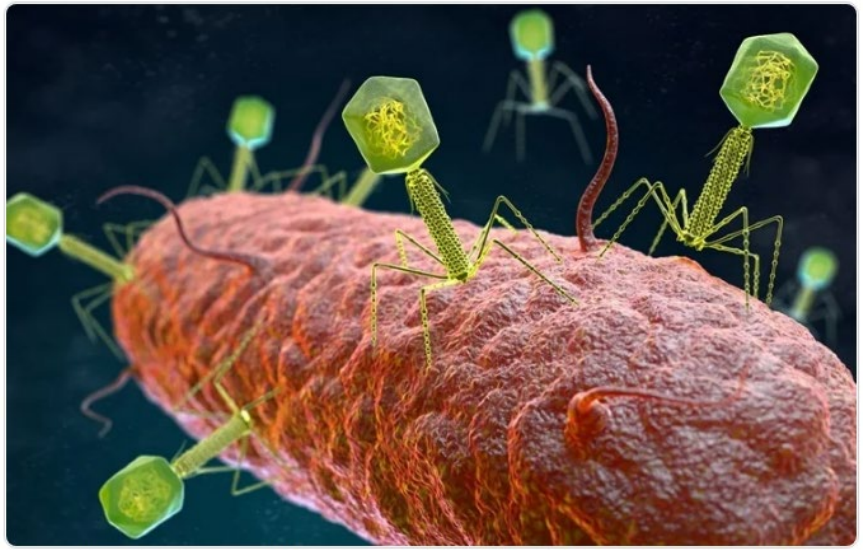
ClinicalTrials.gov ID: NCT05182749
Sponsor: Intralytix, Inc. Last Update Posted: 2023-10-10
https://clinicaltrials.gov/study/NCT05182749

Detailed Description

Purpose: determine if ShigActive is safe and effective in healthy adults in a continuous Phase 1/2a trial

- **Phase 1:** assess the safety of ShigActive in healthy adults
- **Phase 2a:** evaluate the safety and efficacy of ShigActive in healthy adults after a challenge with Shigella

Initiated Feb 2023, estimated completion mid-2025



Study: Phage therapy: From biological mechanisms to future directions. Image Credit: Tatiana Shepeleva/Shutterstock

Verbiage copied from study description:

ShigActive is a collection of bacteriophages. *Bacteriophages (or phages) are viruses that infect only bacteria.*

The phages in ShigActive infect a specific type of bacteria called Shigella, which is the causative agent of shigellosis or dysentery.

ShigActive is intended to ***significantly reduce or eliminate Shigella levels in the human gastrointestinal tract****, which in turn, is anticipated to reduce the incidence and/or severity of shigellosis.*

Influenza → Search for the elusive *universal vaccine*

Influenza Vaccines Research and Development (R&D) Roadmap (IVR)

Created to promote influenza vaccine R&D, through extensive international stakeholder engagement process

Vaccine 39 (2021) 6573–6584

Contents lists available at ScienceDirect

Vaccine

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

Review

A Research and Development (R&D) roadmap for influenza vaccines: Looking toward the future

Kristine A. Moore [a,b,*], Julia T. Ostrowsky [a], Alison M. Kraigsley [a], Angela J. Mehr [a], Joseph S. Bresee [c], Martin H. Friede [d], Bruce G. Gellin [e], Josephine P. Golding [f], Peter J. Hart [f], Ann Moen [d], Charlotte L. Weller [f], Michael T. Osterholm [a], The Influenza Vaccines R&D Roadmap Taskforce William Ampofo [g], Wendy Barclay [h], Marco Cavaleri [i], Cheryl Cohen [j], Benjamin Cowling [k], Rebecca Cox [l], Ian Gust [m], Bruce Innis [n], Gagandeep Kang [o], Jacqueline Katz [p], Florian Krammer [q], Punnee Pitisuttithum [r], Diane Post [s], Larisa Rudenko [t], Marilda Siqueira [u], Jerry Weir [v]

The roadmap covers a 10-year timeframe and is organized into six sections:

1) Virology
2) Immunology
3) Vaccinology for seasonal influenza vaccines
4) Vaccinology for universal influenza vaccines
5) Animal and human influenza virus infection models
6) Policy, finance, and regulation

www.sciencedirect.com/science/article/pii/S0264410X21010288

✓113 specific R&D Milestones

✓ 37 designated “high priority”

Influenza → Defining "*universal influenza vaccine*"

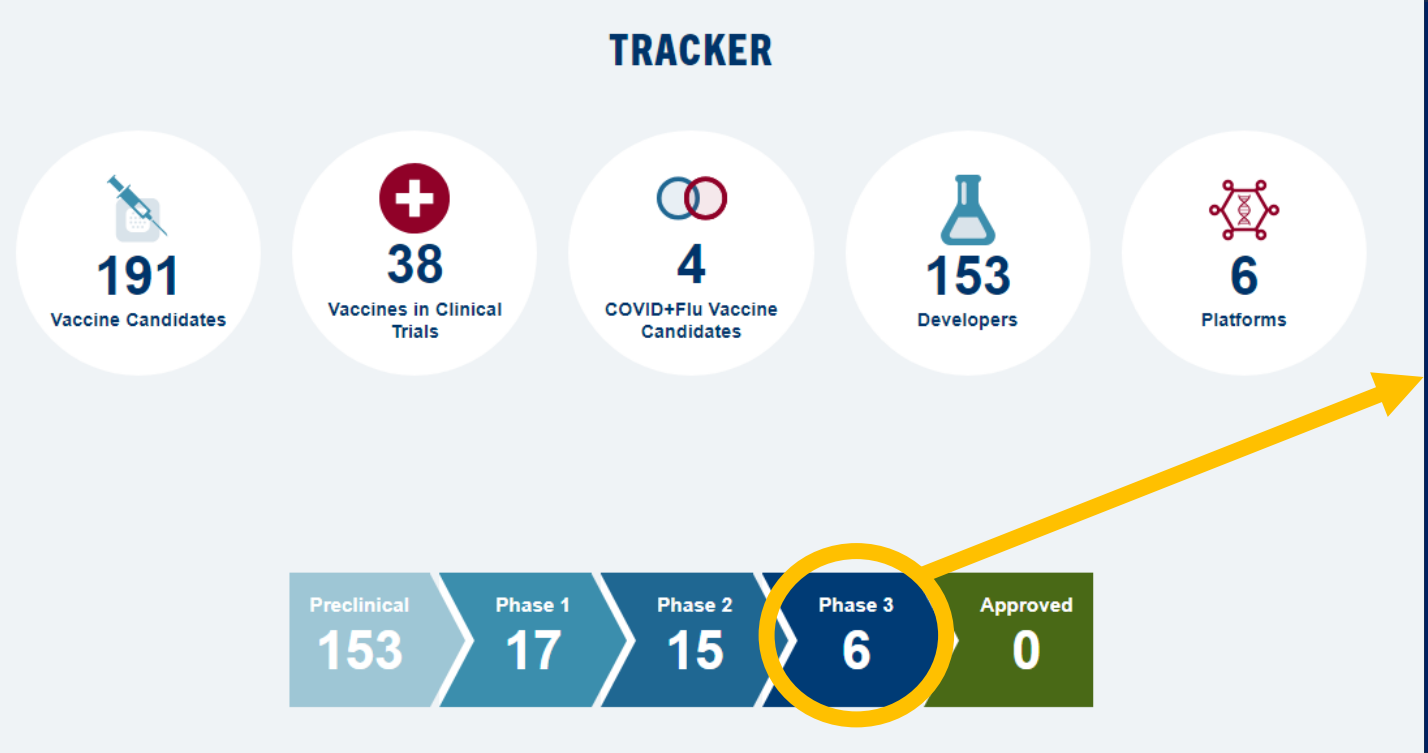
Table 2
Universal Influenza Vaccines: Definitions and Key Features.

