Challenges and opportunities to formulate and stabilize vaccine candidates targeted for use in LMICs

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Department of Pharmaceutical Chemistry

Vaccine Analytics and Formulation Center (VAFC)

2022 Vaccine Technology VII Meeting
Sitges, Spain (Virtual Presentation)
June 16, 2022

Outline of Presentation

Introduction

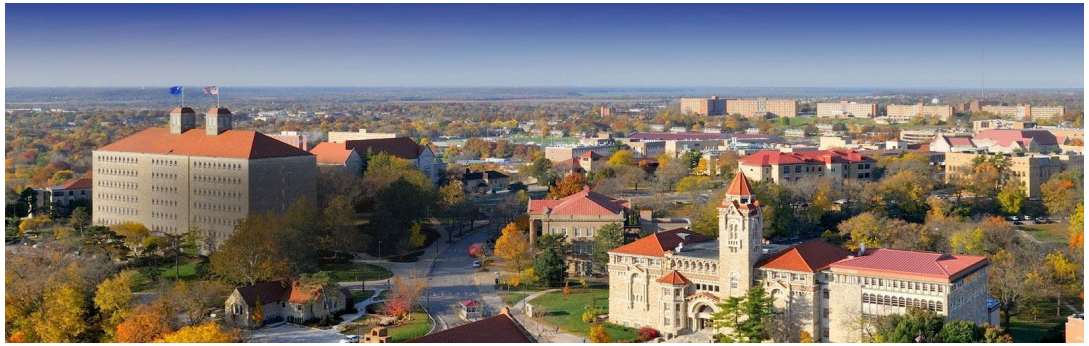
- Vaccine Analytics and Formulation Center (VAFC)
- Different Types of Vaccine Platforms
- Challenges to Formulate and Stabilize Vaccine Platforms

Three Vaccine Formulation Case Studies with Candidates for use in LMICs

Vaccine Analytics and Formulation Center (VAFC)

vafc.ku.edu

Lawrence, KS
45 min
outside of KC



Our focus is the "science of CMC development"

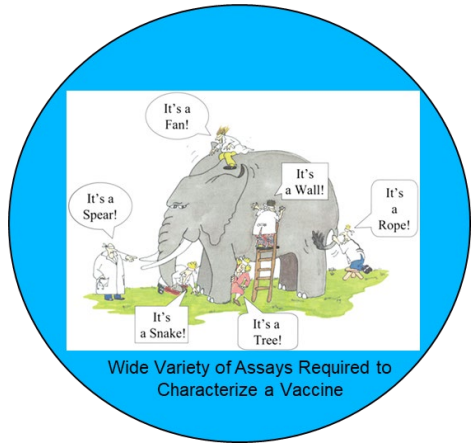
1. *Facilitate translational medicine*
   - Vaccine and biotherapeutic drug candidates into early and late-stage clinical trials
   - Emphasis on use in low- and middle- income countries (LMICs)

2. *Analytical and Formulation Expertise*

   Analytical characterization

   ↓

   - Developability assessments
   - Antigen-Adjuvant interactions
   - Formulation development
   - Stability profiles
   - Comparability studies



3. *Publish and openly communicate results*

4. *Train and employ biopharma/vaccine CMC scientists*

Our KU VAFC Team

Executive Director, co-PI VAFC co-founder

Dr. Sangeeta Joshi

7 staff members have left VAFC for great industry jobs in past 6m!

We are hiring post-docs looking for new opportunities to learn vaccine development!

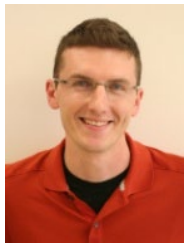
Distinguished Professor, PI VAFC co-founder

Dr. David Volkin

Senior Scientists

Dr. Ozan Kumru

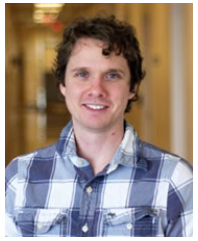
Dr. John Hickey



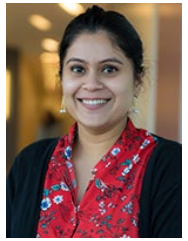
Dr. Prashant Kumar

Post Docs, Research Associates, Visiting Scientists

Dr. David Holland



Dr. Nitya Sharma



Dr. Kathyrn Secrist

Dr. Atsushi Hamana

Graduate Students

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Sakshi Bajoria

Layla Barreto

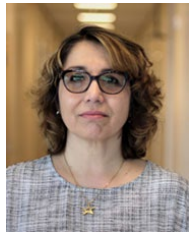
Administrative Staff

Emily Thomas-Dykes

Melinda Fish

Research Assistants

Sara Birdjandi



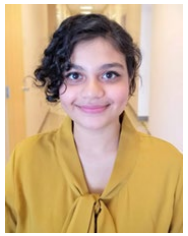
Dara Ogun

Brandy Dotson

Ria Caringal

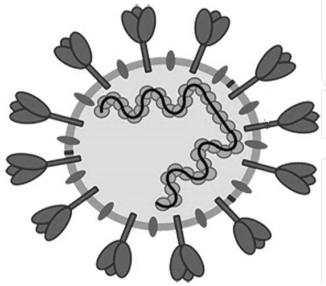
Michael Wang

Poorva Tasker



Overview of Viral Vaccine Platforms
(e.g., COVID-19 Vaccines and Candidates)

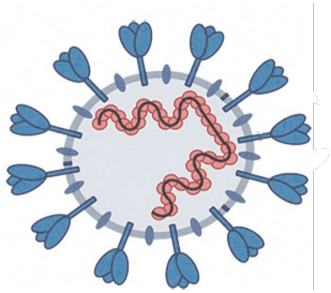
sinovac



Whole-inactivated virus

BHARAT BIOTECH

CODAGENIX INC.



Live-attenuated virus

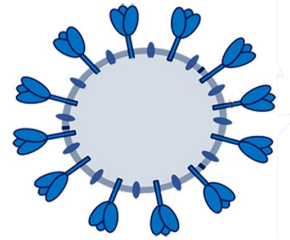
Worldwide COVID-19 Vaccines and Candidates (120 in clinical trials)

PHASE 1	PHASE 1/2	PHASE 2	PHASE 2/3	PHASE 3	AUTHORIZED	APPROVED	ABANDONED
34	21	17	10	38	19	12	15
Vaccines testing safety and dosage	*Combined trials*	Vaccines in expanded safety trials	*Combined trials*	Vaccines in large-scale efficacy tests	Vaccines in early or limited use	Vaccines approved for full use	Vaccines abandoned after trials

NOVAVAX
Creating Tomorrow's Vaccines Today

medicago

Virus-like particles



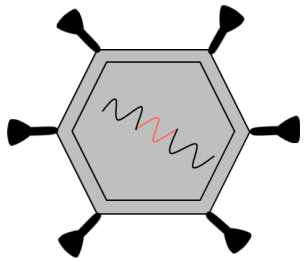
Protein subunit

Biological E. Limited
Celebrating Life Every Day

BAYLOR UNIVERSITY

UNIVERSITY OF OXFORD
AstraZeneca

Replicating viral vector



Non-replicating viral vector

Johnson & Johnson

SINOPHARM

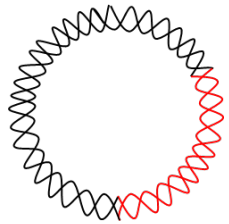
BIONTECH

NIH National Institutes of Health
Turning Discovery Into Health

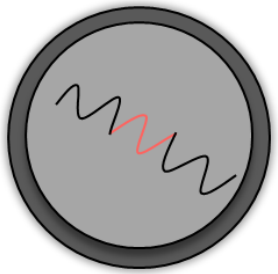
Pfizer

moderna

INOVIO
POWERING DNA MEDICINES



DNA-based



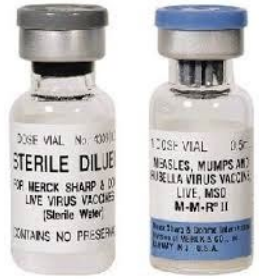
RNA-based

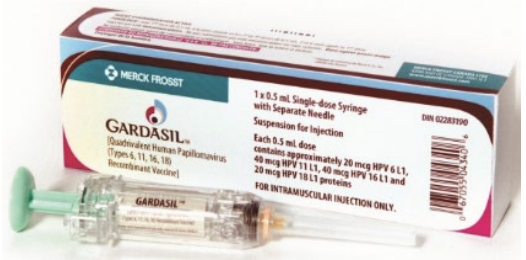
Zimmer, C., Corum, J., & Wee, S. (2020). Coronavirus vaccine tracker. Retrieved May 17, 2022, from https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

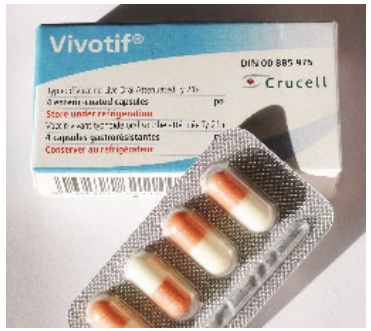
Bringing a New Vaccine Antigen into Clinical Trials Requires Formulation

"Turning Biomolecules and Microorganisms into Medicines"

- ***Vaccine antigen*** at the appropriate dose
- ***Adjuvants*** to enhance desired immune responses
- ***Excipients*** to ensure stability, solubility and tonicity
- ***Primary container*** (vial or prefilled syringe) to hold the vaccine/adjuvant/excipient mixture
- ***Delivery*** device for administration (IM/subQ, ID, oral, nasal)
- Fill-finish ***Manufacturing process*** (liquid, lyo)
- Develop ***Analytical assays*** and specifications
- Define ***Vaccine stability profile***: storage conditions, shelf life, and administration procedures

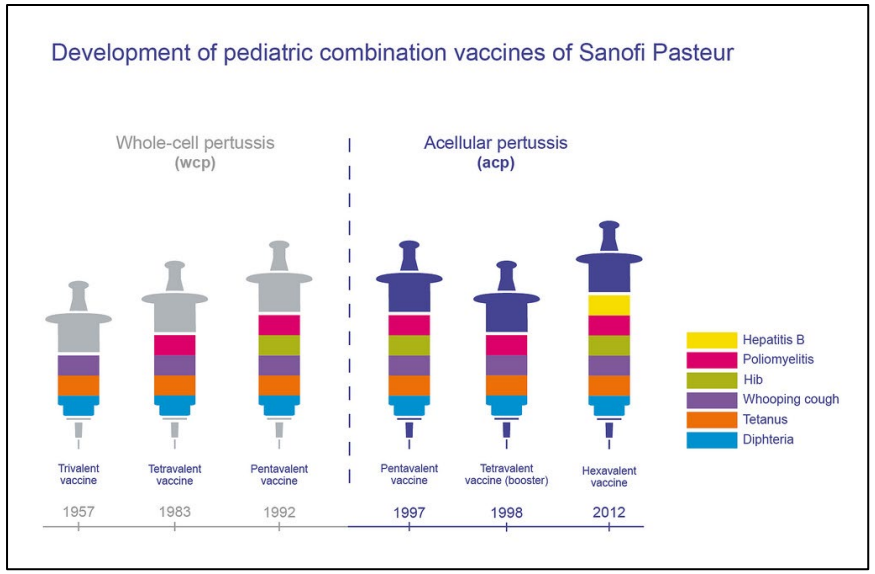






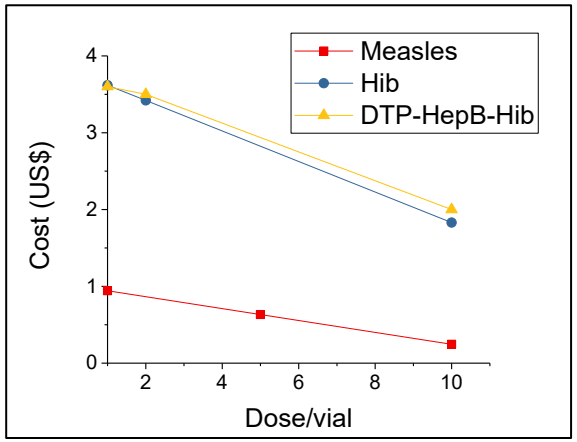
Formulation Development can Lower Costs and Increase Vaccine Coverage for use in LMICs

Combination Vaccines



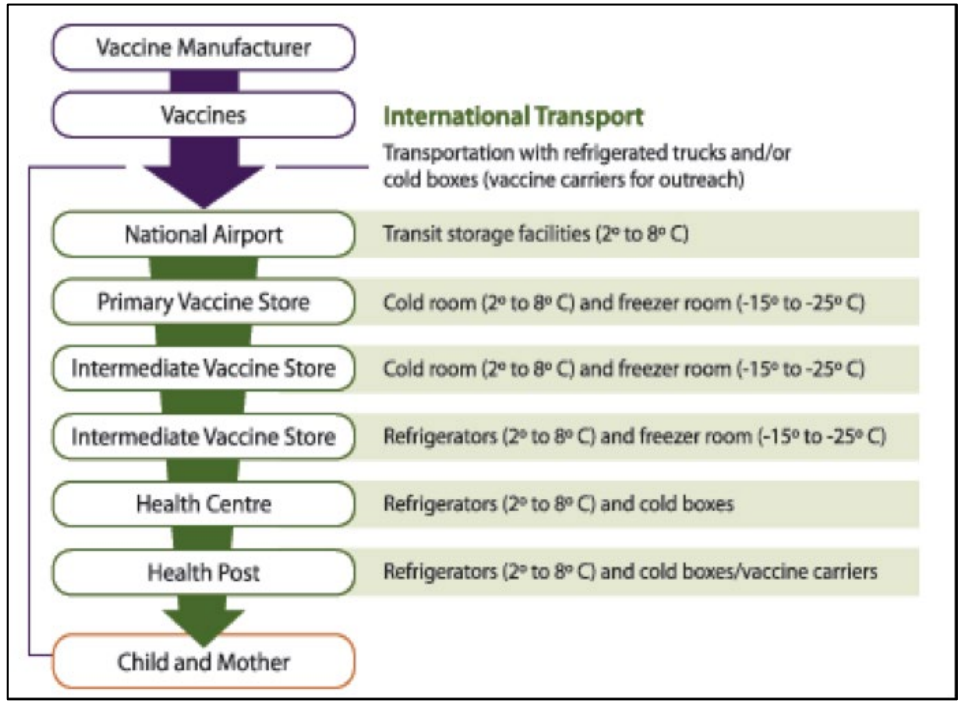
More vaccine antigens per container

Multidose Vaccines



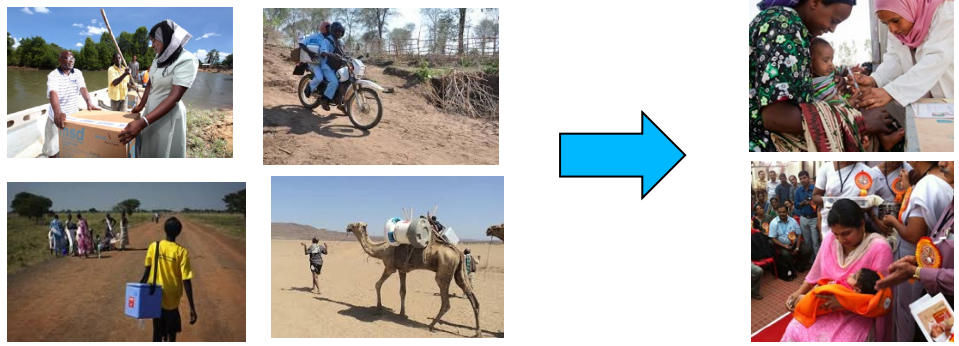
More vaccine doses per container

Vaccine Cold Chain



Improve Stability Across the Cold Chain

The Last Mile:



https://www.gatesfoundation.org/What-We-Do/Global-Development/Vaccine-Delivery http://www.open.edu/openlearncreate/mod/oucontent/view.php?id=53354&printable=1

https://www.flickr.com/photos/sanofi-pasteur/8497938912 Adapted from: Lee *et al*, 2010 "Single versus Multi-Dose Vaccine Vials: An Economic Computational Model"

Outline of Presentation

Introduction

Formulation Case Studies with Vaccine Candidates for use in LMICs:

COVID-19 vaccine candidate

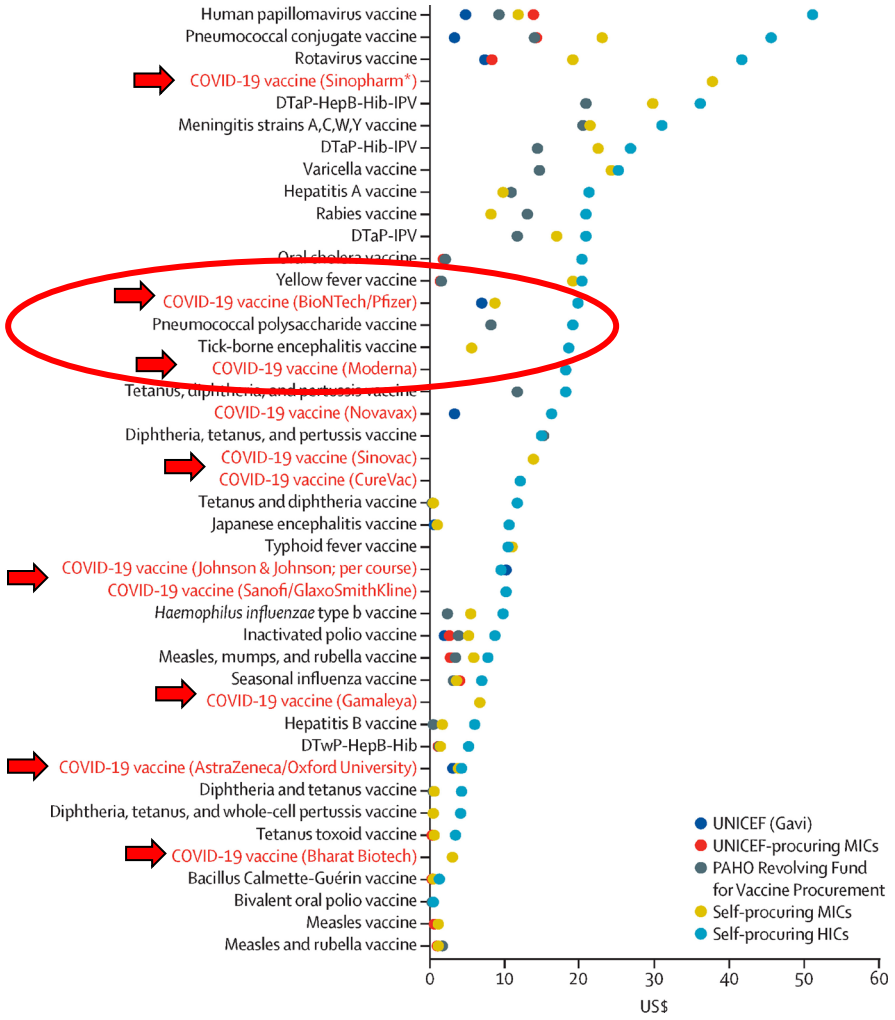
1. *RBD subunit with adjuvants (RBD-J, Alum, CpG)*

Rotavirus vaccine candidates

2. *Live attenuated rotavirus (RV3-BB)*
3. *Trivalent recombinant subunit (t-NRRV)*

COVID-19 vaccine approval is only the first step for worldwide coverage…

(e.g., stability, logistics and costs limit availability in LMICs)



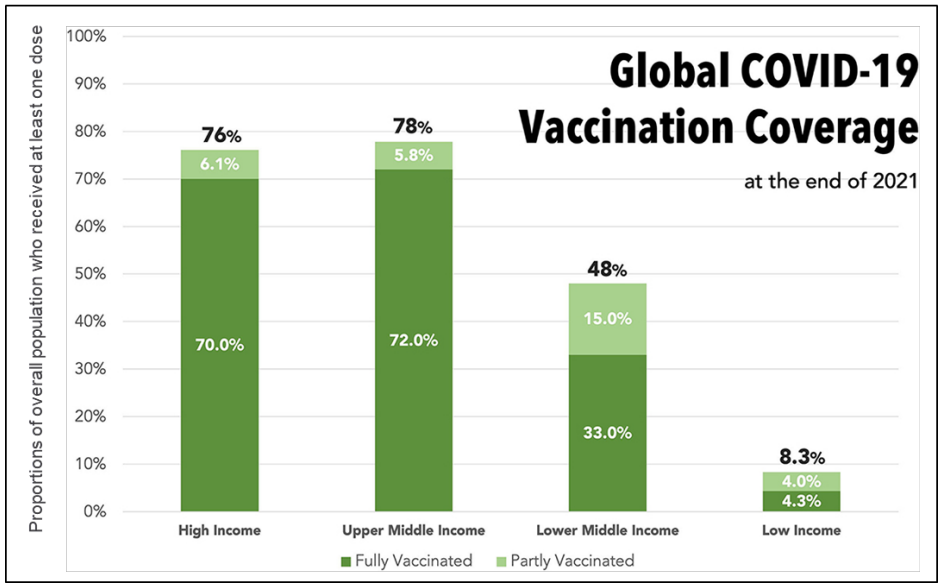
https://www.statista.com/chart/23658/reported-cost-per-dose-of-covid-19-vaccines/

https://launchandscalefaster.org/COVID-19

OJ Wouters et al, Lancet (2021)

Vaccine Formulation Case Study #1:

New COVID-19 Vaccine Candidates Targeted for Use in Low- and Middle- Income Countries (LMICs)



To meet global demand and to ensure access to LMICs:

- Affordable (low-cost production)
- Easily-scalable
- Sufficient stability at refrigerated or ambient temperatures
- Effectively immunogenic

Subunit vaccine formulated with adjuvants as an attractive approach to meet these goals

Front. Public Health, 07 March 2022

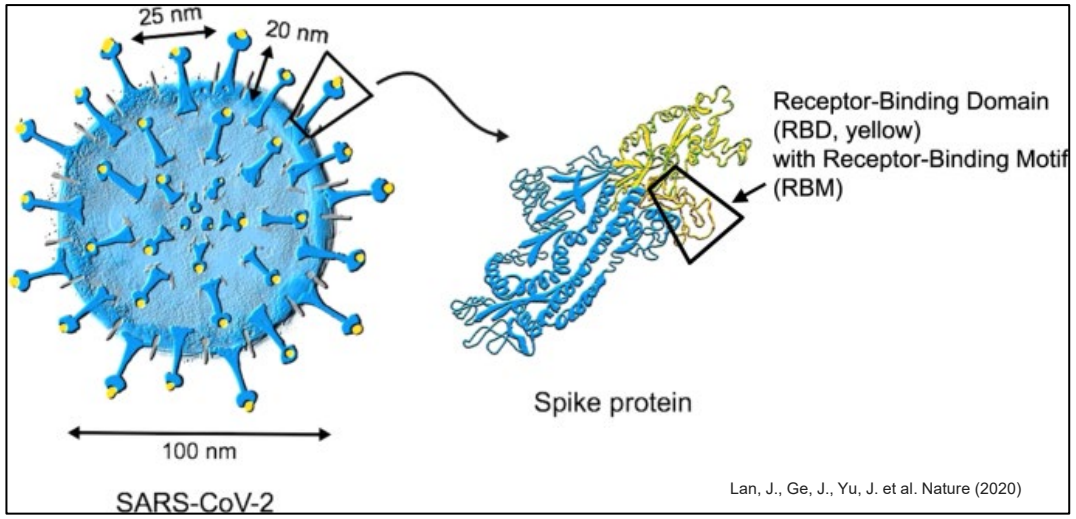
- "ULTRA"-low cost vaccine manufacturing
- Funded by BMGF Grand challenge grant
- Goal: To reduce cost of vaccine manufacturing of recombinant protein antigens to $.015/dose through the integrated automation of a continuous manufacturing process