www.sciencedirect.com/science/article/pii/S0264410X21010288

Source	Definitions	Target viruses	Duration of protection	Target population
Bill & Melinda Gates Foundation Grand Challenges Initiative [15]	• *Universal influenza vaccines*: "protection from morbidity and mortality caused by all subtypes of circulating and emerging (drifted and shifted) influenza A subtype viruses and influenza B lineage viruses for at least 3–5 years."	All influenza A viruses and influenza B viruses	Minimum of 3–5 years	All age groups, especially in developing countries
European Commission European Union–India Collaboration for Next Generation Influenza Vaccines [14]	• *Next-generation influenza vaccines*: improved efficacy and safety; improved duration of immunity; reactivity against an increased breadth of influenza strains and/or from the outset of a large-scale influenza pandemic; suitable for different populations and LMICs.	Increased breadth of influenza strains	Improved duration of immunity	Different populations and LMICs
Global Funders Consortium for Universal Influenza Vaccine Development [26]	• *Universal influenza vaccine*: high efficacy; induces immunity to a broad array of influenza A viruses (and perhaps influenza B viruses); prevents severe disease; confers more durable immunity than current vaccines; prevents seasonal and pandemic influenza; cost-effective for low- and high-resource settings.	Influenza A viruses and perhaps influenza B viruses	More durable than current influenza vaccines	All
National Institute of Allergy & Infectious Diseases A Universal Influenza Vaccine: The Strategic Plan for the NIAID [16]	• *Universal influenza vaccine*: goal of at least 75% effectiveness against symptomatic influenza virus infection; protects against Groups 1 and Group 2 influenza A viruses (secondary target, influenza B viruses); durable protection for at least 1 year and preferably through multiple seasons; suitable for all age groups.	Group 1 and Group 2 influenza A viruses	Durable protection for at least 1 year	All age groups
Sabin-Aspen Vaccine Science & Policy Group Accelerating the Development of Universal Influenza Vaccine [25]	• *Universal influenza vaccine*: safe and highly effective in all age groups, against any strain; confers lifelong immunity.	All influenza viruses	Lifelong	All age groups
World Health Organization Preferred Product Characteristics for Next-Generation Influenza Vaccines [8]	• *Universal-type influenza A vaccines:* protection against severe influenza A virus illness for at least 5 years; suitable for high-risk groups in LMICs.	Influenza A viruses	At least 5 years	High-risk groups in LMICs

Abbreviations: LMICs, low- and middle-income countries; NIAID, US National Institute of Allergy and Infectious Diseases.

Influenza → Search for the elusive *universal vaccine*



3 Nucleic acid-based
Moderna (2)
Pfizer/BioNTech (1)

1 Non-VLP nanoparticles
Novovax/Emergent BioSolutions (1)

1 Recombinant protein
BiondVax Pharmaceuticals (1)

1 Virus-like particles (VLP)
Medicago (1)

Phase 3 trials

the IVR initiative
INFLUENZA VACCINES ROADMAP

https://ivr.cidrap.umn.edu/universal-influenza-vaccine-technology-landscape

Pathogen targets for vaccine product development

NEW

- ✓ ***Borrelia burgdorferi*** (Lyme disease)
- ✓ **CMV** (specific populations)

HIV

EBV
HSV
Gonorrhea

Zika virus

Norovirus
C. difficile

Group A Strep
Group B Strep

✓ **Chikungunya**

✓ **Shigella**
Salmonella paratyphi

IMPROVE on existing

- ✓ **Influenza - Universal**

RSV (active and passive immunity)
SARS-CoV-2

Measles
HPV

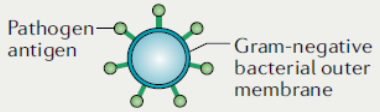
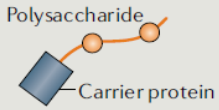
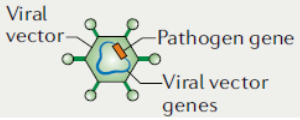
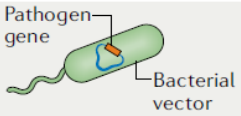
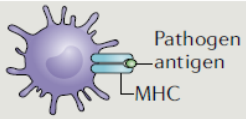
✓ **Tuberculosis**
Malaria

Ebola
Salmonella typhi

…and many more in early studies…

Mechanisms of immune modulation that guide vaccine development

Types of Vaccines

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		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	–

Currently available vaccine types

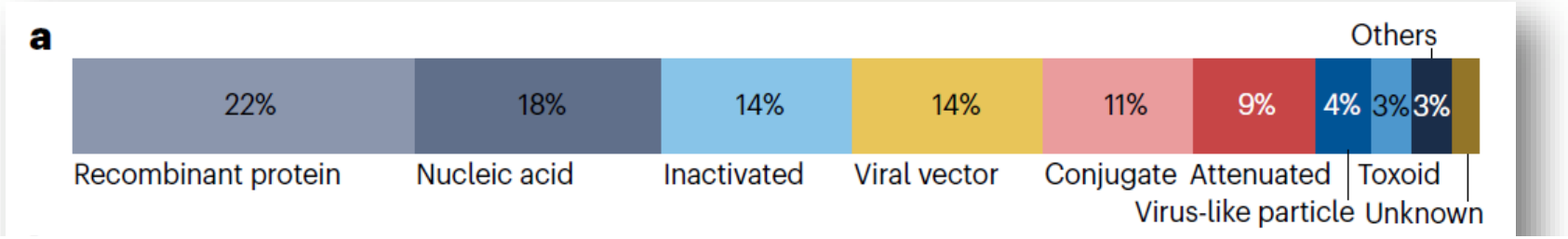
- ❑ **Live attenuated**
- ❑ **Killed/Inactivated (whole organism)**
- ❑ **Toxoid**
- ❑ **Subunit** (Purified protein, recombinant protein, polysaccharide, peptide)
- ❑ **Virus-like particle (VLP)**
- ❑ **Outer membrane vesicle**
- ❑ **Protein-polysaccharide conjugate**
- ❑ **Viral vectored** *(Ebola)*
- ❑ **Nucleic acid vaccine** *(SARS-CoV-2)*

Fig. 2 | Different types of vaccine. Schematic representation of different types of vaccine against pathogens; the text indicates against which pathogens certain vaccines are licensed and when each type of vaccine was first introduced.
BCG, Mycobacterium bovis bacillus Calmette–Guérin.

A guide to vaccinology: from basic principles to new developments
Andrew J. Pollard, Else M. Bijker1
NATURE REVIEWS | IMMUNOLOGY VOLUME 21 | FEBRUARY 2021

Fig. 1 | Landscape of vaccine candidates by technology platform, R&D phase and disease

www.nature.com/articles/d41573-023-00119-4

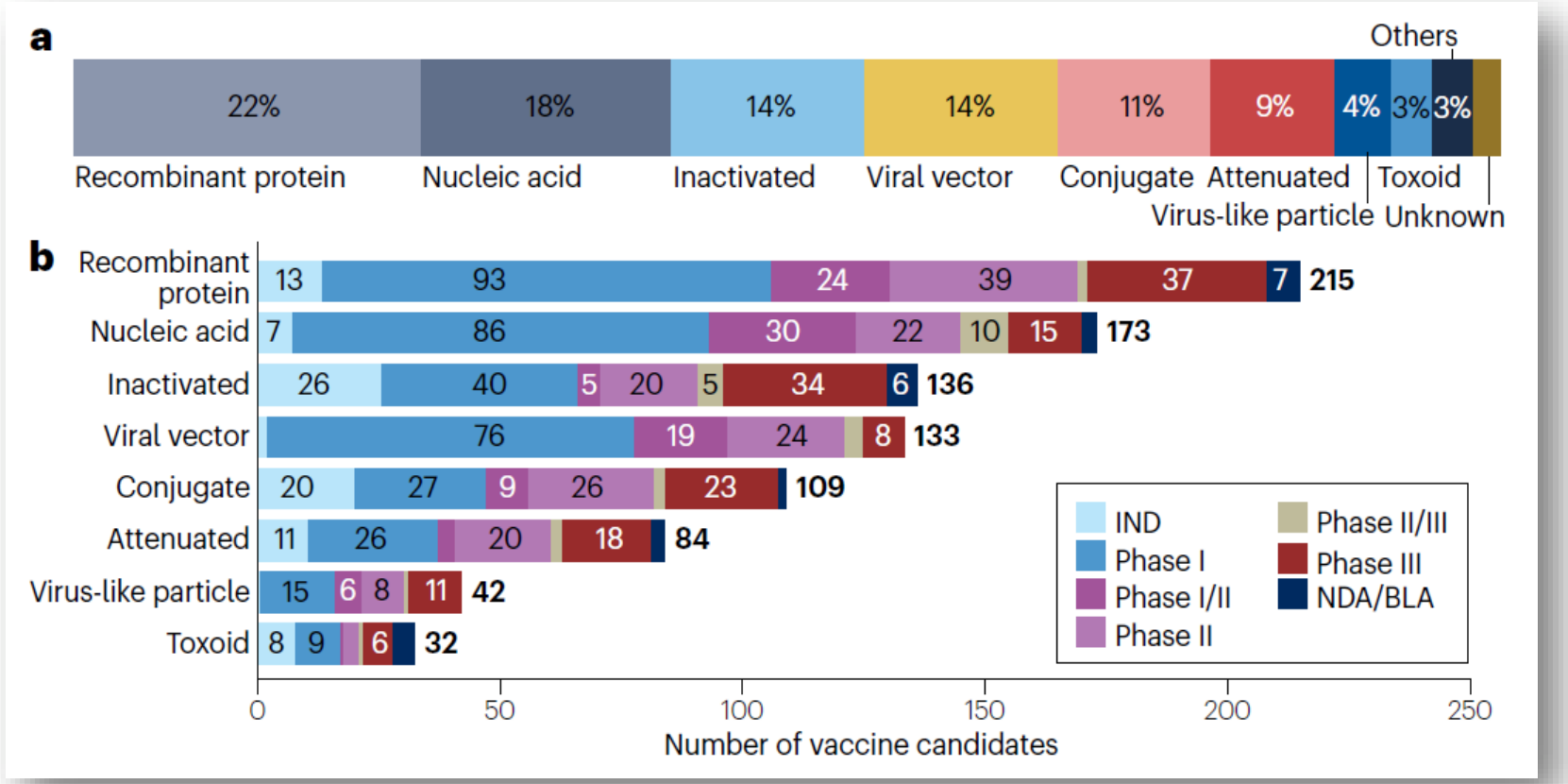


a) The **966 vaccine candidates were classified into the categories shown based on the underlying technology platforms**.

Products with inadequate information for classification were included in an ‘Unknown’ group, and those not fitting into the main groups were included in an ‘Others’ group.

Fig. 1 | Landscape of vaccine candidates by technology platform, R&D phase and disease

www.nature.com/articles/d41573-023-00119-4



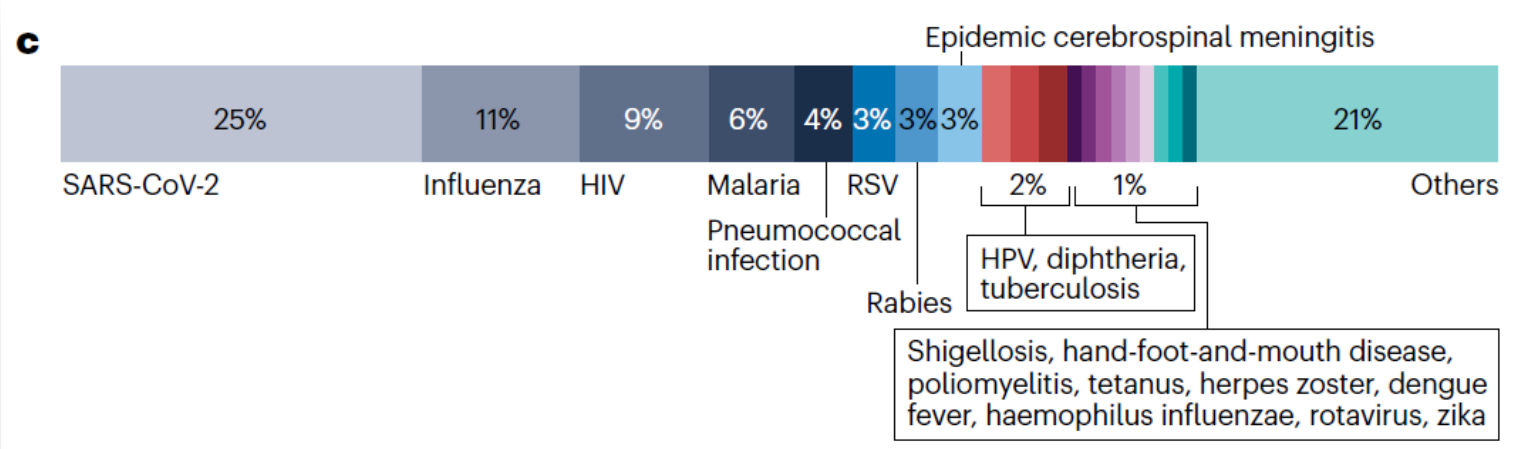
a) The **966 vaccine candidates were classified into the categories shown based on the underlying technology platforms**.

Products with inadequate information for classification were included in an 'Unknown' group, and those not fitting into the main groups were included in an 'Others' group.

b) All candidates excluding 'Unknown' and 'Others' are shown in the bar chart, classified by R&D phase.

Fig. 1 | Landscape of vaccine candidates by technology platform, R&D phase and disease

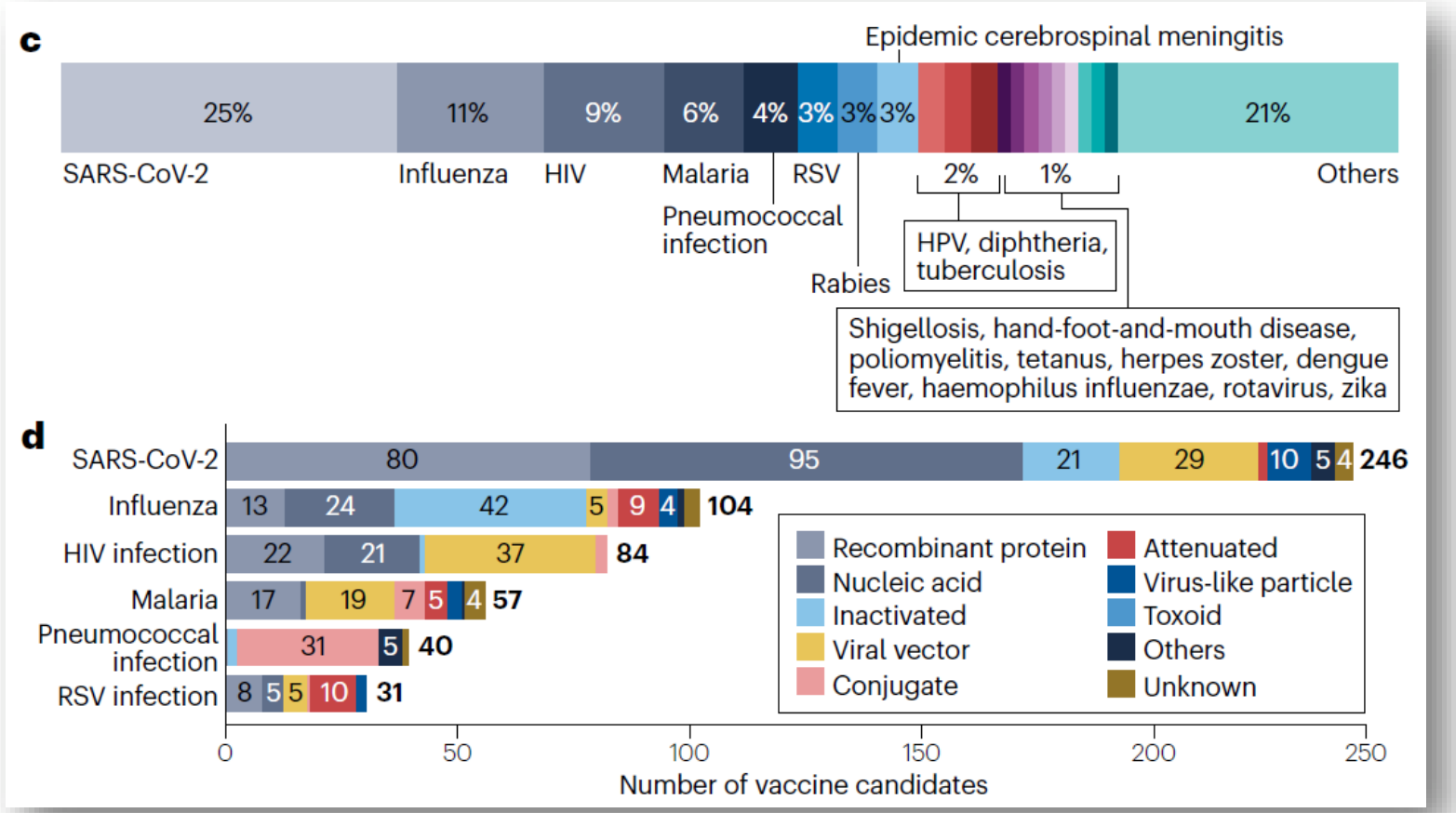
www.nature.com/articles/d41573-023-00119-4



c) **Proportion of vaccine candidates against different diseases.** Diseases with less than ten candidates were included in the 'Others' group.

Fig. 1 | Landscape of vaccine candidates by technology platform, R&D phase and disease

www.nature.com/articles/d41573-023-00119-4



c) **Proportion of vaccine candidates against different diseases.** Diseases with less than ten candidates were included in the 'Others' group.

d) **Candidates for the top six diseases for vaccine development**, by technology platform.