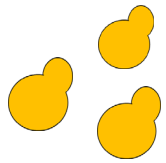
Production of low-cost vaccines by creating a generic, integrated, and automated vaccine manufacturing platform

Massachusetts Institute of Technology	UCL	KU THE UNIVERSITY OF KANSAS
Strain engineering, laboratory scale process	Process development and scale-up	Analytical characterization, formulation development

- Recombinant protein antigens evaluated:
  - NRRV antigens (rotavirus vaccine candidate)
  - RBD antigens (Covid-19 vaccine candidate)

Recombinant RBD variant as subunit COVID-19 vaccine candidate





Expressed, secreted and purified variants from ULTRA platform (K. phaffi)

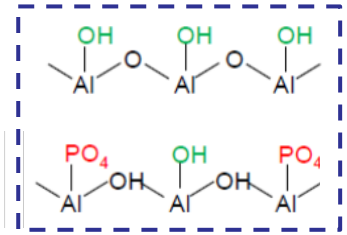
Massachusetts Institute of Technology

	Position											
	1	13	121	122	123	124	125	126	158	159	160
SARS CoV	N	N	Y	K	Y	R	Y	L	C	Y	W
SARS CoV-2	N	N	Y	L	Y	R	L	F	C	Y	F
RBD variants expressed in *K. phaffii*	N	Q	Y	L	Y	R	L	F	C	Y	F
	del	Q	Y	L	Y	R	L	F	C	Y	F
	del	N	Y	L	Y	R	L	F	C	Y	F
	del	N	Y	K	Y	R	L	F	C	Y	W

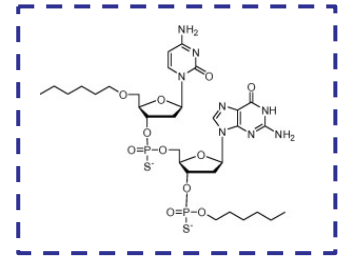
Developability Assessments

Structural attribute	Method
Protein concentration, purity and aggregation	UV-Vis Spectroscopy
	SDS PAGE
Size/ Aggregation	Size Exclusion Chromatography
Primary structure and post-translational modifications	Intact MS
	N-glycan analysis
Higher-order structure	Circular Dichroism (CD)
	Intrinsic fluorescence spectroscopy
	Differential Scanning Calorimetry (DSC)
Ligand binding	Bio-layer Interferometry (BLI)

Aluminum salt adjuvants



CpG 1018

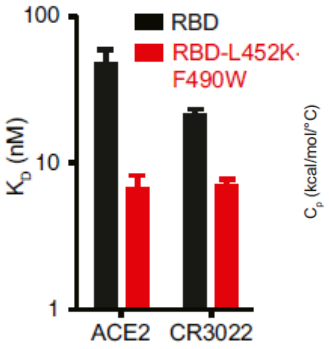


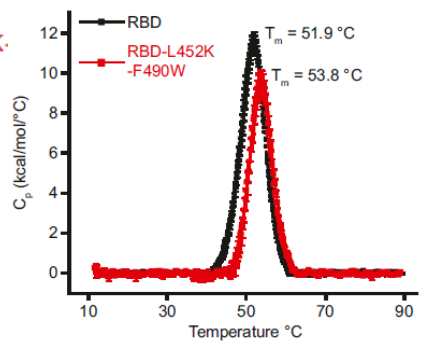
Formulated with adjuvants

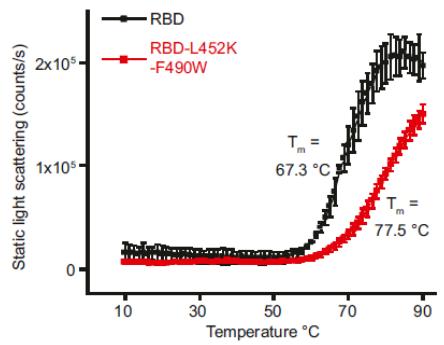
Preclinical Animal Studies

Dalvie *et al.*,
Proc Natl Acad Sci, 118 (38) (2021)

***Down-selected*: RBD-L452K-F490W or RBD-J**

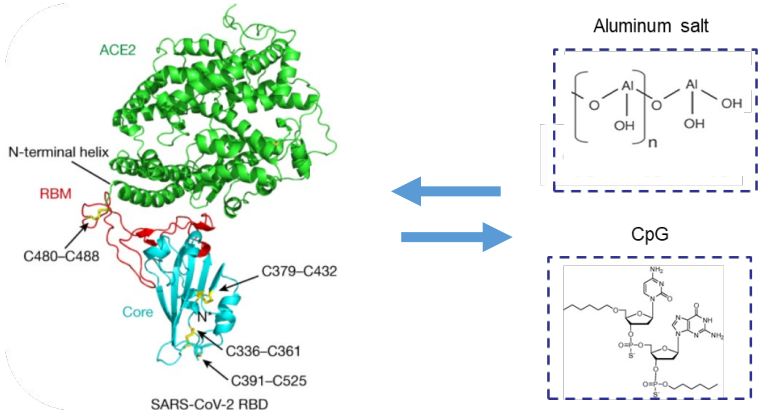






RBD-J Adjuvanted Formulations:

Inter-relationships between Antigen-Adjuvant Interactions, Immunogenicity and Stability

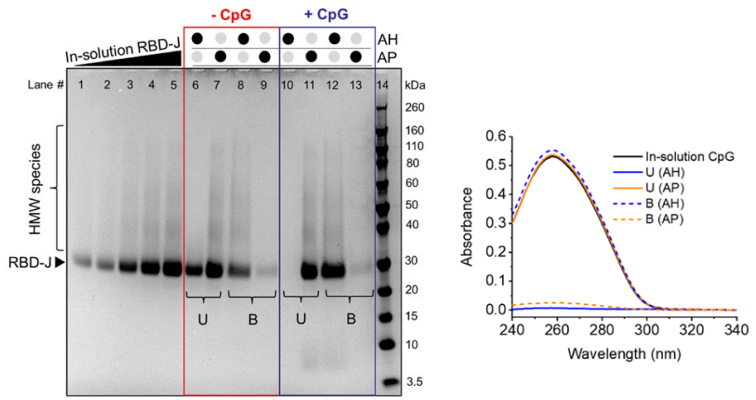


Antigen-Adjuvant Interactions

- SDS PAGE
- UV visible spectroscopy

In vivo immunogenicity

In vitro storage stability



Aluminum adjuvant	% Bound RBD-J - CpG	% Bound RBD-J + CpG	% Bound CpG
AH	~ 50	~ 100	100
AP	< 15*	< 15*	0

Formulation	Adjuvant	% Bound to aluminum adjuvant: RBD-J	% Bound to aluminum adjuvant: CpG 1018
F1	AH	~ 50	-
F2	AH	~ 100	-
F3	AH+CpG	~ 100	100
F4	AP	< 15	-
F5	AP+CpG	< 15	0
F6	CpG	-	-
F7	No adjuvant	-	-

- RBD-J partially binds AH
- RBD-J 100% AH bound with CpG
- RBD-J does not bind AP

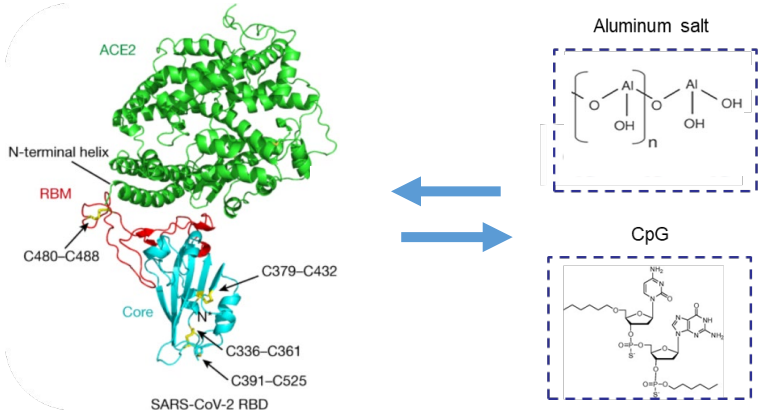
Prepared different adjuvanted RBD-J formulations

- AH vs AP
- CpG vs no CpG
- Bound vs unbound

Bajoria *et al.*, *Human Vaccin Immunother* (2022), epub

RBD-J Adjuvanted Formulations:

Inter-relationships between Antigen-Adjuvant Interactions, Immunogenicity and Stability



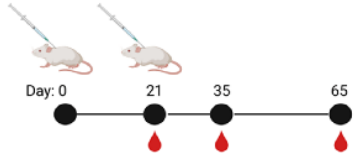
Antigen-Adjuvant Interactions

In vivo Immunogenicity

- Mouse studies
- Total antibodies
- Neutralizing antibodies

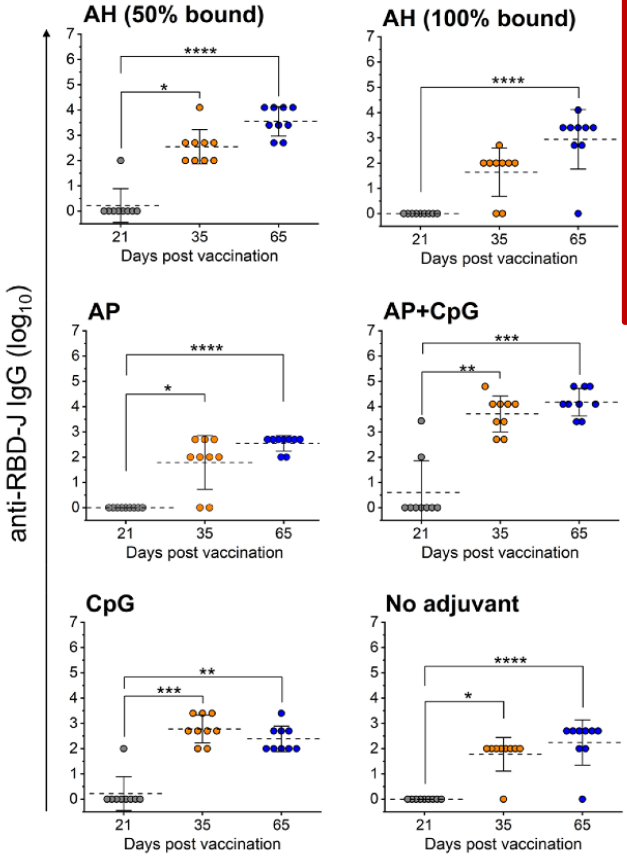
In vitro Storage Stability

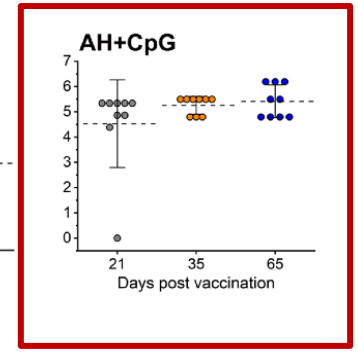
Bajoria *et al.*, *Human Vaccin Immunother* (2022), epub