Future potential of mRNA vaccines

Signal Transduction and Targeted Therapy

www.nature.com/sigtrans

REVIEW ARTICLE OPEN

mRNA vaccines in disease prevention and treatment

Gang Zhang[1,2,3,4,5], Tianyu Tang[1,2,3,4,5], Yinfeng Chen[1,2,3,4,5], Xing Huang[1,2,3,4,5]✉ and Tingbo Liang[1,2,3,4,5]✉

mRNA vaccines have emerged as highly effective strategies in the prophylaxis and treatment of diseases, thanks largely although not totally to their extraordinary performance in recent years against the worldwide plague COVID-19. The huge superiority of mRNA vaccines regarding their efficacy, safety, and large-scale manufacture encourages pharmaceutical industries and biotechnology companies to expand their application to a diverse array of diseases, despite the nonnegligible problems in design, fabrication, and mode of administration. This review delves into the technical underpinnings of mRNA vaccines, covering mRNA design, synthesis, delivery, and adjuvant technologies. Moreover, this review presents a systematic retrospective analysis in a logical and well-organized manner, shedding light on representative mRNA vaccines employed in various diseases. The scope extends across infectious diseases, cancers, immunological diseases, tissue damages, and rare diseases, showcasing the versatility and potential of mRNA vaccines in diverse therapeutic areas. Furthermore, this review engages in a prospective discussion regarding the current challenge and potential direction for the advancement and utilization of mRNA vaccines. Overall, this comprehensive review serves as a valuable resource for researchers, clinicians, and industry professionals, providing a comprehensive understanding of the technical aspects, historical context, and future prospects of mRNA vaccines in the fight against various diseases.

Signal Transduction and Targeted Therapy (2023)8:365 ; https://doi.org/10.1038/s41392-023-01579-1

www.nature.com/articles/s41392-023-01579-1

Future potential of mRNA vaccines

Major mRNA vaccine trial results expected in 2023

MRNA vaccine	Indication	Event	Trial size
Moderna's mRNA-1010	Seasonal influenza	Phase III results expected Q1	6,102 subjects
Pfizer's modRNA vaccine	Seasonal influenza	Phase III results expected 2023	36,200 subjects
Roche's/BioNTech's RO7198457	Advanced melanoma	Phase II results expected H1	131 subjects
BioNTech's BNT-163	Herpes lesions	Phase I results expected H2	108 subjects

Source: GlobalData

www.clinicaltrialsarena.com/features/mrna-vaccine-trials-to-watch/?cf-view

Future potential of mRNA vaccines

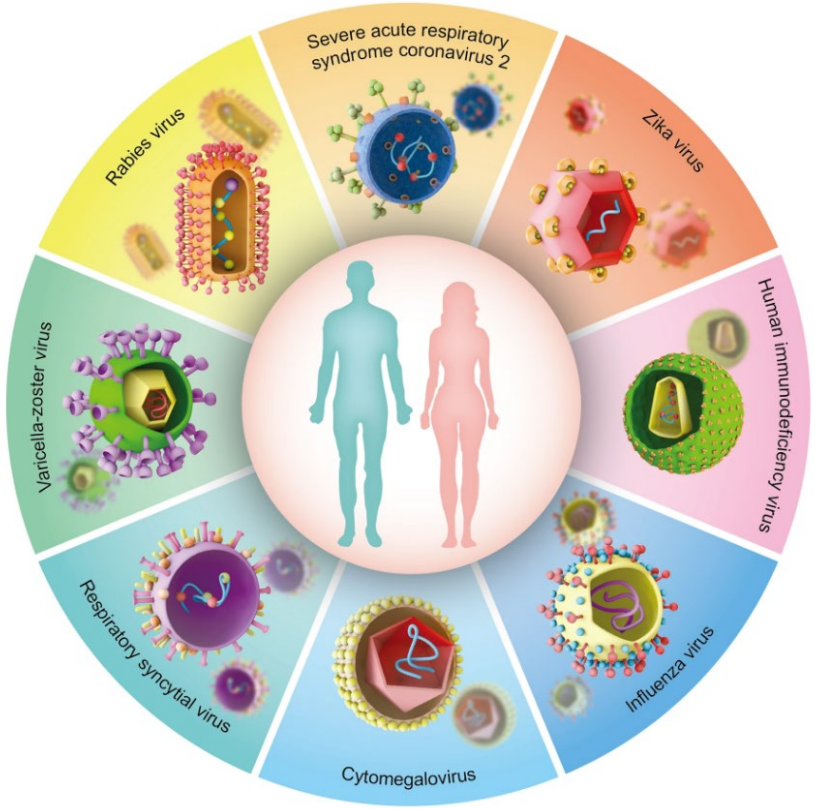


Fig. 3 Landscape of mRNA vaccines in infectious diseases
mRNA vaccines have been developed against multiple infectious diseases to date, including severe acute respiratory syndrome coronavirus 2, zika virus, human immunodeficiency virus, influenza virus, cytomegalovirus, respiratory syncytial virus, varicella-zoster virus, and rabies virus.

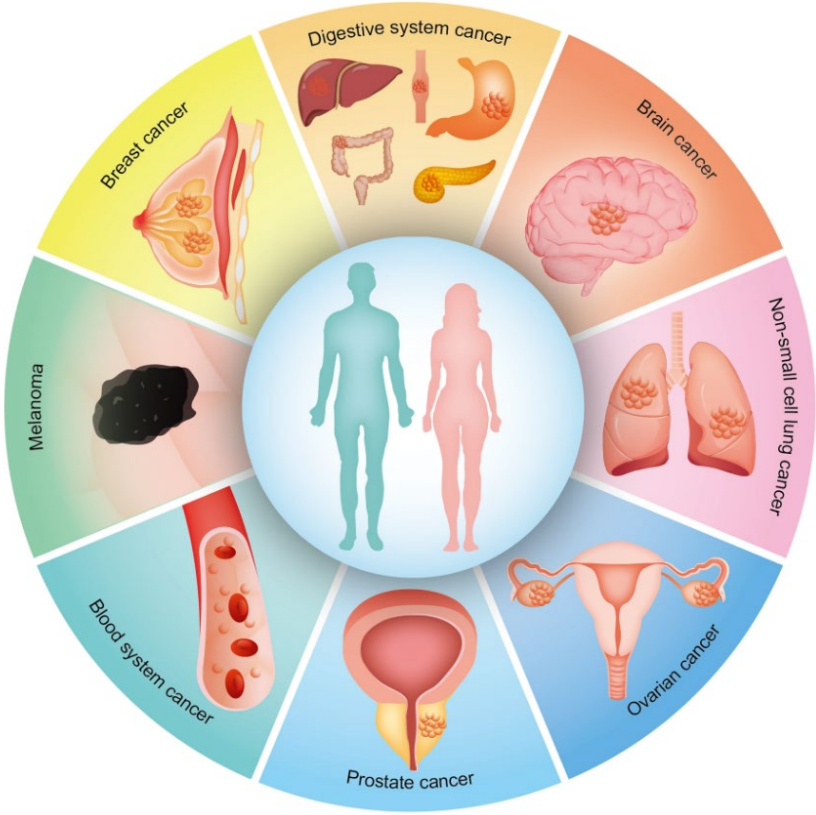


Fig. 4 Landscape of mRNA vaccines in cancers
mRNA vaccines have been developed against multiple cancers to date, including melanoma, brain cancer, non-small cell lung cancer, ovarian cancer, prostate cancer, blood system cancer, digestive system cancer, and breast cancer.

Zhang, G; Tang, T; Chen, Y. et al. **mRNA vaccines in disease prevention and treatment.** *Sig Transduct Target Ther.* **2023**; 8: 365. www.nature.com/articles/s41392-023-01579-1

Research efforts in novel vaccine delivery methods

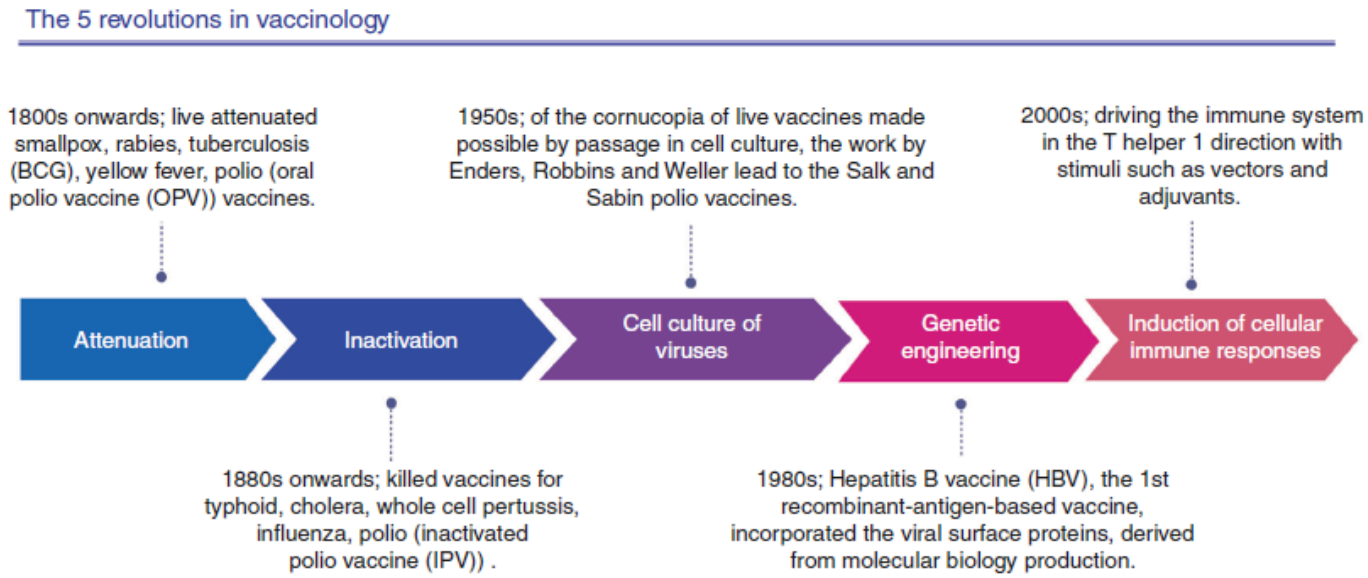
Vaccine Platforms & Delivery Methods

REVIEW ARTICLE **OPEN**

The sixth revolution in pediatric vaccinology: immunoengineering and delivery systems

Dheeraj Soni[1,2], Sharan Bobbala[3], Sophia Li[3], Evan A. Scott[3] and David J. Dowling[1,2]

Pediatric Research (2021) 89:1364–1372 www.nature.com/articles/s41390-020-01112-y



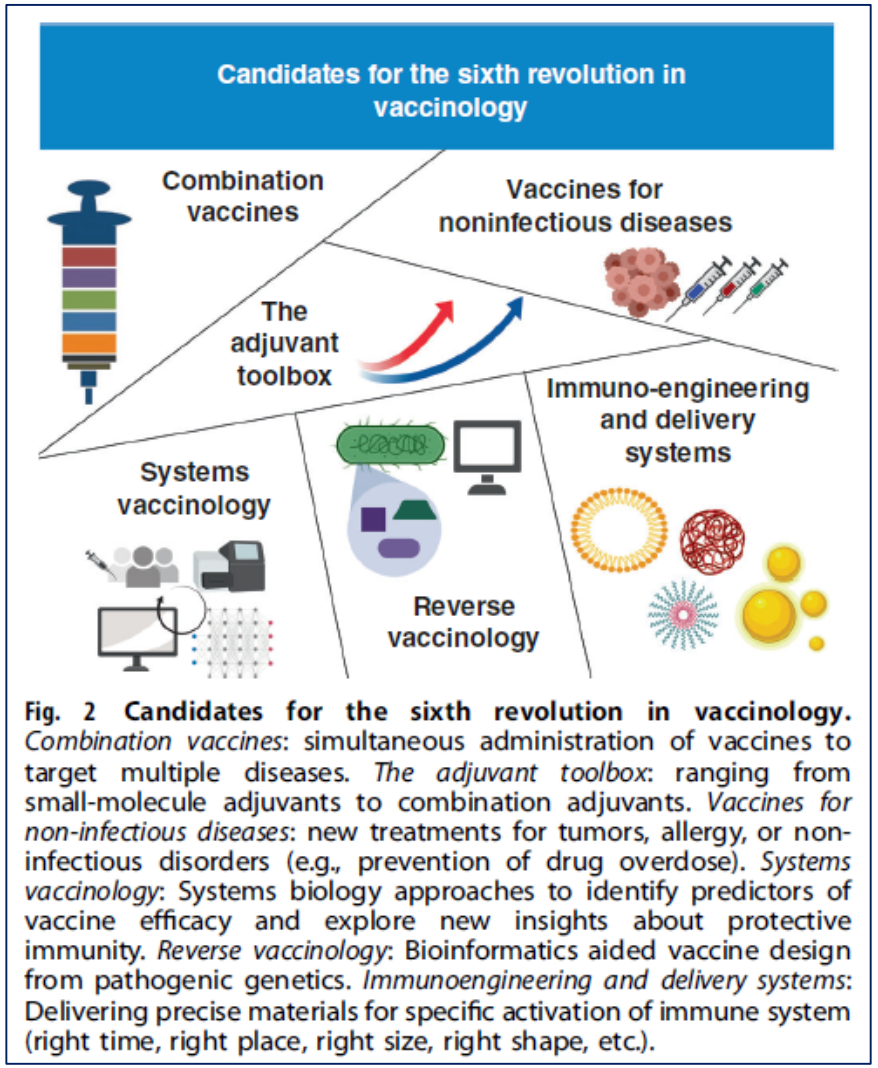


Fig. 2 Candidates for the sixth revolution in vaccinology. *Combination vaccines*: simultaneous administration of vaccines to target multiple diseases. *The adjuvant toolbox*: ranging from small-molecule adjuvants to combination adjuvants. *Vaccines for non-infectious diseases*: new treatments for tumors, allergy, or non-infectious disorders (e.g., prevention of drug overdose). *Systems vaccinology*: Systems biology approaches to identify predictors of vaccine efficacy and explore new insights about protective immunity. *Reverse vaccinology*: Bioinformatics aided vaccine design from pathogenic genetics. *Immunoengineering and delivery systems*: Delivering precise materials for specific activation of immune system (right time, right place, right size, right shape, etc.).

Vaccine Delivery Methods

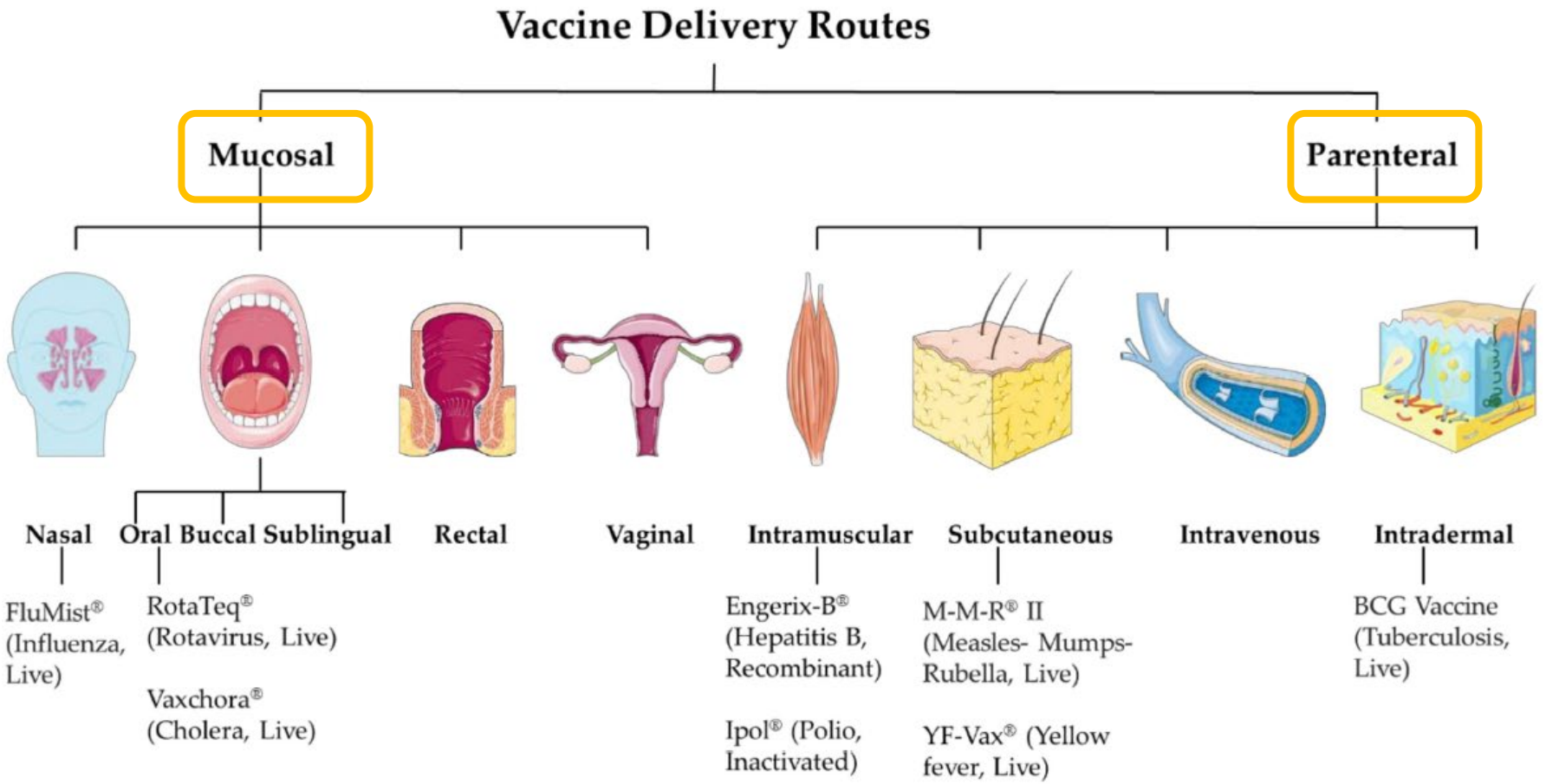


Figure 1. Vaccine delivery routes.