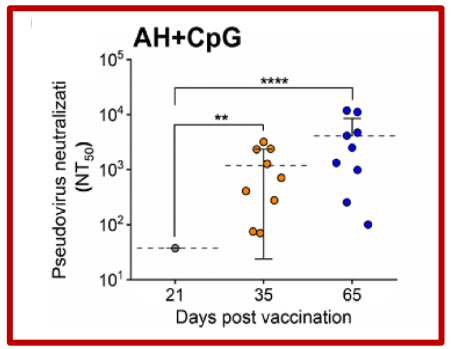


Total antibody

Neutralizing antibody





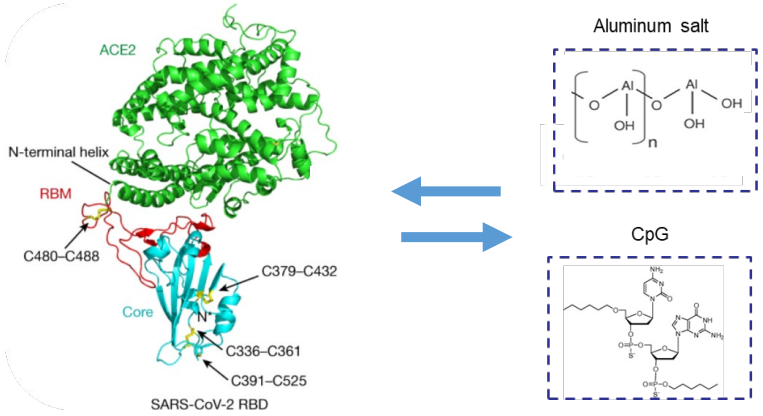


RBD-J +AH + CpG

- Highest and earliest total antibody response
- Only formulation to show a potent neutralizing response

RBD-J Adjuvanted Formulations:

Inter-relationships between Antigen-Adjuvant Interactions, Immunogenicity and Stability

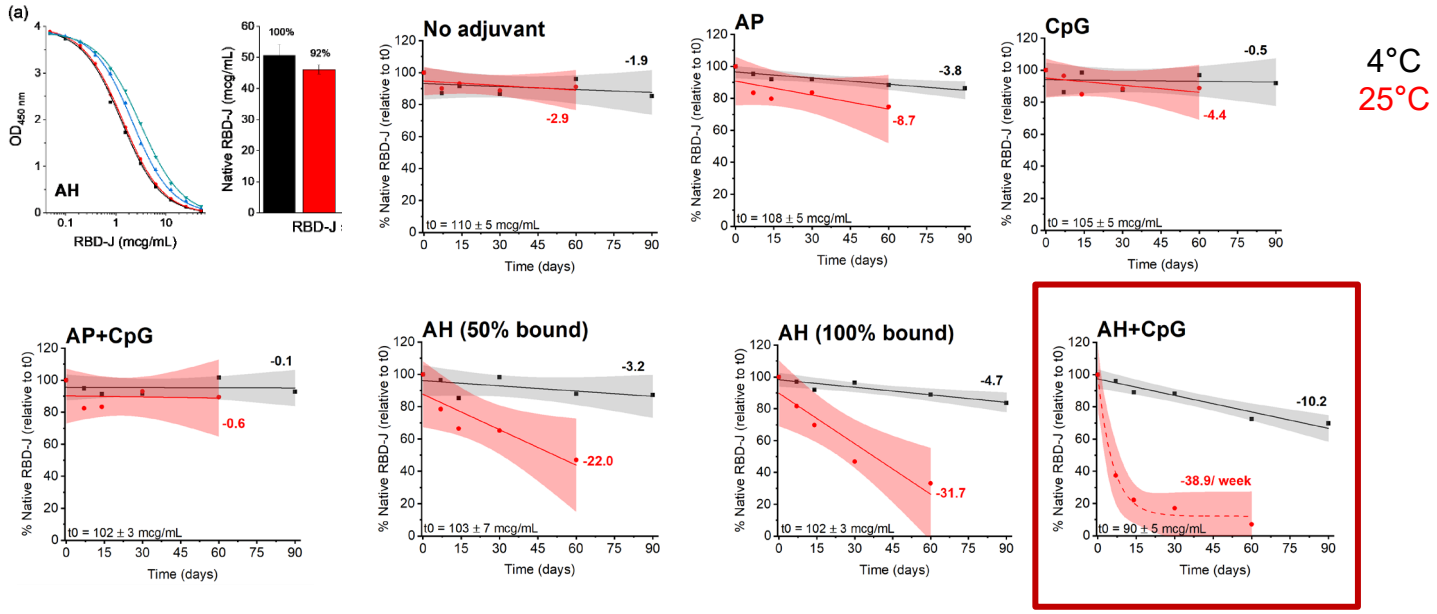


Antigen-Adjuvant Interactions

In vivo Immunogenicity

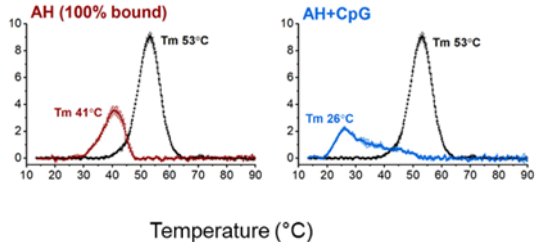
In vitro Storage Stability

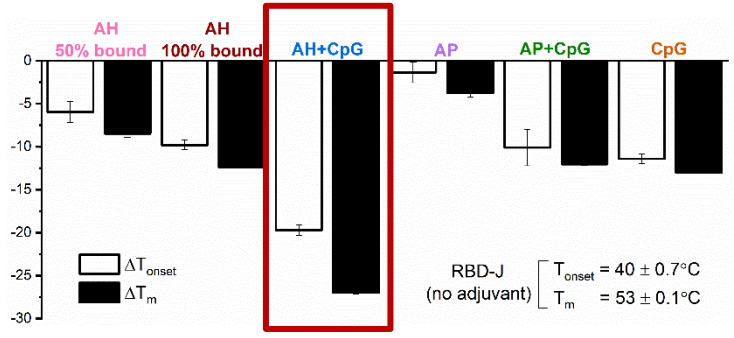
- Competitive ELISA binding to ACE2
- Differential Scanning Calorimetry (DSC)



RBD-J +AH + CpG

- Least stable formulation during storage
- Lowest conformational stability

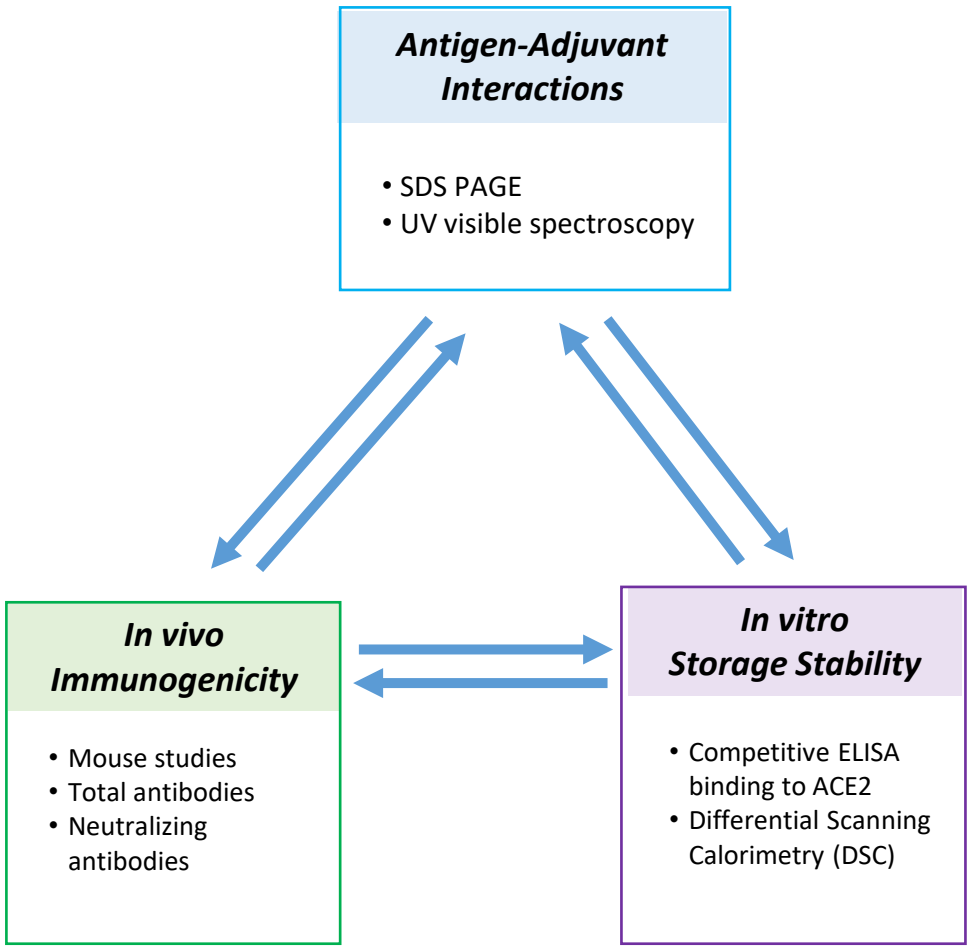


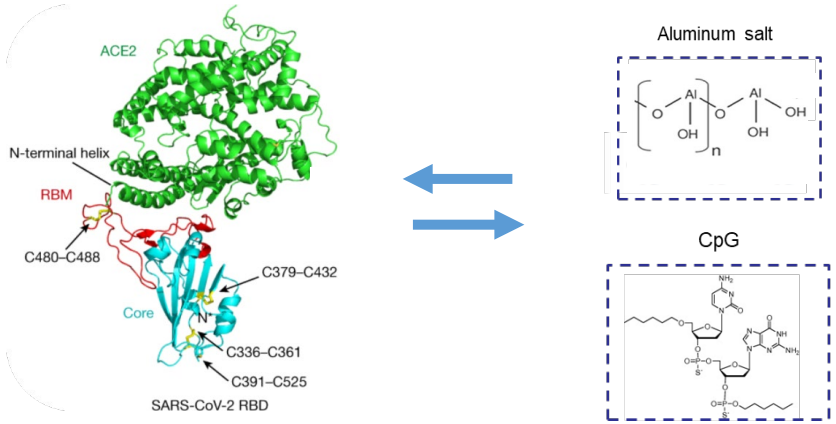


Bajoria *et al.*, *Human Vaccin Immunother* (2022), epub

RBD-J Adjuvanted Formulations:

Summary of Inter-relationships between Antigen-Adjuvant Interactions, Immunogenicity and Stability





- RBD-J formulations can be rationally designed to vary interactions between antigen-adjuvants and adjuvants-adjuvants
- Nature of these inter-relationships is expected to antigen specific ("case-by-case"), *even for different variants of RBD*!
- Optimizing these formulation variables is key to successfully develop *efficacious* and *stable* adjuvanted subunit vaccine candidates

Bajoria *et al.*, *Human Vaccin Immunother* (2022), epub

Outline of Presentation

Introduction

Formulation Case Studies with Vaccine Candidates for use in LMICs:

COVID-19 vaccine candidate

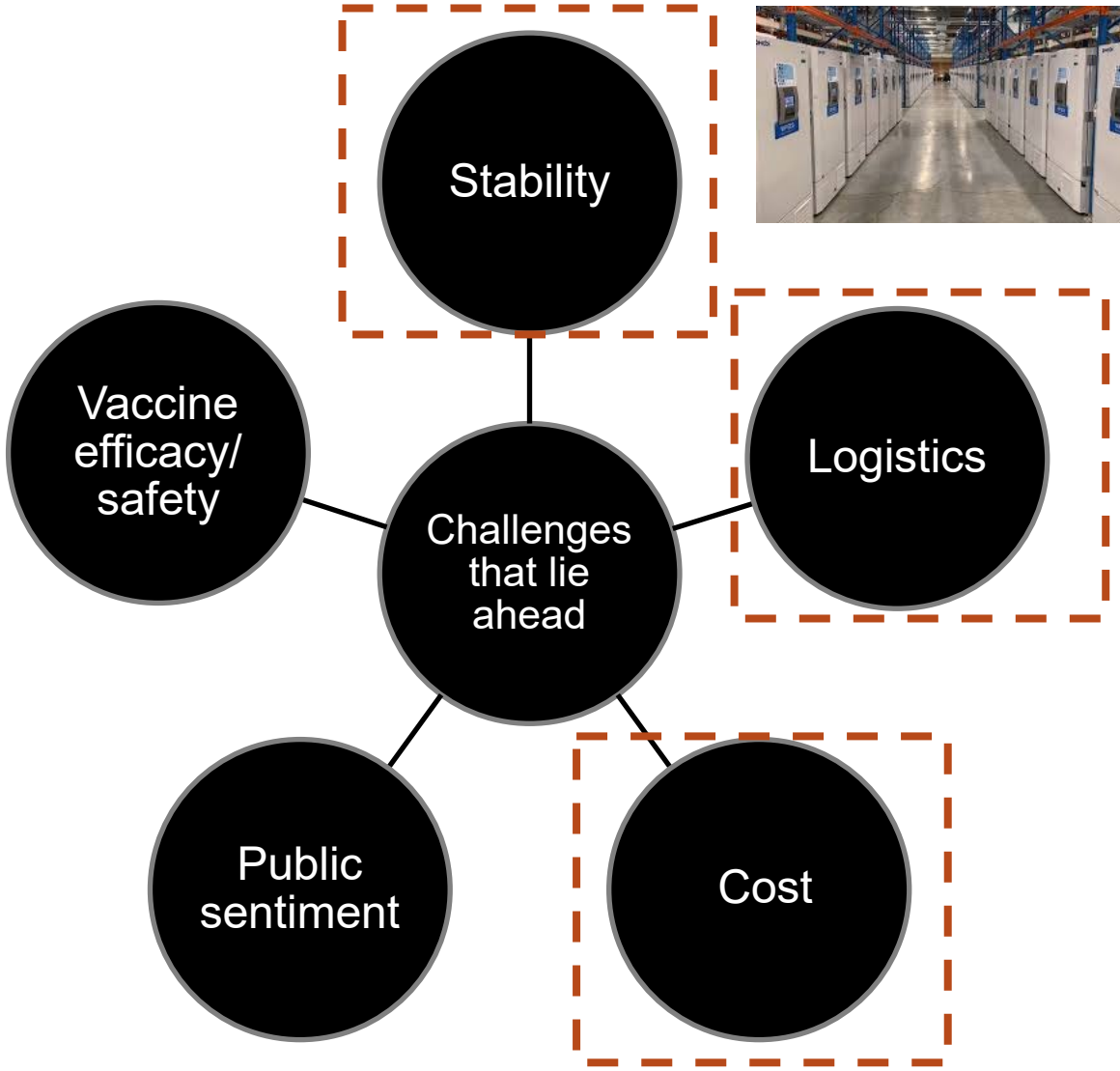
1. *RBD subunit with adjuvants (RBD-J, Alum, CpG)*

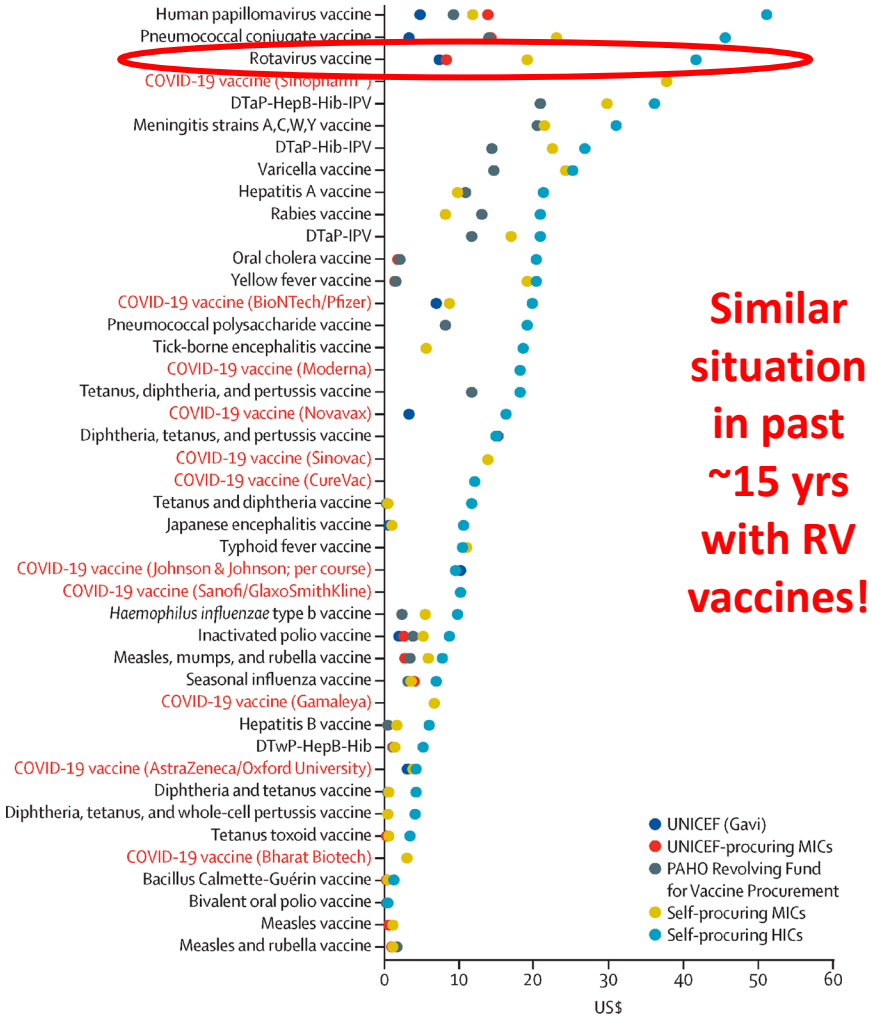
Rotavirus vaccine candidates

2. *Live attenuated rotavirus (RV3-BB)*
3. *Trivalent recombinant subunit (t-NRRV)*

Vaccine approval is only the first step for worldwide coverage…

(e.g., stability, logistics and costs limit availability in LMICs)





Similar situation in past ~15 yrs with RV vaccines!

https://www.statista.com/chart/23658/reported-cost-per-dose-of-covid-19-vaccines/

https://launchandscalefaster.org/COVID-19

OJ Wouters et al, Lancet (2021)

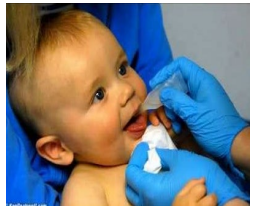
Rotavirus Vaccines

RotaTeq: 2006, pentavalent rotavirus vaccine (RV5)

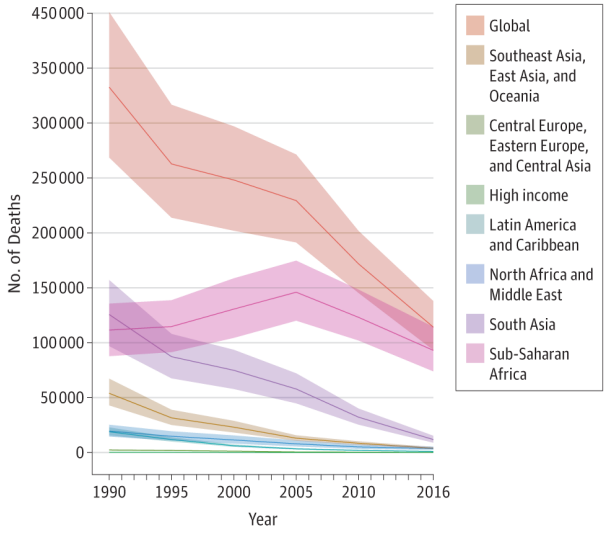
Rotarix: 2008, monovalent rotavirus vaccine (RV1)

In 2018, two additional WHO prequalified RV vaccines available from Indian vaccine manufacturers

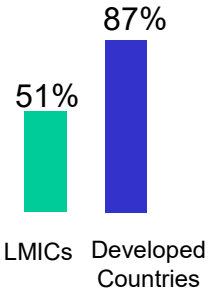
live attenuated rotavirus strain + Oral delivery of liquid formulation



Rotavirus mortality rate over time



Vaccine efficacy



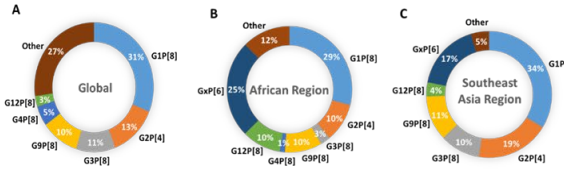
Low Global Coverage

~30%

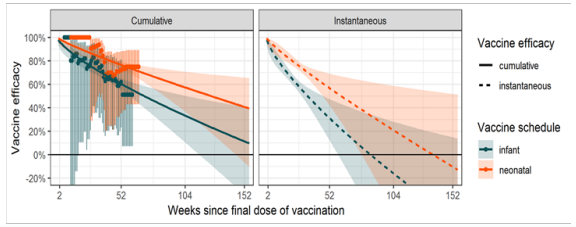
High cost + limited manufacturing capacity

Need for New Rotavirus Vaccines in LMICs

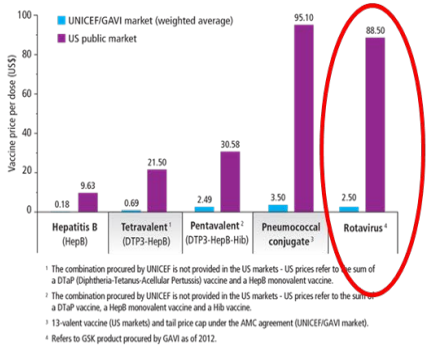
1. Improve vaccine efficacy by broader serotype coverage against prevalent strains in LMICs



2. Improved duration of protective response and reduce risk of intussusception



3. Further reduce RV vaccine prices (<$3.50 for three doses) by lowering production costs and implementing low-cost, thermostable formulations

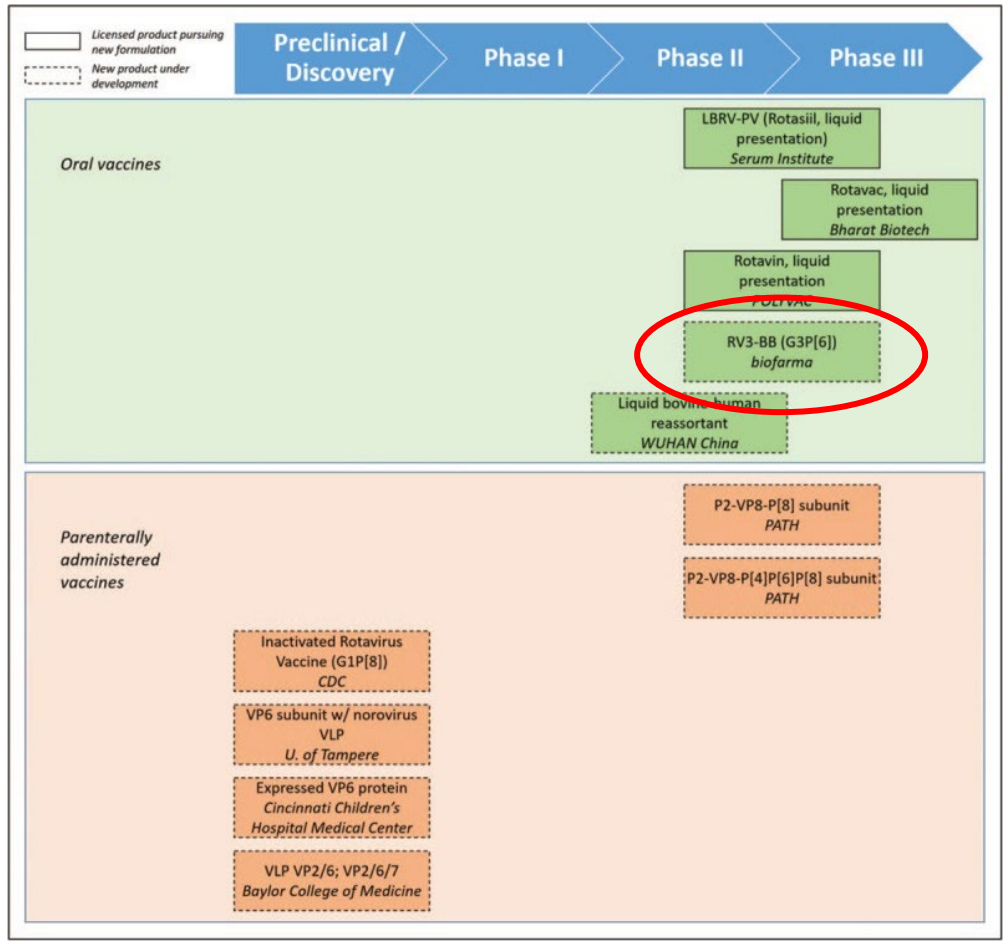


Troeger et al, *JAMA Pediatr*.172:958 (2018)