Menon I, Bagwe P, et al. **Microneedles: A New Generation Vaccine Delivery System.** Micromachines. 2021; 12(4):435 www.mdpi.com/2072-666X/12/4/435

Microarray Patches (MAPs)

EXPERT REVIEW OF VACCINES
2023, VOL. 22, NO. 1, 937–955
https://doi.org/10.1080/14760584.2023.2270598

Taylor & Francis
Taylor & Francis Group

REVIEW

OPEN ACCESS Check for updates

Microarray patches: scratching the surface of vaccine delivery

Jovin J. Y. Choo[a], Christopher L. D. McMillan[a,b], Paul R. Young[a,b] and David A. Muller[a,b]

[a]School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, QLD, Australia; [b]Australian Infectious Diseases Research Centre, School of Chemistry and Molecular Biosciences, The University of Queensland, Brisbane, QLD, Australia

www.tandfonline.com/doi/epdf/10.1080/14760584.2023.2270598?needAccess=true

"…highlights the significant potential of MAPs for vaccine delivery and underscores their versatility, safety, and potential for large-scale implementation.

The development and refinement of **MAP-based vaccination** approaches have the **potential to transform the field of immunization,** overcoming several barriers associated with traditional N&S injections."

Novel delivery method: Microneedle/Microarray Systems

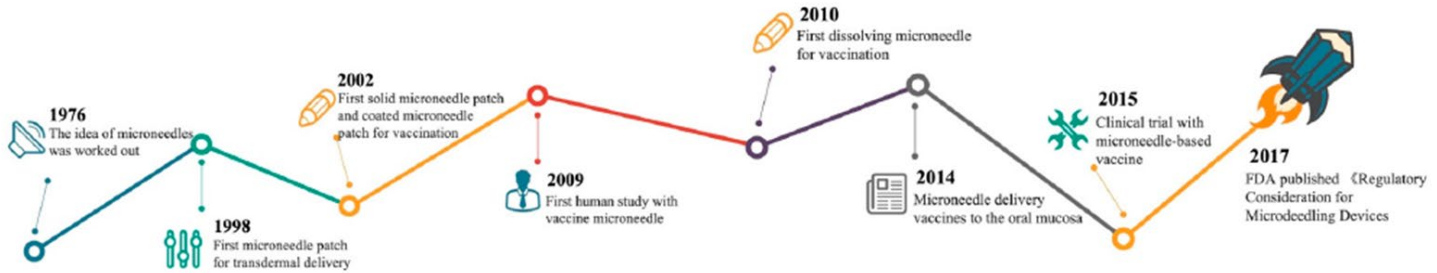


Figure 2. Timeline of Microneedle Research Development.

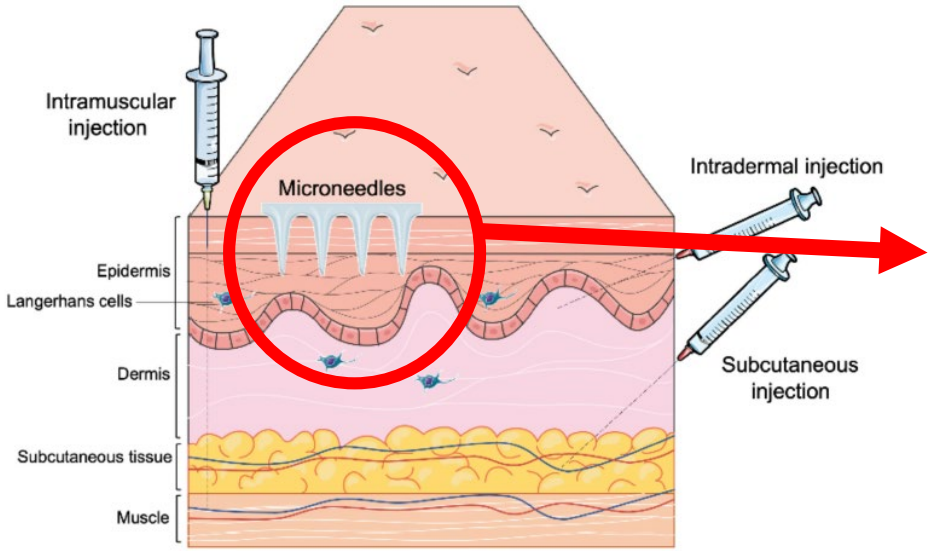


Figure 2. Different parenteral routes of vaccine administration.

Menon I, Bagwe P, et al. **Microneedles: A New Generation Vaccine Delivery System.** Micromachines. 2021; 12(4):435 www.mdpi.com/2072-666X/12/4/435

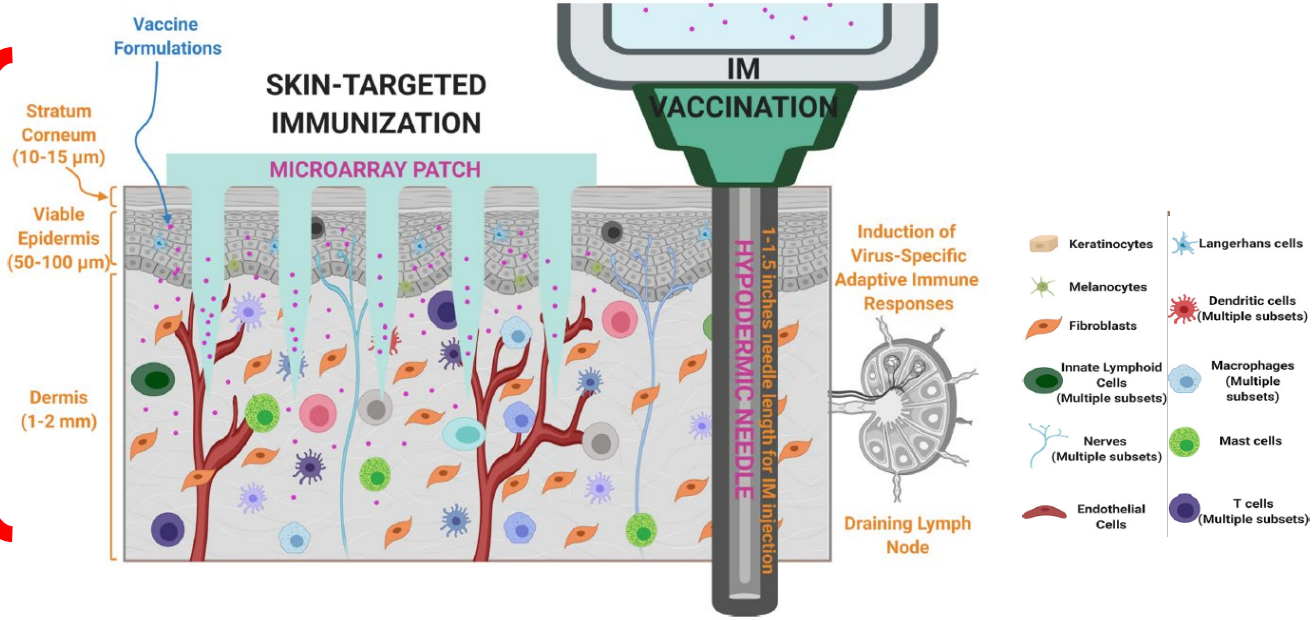


Fig. 4. Microarray patches (MAPs) enable precise, consistent, and minimally invasive administration of vaccine formulations (antigen ± adjuvant) to immunologically rich cutaneous microenvironments, whereas conventional intramuscular (IM) immunization bypasses the skin immune system, results in systemic exposure to vaccine ingredients, and causes pain.

Korkmaz E, Balmert SC, et al. **Microarray patches enable the development of skin-targeted vaccines against COVID-19.** Adv Drug Deliv Rev. 2021; 171:164-186. www.sciencedirect.com/science/article/pii/S0169409X2100034X

Microarray Patches (MAPs): 5 types

SOLID

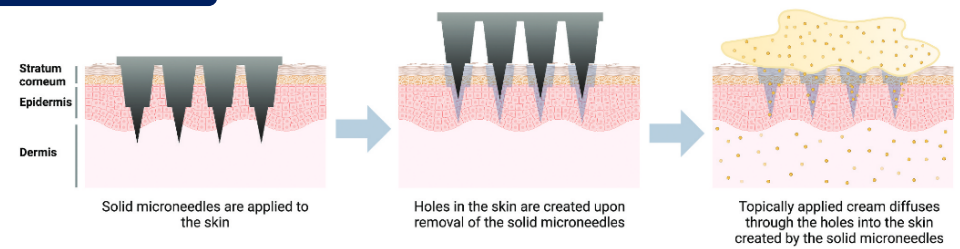


Figure 1. Schematic representation of the 'poke and patch' technique by the solid MAP. solid MAPs are commonly used to penetrate the skin before topical application of desired drug or vaccine, allowing them to diffuse through the holes created by the microneedles. Created with BioRender.com.

COATED

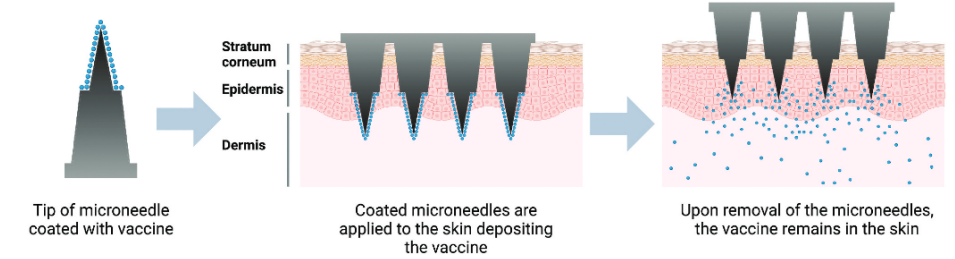


Figure 2. Schematic representation of the coated MAP. vaccines are dry coated onto the tips of the microprojections before application to the skin. Created with BioRender.com.

DISSOLVABLE

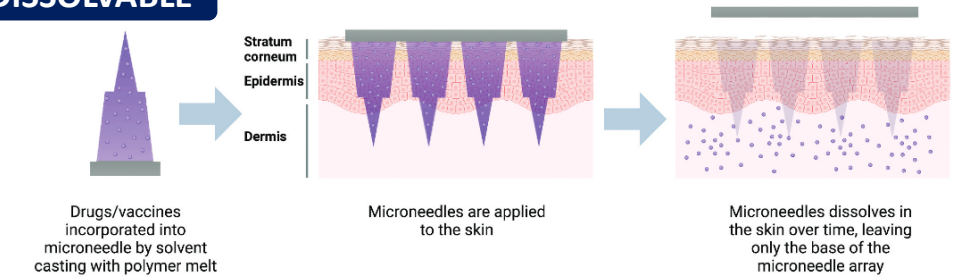


Figure 3. Schematic representation of the dissolvable MAP. the desired drugs or vaccines are integrated together with the microprojections which dissolves into the skin over time after application. Created with BioRender.com.

HOLLOW

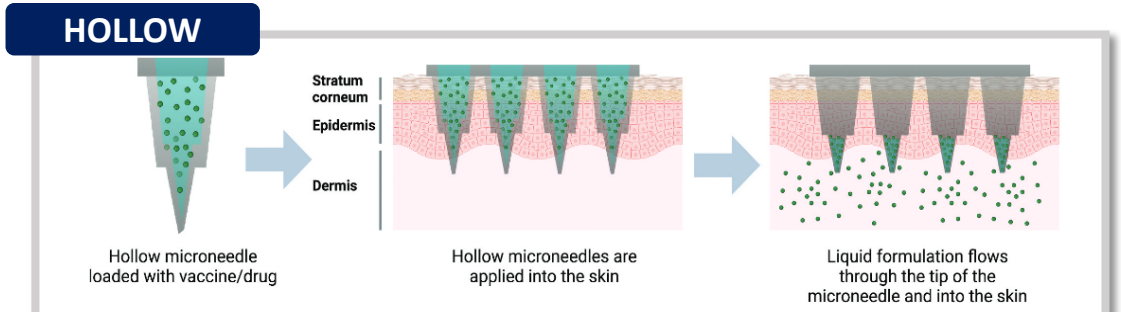


Figure 4. Schematic representation of the hollow MAP. vaccines/drugs are loaded into channels of the microneedle that flows through and into the penetrated pores of the skin when administered. Created with BioRender.com.

HYDROGEL

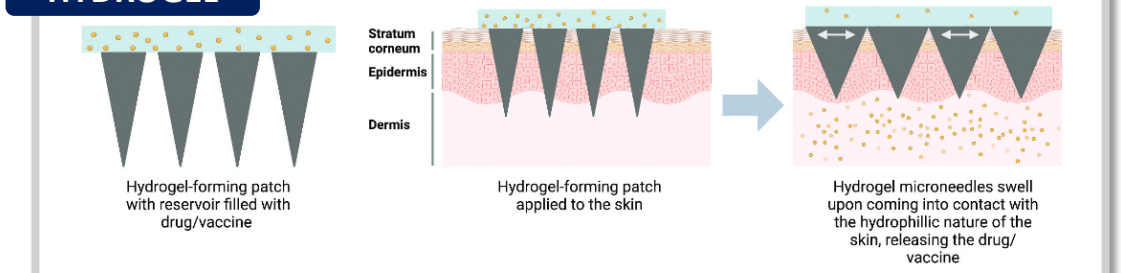


Figure 5. Schematic representation of the hydrogel-forming MAP. hydrogel-forming MAPs are fabricated with polymers crosslinked with gelatin which rapidly swells upon penetration into the skin and eventually releases the drug/vaccines into the microenvironment. Created with BioRender.com.

www.tandfonline.com/doi/epdf/10.1080/14760584.2023.2270598?needAccess=true

Microarray Patches (MAPs)

Fig. 5. Representative images of different MAP concepts presented in the literature

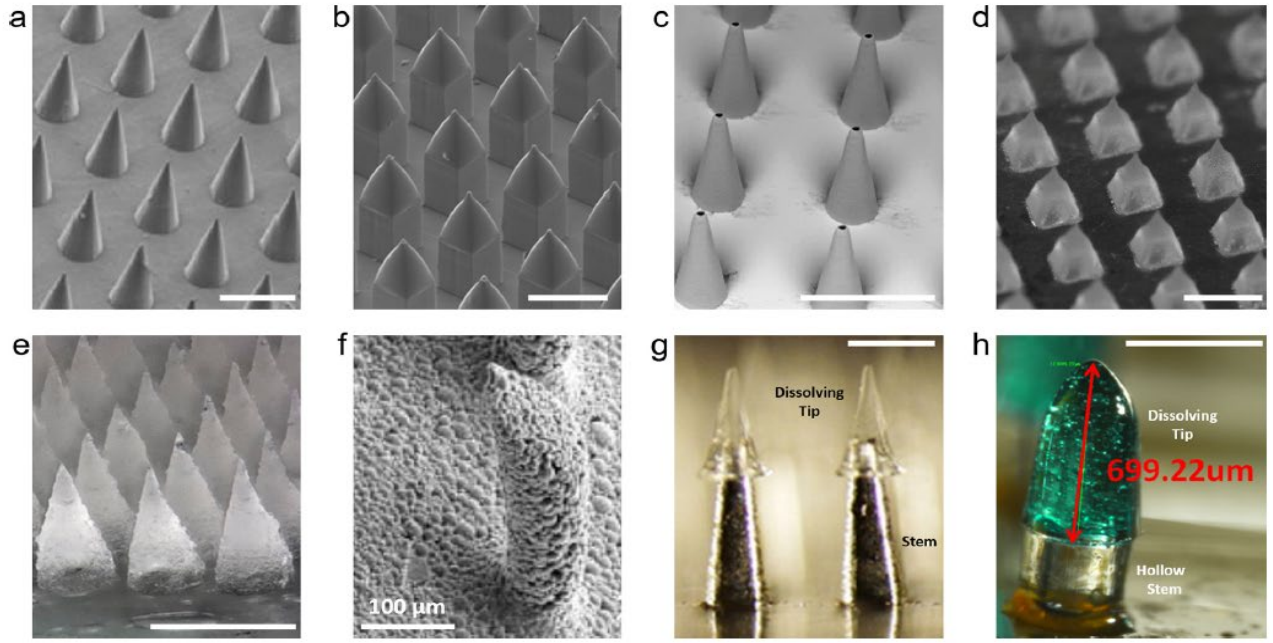
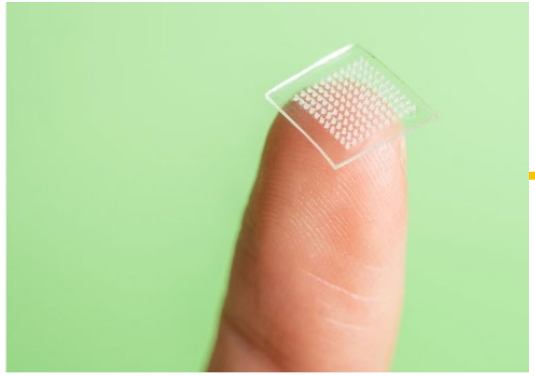