Infection, Genetics and Evolution 28 446 (2014); *Lancet Infectious Diseases* 19, 717 (2019); GAVI progress report

Vaccine Formulation Case Study #2:

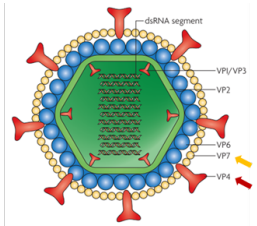
New Rotavirus Vaccine Candidates Targeted for Use in Low- and Middle- Income Countries (LMICs)



Curr Opin Inf Dis 32, 435-44 (2019)

Case study #2

- 70 nm viral particle
- inner core contains 11 double stranded RNA segments,
- internal capsid and
- outer capsid with 60 spikes between 10-12 nm length



VP4 and VP7 are targets of neutralizing antibodies

Live, attenuated virus

formulated as 2-8°C stable liquid for oral delivery

Murdoch Childrens Research Institute

RV3-BB rotavirus strain

- Discovered natural, attenuated strain
- Developed RV3-BB vaccine to proof-of-concept (Phase IIB)
- Owns vaccine IP (Non-exclusively licensed IP to BioFarma)

BATAVIA biosciences

Process development

- Upstream process development
- Downstream process development
- Analytical development
- Scale-up
- Tech transfer

KU THE UNIVERSITY OF KANSAS

Formulation development

- Stable liquid formulation at 2-8 °C
- Oral delivery without need for preneutralization of gastric acid

biofarma

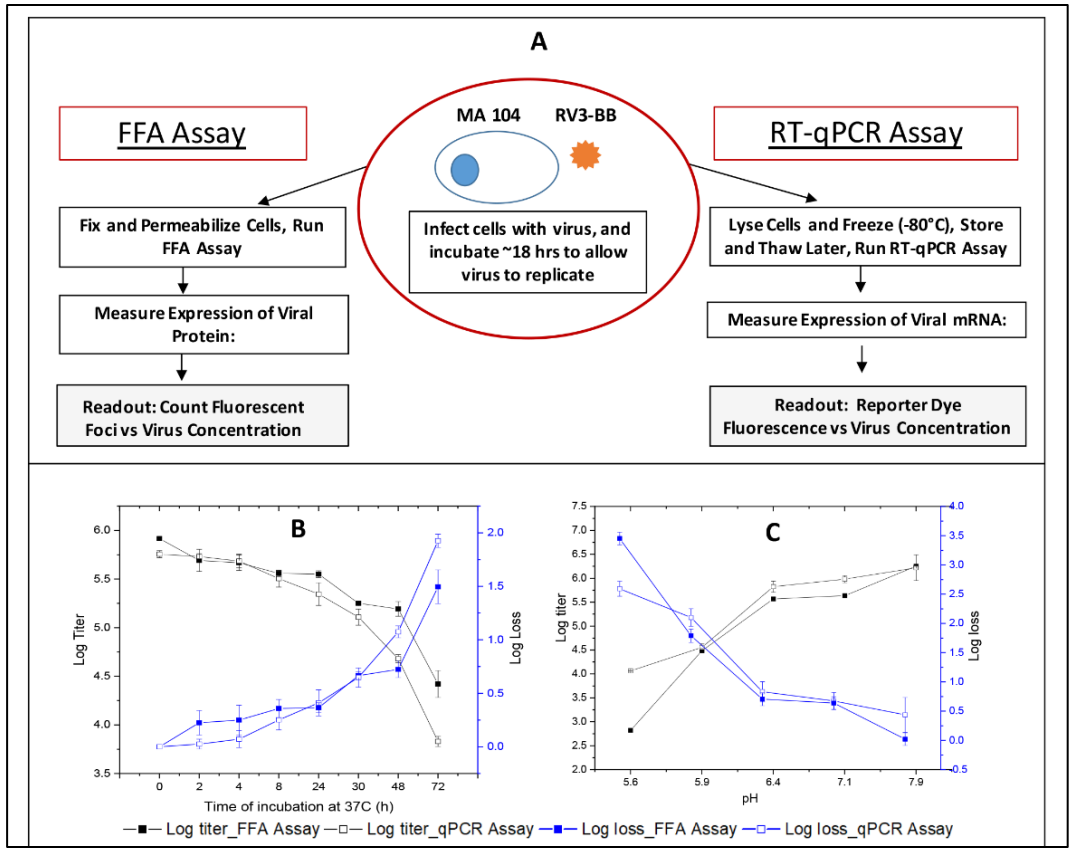
Market authorization and commercial manufacturing

- Clinical Trial Manufacturing for Phase 1, 2 and 3
- Market Authorization
- Commercial Manufacturing

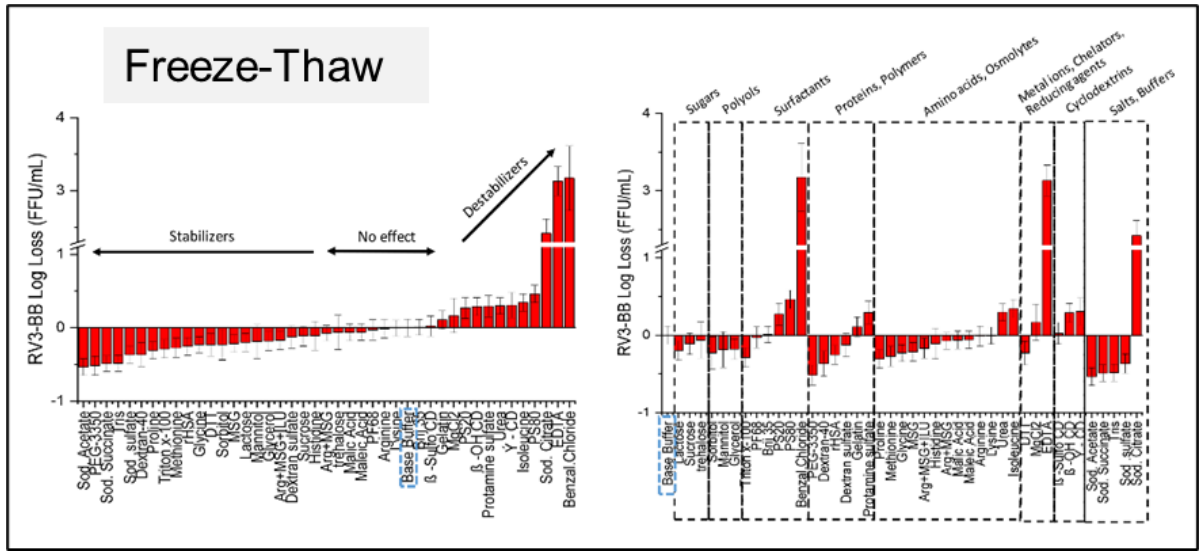
Funding from:

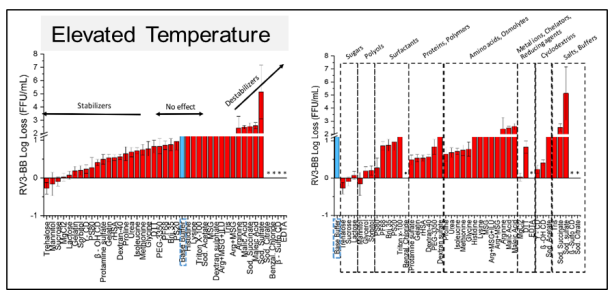
BILL & MELINDA GATES foundation

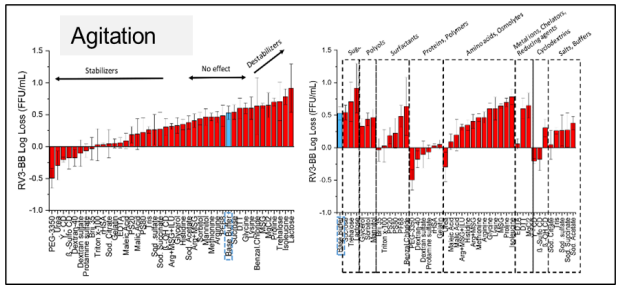
Implementation of a high-throughput RT-qPCR viral infectivity assay to enable RV3-BB formulation work

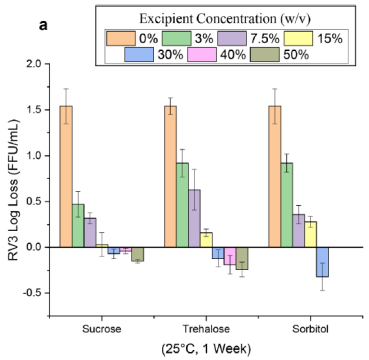


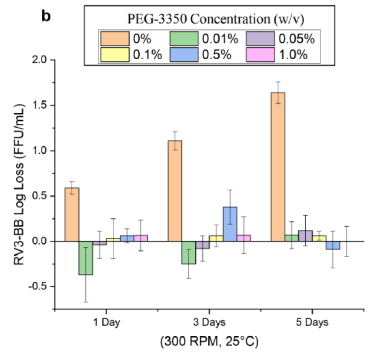
Screening of ~50 Excipients to Stabilize RV3-BB Virus Against Various Stresses (*Log loss of titers using RT-qPCR assay)*