Fig. 5. Representative images of different MAP concepts presented in the literature. a. Solid MAPs manufactured from polylactic acid (PLA). Adapted with permission from [220]. Copyright 2010, Elsevier. b. Coated MAPs fabricated from PLA. Adapted with permission from [221] under terms of the CC-BY 4.0 license (https://creativecommons.org/licenses/by/4.0/). Copyright 2020, the Authors. c. Polymer hollow MAPs. Adapted with permission from [222] under terms of the CC-BY 4.0 license. Copyright 2019, the Authors. d. Dissolvable MAPs produced from a mixture of carboxymethylcellulose and trehalose. Adapted with permission from [223]. Copyright 2011, Wiley-VCH. e. Hydrogel-forming MAPs created from a blend of poly (methylvinylether-co-maleic acid), poly(ethylene glycol), and sodium carbonate. Adapted with permission from [224]. Copyright 2018, American Chemical Society. f. Porous MAPs fabricated from PLA. Adapted with permission from [225]. Copyright 2007, Springer Nature. g. Hybrid MAPs with stainless steel stems and dissolving poly(vinyl alcohol)/sucrose tips. Adapted with permission from [226]. Copyright 2011, Elsevier. h. Hybrid MAPs with SU-8 microtube stems and dissolving maltose tips after 3 min skin application. Adapted with permission from [227]. Copyright 2013, American Institute of Physics. Unless otherwise indicated, scale bars = 500 µm.



Queen's University Belfast prototype dissolving microarray patch. Photo: PATH/Patrick McKern.

Georgia Tech/Micron Biomedical prototype dissolving microarray patch. Photo: PATH/Patrick McKern.

Credit: Vaxxas, https://www.vaxxas.com/

Korkmaz E, Balmert SC, et al. **Microarray patches enable the development of skin-targeted vaccines against COVID-19.** Adv Drug Deliv Rev. 2021; 171:164-186.

www.sciencedirect.com/science/article/pii/S0169409X2100034X

www.path.org/programs/mdht/mapresources/

Microarray Patches (MAPs)

Table 3. Advantages and limitations of the different MAP designs.

Type of MAP	Advantages	Limitations	Reference
Solid MAPs	• Easy application and manufacturing • Sharp tips with good mechanical strength	• Reliability and reproducibility of vaccine delivery • Lack of precise dosing • Reformulation of the drug for different types of vaccine	[55,61,71–73,154–162]
Coated MAPs	• Minimal vaccine dosage needed • Allows for drug diffusion to deeper epidermal layers • Dosage uniformity • Reduced sensitivity to humidity	• Limitations in coating the necessary vaccine dosage • Vaccine stability during the drying and storage process • Retention of vaccine potency	[51,64–68,74–77,79–85,88–95,97–106,146,163–172]
Dissolvable MAPs	• Larger capacity to hold greater drug/vaccine payloads while ensuring a precise and consistent release of dosage • Able to have higher concentrations of excipients	• Vaccine compatibility and stability with solvent materials • Effects of biodegradable materials on the mechanical strength of the MAPs	[96,106–115,117–127,129–137,173–180]
Hollow/ porous MAPs	• Serves as a reservoir to allow for passive diffusion • Allows greater volume of liquid formulations to be delivered into the skin	• Potential of vaccine leakage, clogging of channel openings, and the collapse of microprojections due to their weak structure	[60,141,148,181–188]
Hydrogel-forming MAPs	• Uses a reservoir to store the drug/vaccine, enabling a higher volume/dosage to be administered	• Newly emerging technology that requires more research to understand the delivery efficacy, mechanism, safety, and other adverse effect • Have not been thoroughly investigated in pre-clinically in animal models for skin-targeted immunization against viral pathogens	[54,174,189–191]

www.tandfonline.com/doi/epdf/10.1080/14760584.2023.2270598?needAccess=true

Microarray Patches (MAPs)

Delivery Innovation: Measles-Rubella Microarray Patches

phase 2b proof-of-concept data expected May 2023

WHO continues to enable and accelerate development through the Vaccine Innovation Prioritization Strategy

Results are published or anticipated for MR, Influenza, SARS-CoV-2, Hep B and JE in Phase 1, as well as Phase 2 studies for MR and SARS-CoV-2

Placebo	Phase 1			Phase 2
Adult **placebo** (GT/Micron)	**Influenza** Phase 1 (Cosmed)	JE Phase 1 (Fujifilm)	**Influenza** Phase 1 (Vaxess)	**MR** Phase 1/2 (Micron)
Adult placebo (Vaxxas)	**Influenza** Phase 1 (GT/Micron)	**Influenza** Phase 1 (Zosano)	Influenza + adjuvant Phase 1 (Vaxxas)	**SARS-CoV-2** Phase 2a (MyLife)
Pediatric **placebo** (Micron)	**Influenza** Phase 1 (Vaxxas)	**Hep B** Phase 1 (LTS)	SARS-CoV-2 Phase 1 (Vaxess)	**MR** Phase 1/2 (Vaxxas)
Pediatric **placebo** (Vaxxas)	**Influenza** Phase 1 dose sparing (Vaxxas)	**MR** Phase 1 (Vaxxas)	**SARS-CoV-2** Phase 1 Vaxxas	**MR** Phase 2 (Micron)

Published Completed In progress Planned

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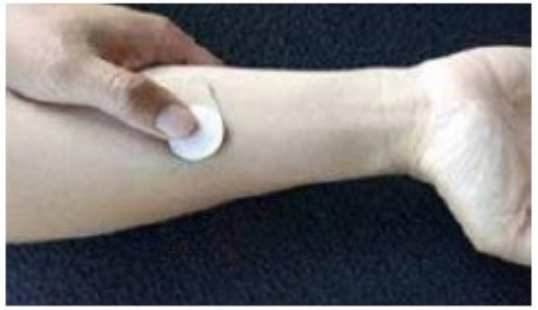
IVB Director's Report to SAGE 11

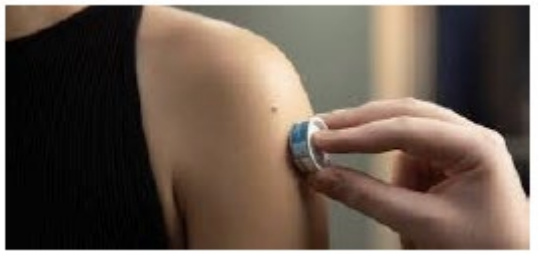
Slide from presentation during World Immunization Week, April 26, 2023
"Game Changers: Vaccine Innovations on the Horizon" - *Moss W, Giersing B, Hill A, Karron R, Talaat K, Limaye R*
Available at: https://publichealth.jhu.edu/2023/game-changing-vaccine-developments

Microneedle Vaccine Delivery Systems

Table 2. Companies developing microneedles for vaccine delivery.

Company	Type of Microneedle	Disease
Micron Biomedical	Dissolving microneedle	Inactivated rotavirus
3M (Kindeva)	Hollow microneedle	Cancer vaccines
BD Technologies (BS Soluvia)	Stainless steel microneedles	Influenza
Flugen	Metal microneedles	Influenza
Debiotech	Hollow microneedles	COVID-19
Verndari (Vaxipatch)	Stainless steel microneedle	Influenza, COVID-19
Nanopass (MicroJet™)	Silicon microneedles	Influenza, Polio, Varicella-Zoster, Cancers, Hepatitis B, COVID-19
BioSerenTach Inc.	Dissolving microneedles	Vaccine
Sorrento therapeutics (Sofusa®)	Nanotopographical imprinted microneedles (coated)	Immuno-oncology
Vaxxas (Nanopatch™)	Coated microneedles array patch	Influenza, COVID-19
Quadmedicine	Dissolving microneedles	Influenza, Canine Influenza
Vaxess	Dissolving microneedles	Influenza, COVID-19, skin cancer
Raphas	Dissolving microneedles	HPV, Polio, Tdap, HBV, IPV, and Hepatitis B





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Thank you

Jeremy Farrar, Director of the Wellcome Trust, said *"No matter how great your idea, how exciting your new treatment, or how robust your science, it must be accepted by the people who stand to benefit from it. Vaccines, for example, are one of our most powerful public health tools, and we need people to have confidence in them if they are to be most effective."*