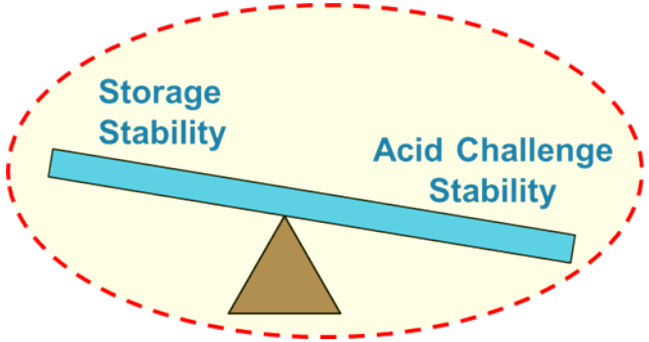




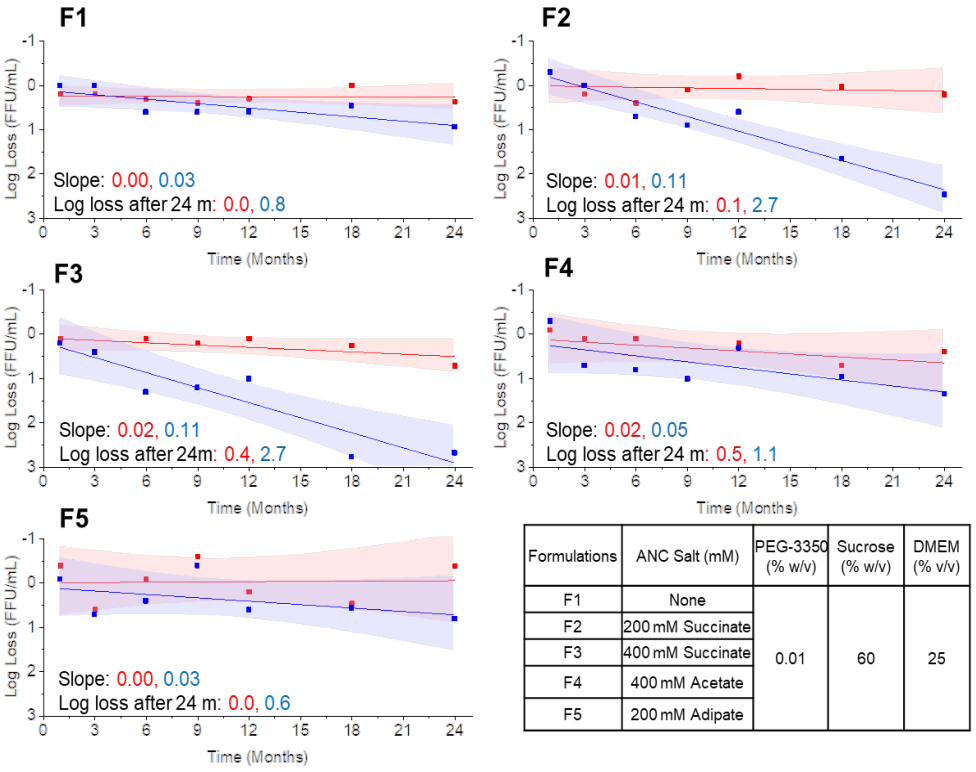


Kumar and Shukla *et al.*, *Human Vaccin Immunother* 17: 2298 (2021)

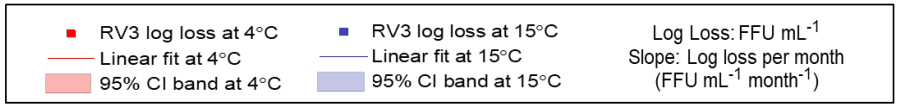
Candidate RV3-BB formulations demonstrate excellent storage stability



in vitro digestion models suggest candidate formulations protect RV3-BB during *in vivo* oral delivery



Formulations	ANC Salt (mM)	PEG-3350 (% w/v)	Sucrose (% w/v)	DMEM (% v/v)
F1	None	0.01	60	25
F2	200 mM Succinate			
F3	400 mM Succinate			
F4	400 mM Acetate			
F5	200 mM Adipate			



Hamidi *et al.*, *Vaccine* 39: 2048-2059 (2021)

(B) Sequential Addition Model

Sequential addition of either HCl + SGF ± infant formula or Mylanta ± WFI

↓ Pre-incubate 37°C, 0.5 hr.

Addition of pepsin (2,000 U/mL)

↓

Addition of RV3-BB formulation (2 mL)

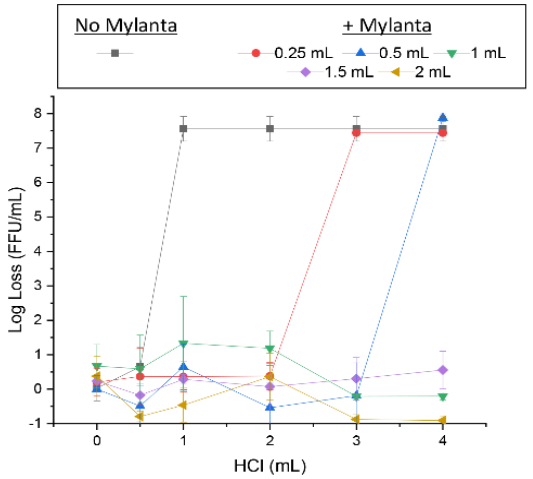
↓ Incubate 37°C, 1 hr Measure pH

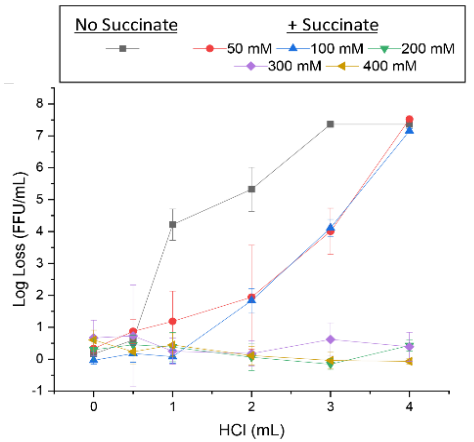
Dilution in DMEM + trypsin

↓ 50 fold dilution

Analyze with Infectivity RT-qPCR

Readout: RV3-BB titer (log FFU/mL)

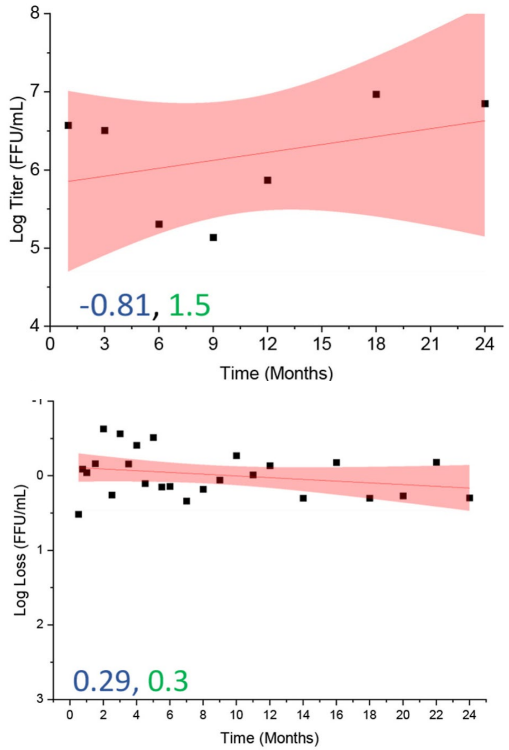




Kumar and Pullagurla *et al.*, *J Pharm Sci* 110: 760-770 (2021)

"Lessons Learned" from RV3-BB Work:
Enable More Rapid Formulation Development of Live Virus Vaccine Candidates

Improved experimental set-up

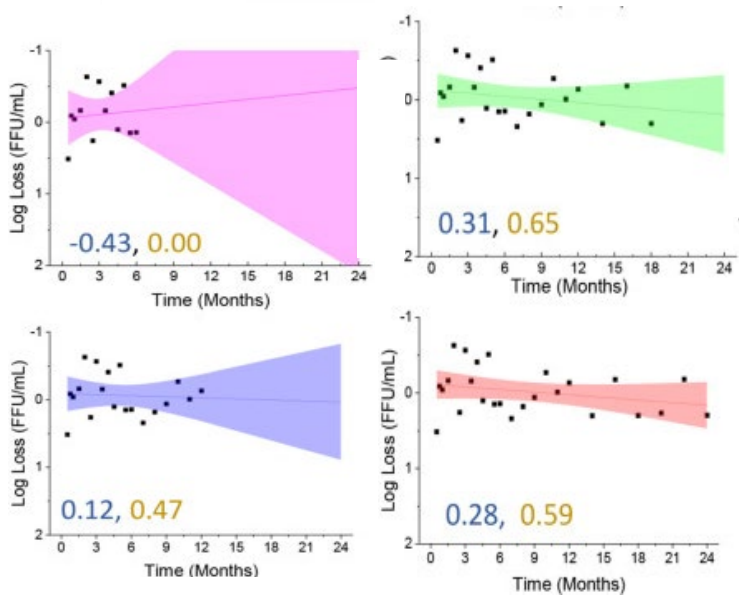


(1) high-throughput RT-qPCR assay to measure viral titers,

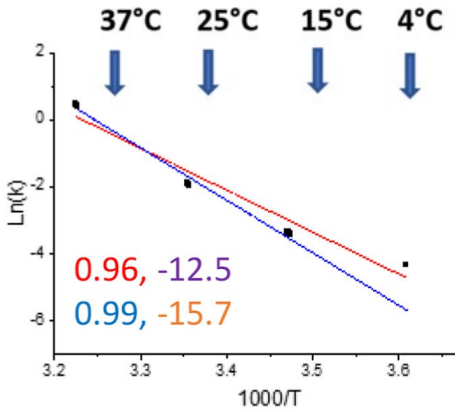
(2) additional assay replicates and stability time-points, and

(3) −80 °C control for each formulation to benchmark results at each stability time-point and temperature.

Extrapolation of real-time 2-8°C stability data



Arrhenius extrapolations of accelerated stability data



Pullagurla and Kumar *et al.*, *Biologicals* 75 :21 (2022)

Instead of accumulating two-year, 2–8 °C storage stability data

Same rank-ordering of the three RV3-BB formulations could have been achieved by modeling

- 37°C, 1 month
- 25°C, 3 month
- 15°C, 9-12 months
- 2-8°C, 12 months

Current Status of Live, RV3-BB Vaccine Candidate and Formulations

Completed Ph 2 dose ranging clinical trials in Africa

Lancet Infect Dis. 22(5):668-678 (2022)

Neonatal rotavirus vaccine (RV3-BB) immunogenicity and safety in a neonatal and infant administration schedule in Malawi: a randomised, double-blind, four-arm parallel group dose-ranging study

Ongoing Phase 3 clinical trials in Indonesia

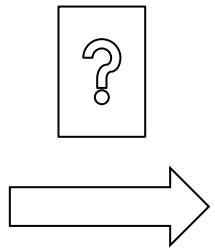
https://clinicaltrials.gov/ct2/show/NCT04185545

This phase III trial aims to assess the efficacy, safety and immunogenicity of Rotavirus RV3 Vaccine (Bio Farma) in neonates, lot-to-lot consistency, and antigen interference with co-administered EPI vaccines

Current Formulation (in Ph 2 and 3 clinical trials)

Prior to oral administration:

- Frozen Liquid that must be thawed
- Preneutralization with Mylanta



New Formulation (not implemented yet)

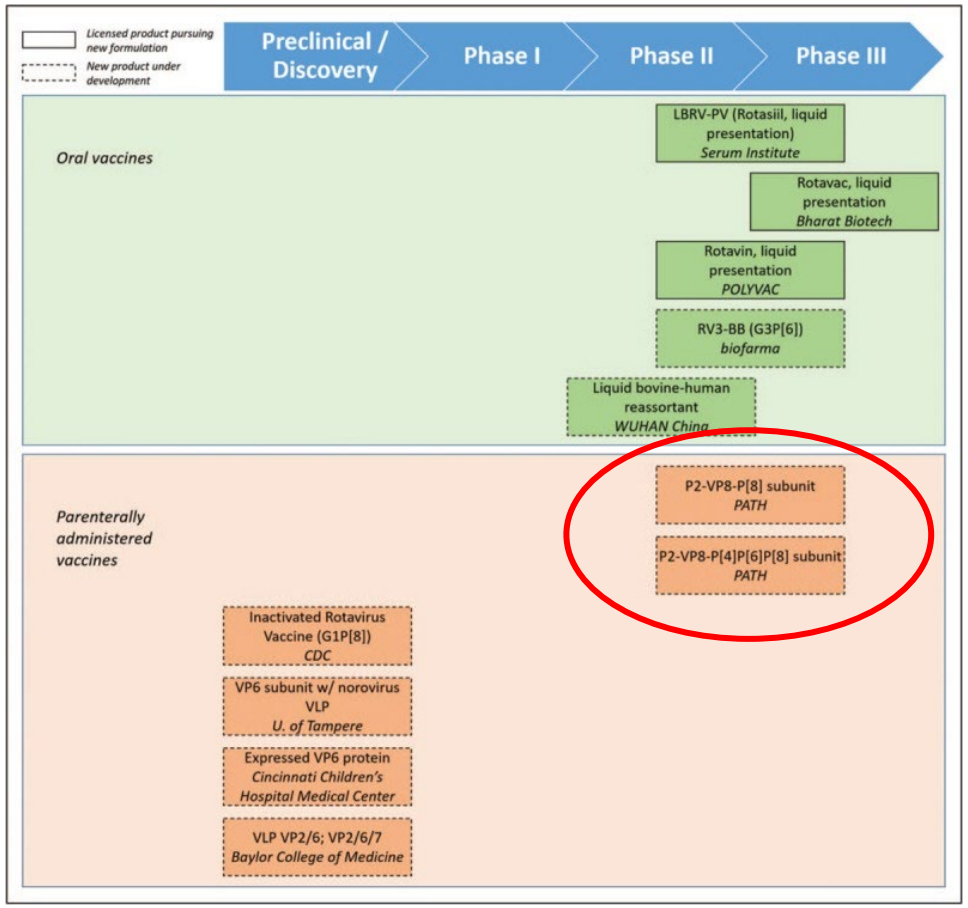
Ready to use:

Liquid, refrigerator stable

No preneutralization needed

Vaccine Formulation Case Study #3:

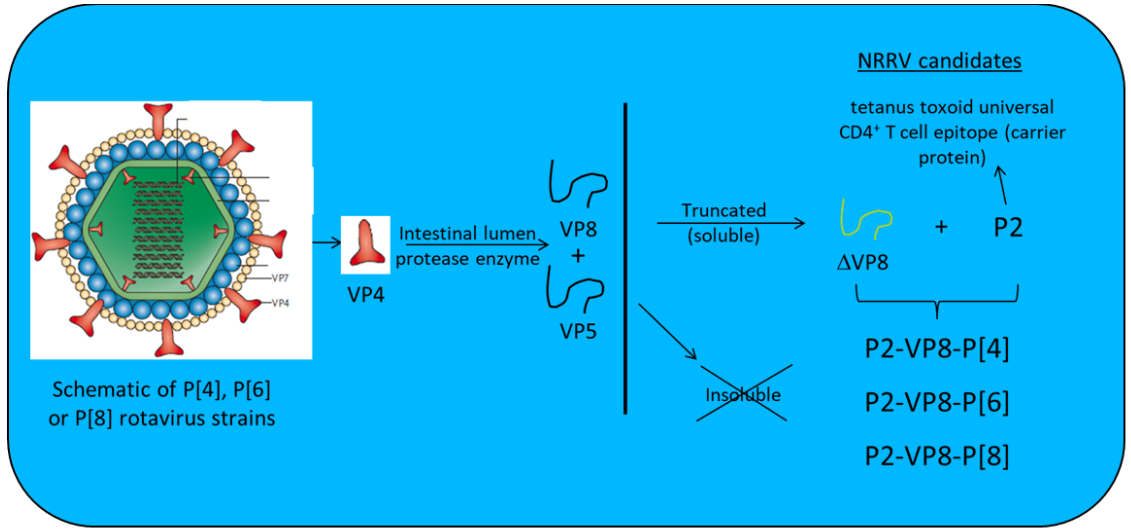
New Rotavirus Vaccine Candidates Targeted for Use in Low- and Middle- Income Countries (LMICs)



Curr Opin Inf Dis 32, 435-44 (2019)

Case study #3

Trivalent Recombinant protein formulated with aluminum adjuvant for injection



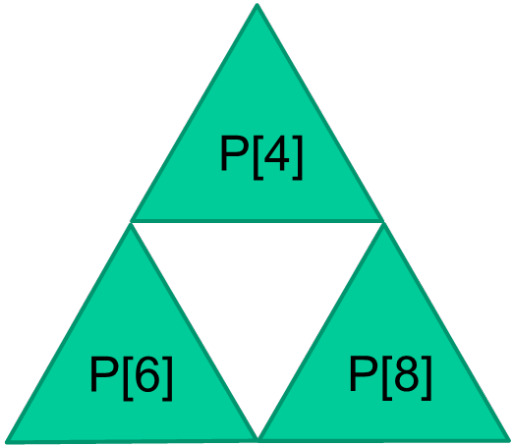
History of Development

- Discovered and designed by NIH
  - *Vaccine* 30 (2012) 6121
  - *Vaccine* 32 (2014) 4420
- Clinical and CMC development by PATH
  - *Vaccine* 33 (2015) 3766
  - *Lancet* 20 (2020) 851
  - *Human Vaccines & Immuno* 16 (2020) 1957
  - *J Immunol Methods* 494 (2021) 113056
- Analytical and formulation development performed at KU in collaboration with PATH
  - *J Pharm Sci.* 109 (2020) 380
  - *J Pharm Sci.* 109 (2020) 394
  - *J Pharm Sci.* 109 (2020) 476
  - *J Pharm Sci.* 110 (2021) 1042
  - *J Pharm Sci* 110 (2021) 1054
  - *J Pharm Sci* 111 (2022) 970

Funding from:
BILL & MELINDA GATES foundation

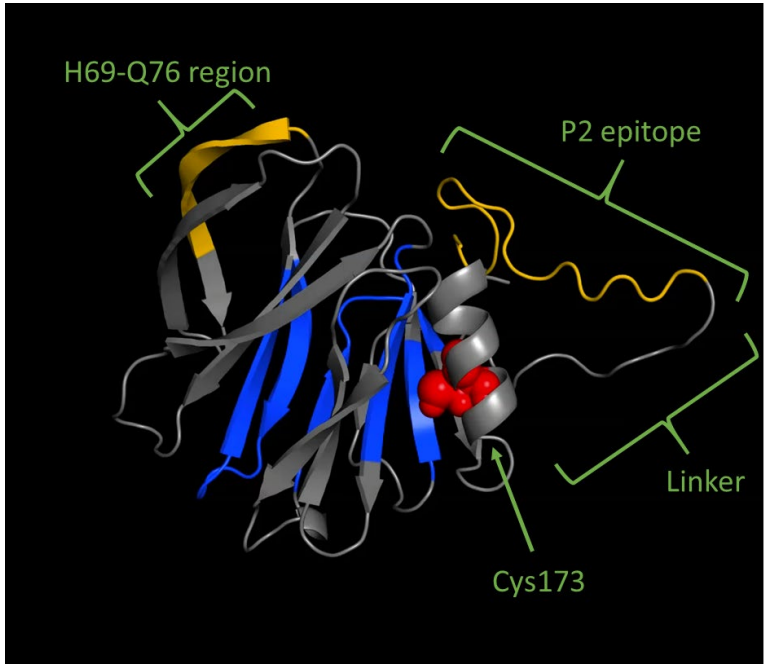
Structural Analysis and Preformulation Characterization of NRRV Antigens

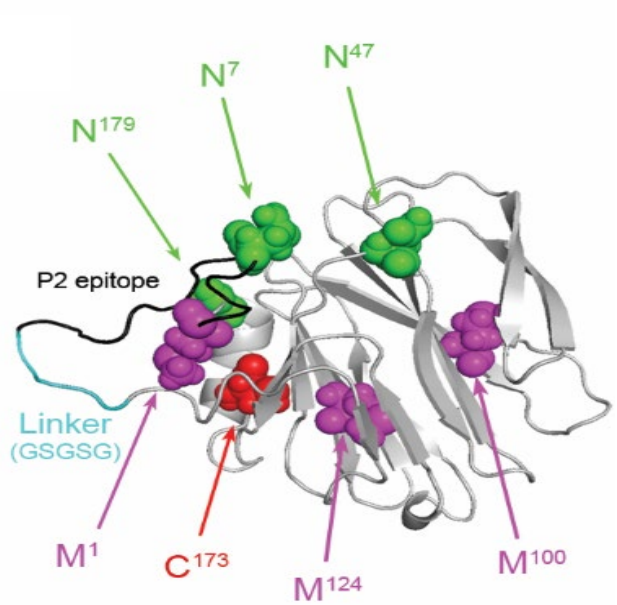
Trivalent NRRV vaccine antigens



1. X-ray structure of VP8-P4 available
2. Performed I-Tasser Modeling of P2-VP8-P4
3. Performed HDX-MS analysis of relative flexibility

Fast exchange region (higher flexibility)
Moderate exchange region (intermediate flexibility)
Slow exchange region (lower flexibility)





Labile Amino Acid Residues

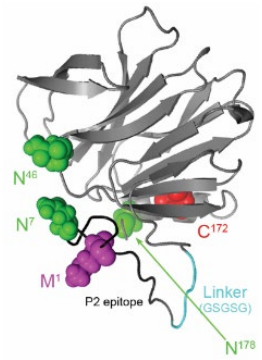
- Met^{1} most susceptible to oxidation followed by Met^{100} and Met^{124}
- Single Cys residue forms inter-molecular disulfide bonds
- Asn^{7} (and two Asn-Gly sites) deamidation

Agarwal S *et al.*, *J Pharm Sci* 109: 394 (2020)

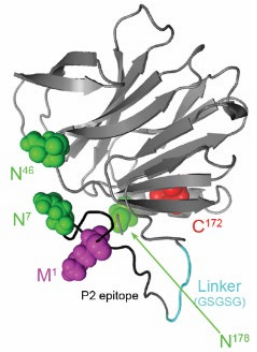
Kaur and Jiang *et al.*, *J Pharm Sci* 110: 1054 (2021)

Formulation of t-NRRV with Aluminum Adjuvants and Preservatives

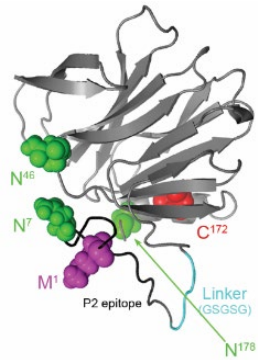
P[4]

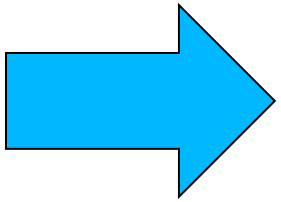


P[6]



P[8]





Vaccine Drug Product Goals:

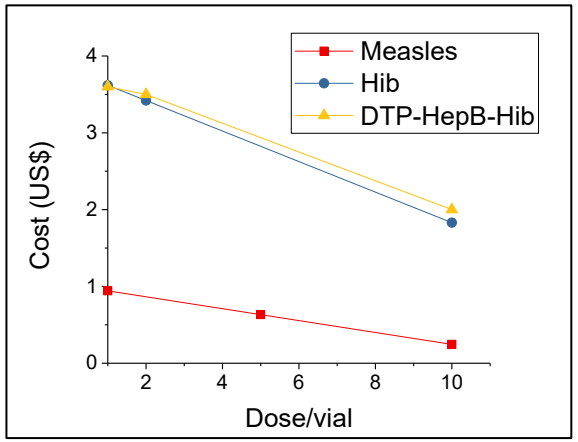
Liquid formulation, refrigerator stable, compatible with aluminum adjuvant and vaccine preservatives

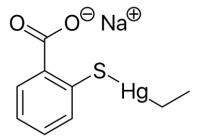
Alhydrogel®

- Aluminum hydroxide
- Long history of use in vaccines
- Readily available and low cost

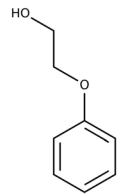
Antimicrobial preservatives

- Multidose vaccines lower costs
- TH and 2-PE most commonly used in vaccines





Thimerosal (TH)



2-phenoxy-ethanol (2-PE)

https://www.researchgate.net/figure/TEM-images-of-Alhydrogel-fig4_313433947

https://www.americanpharmaceuticalreview.com/Featured-Articles/358863

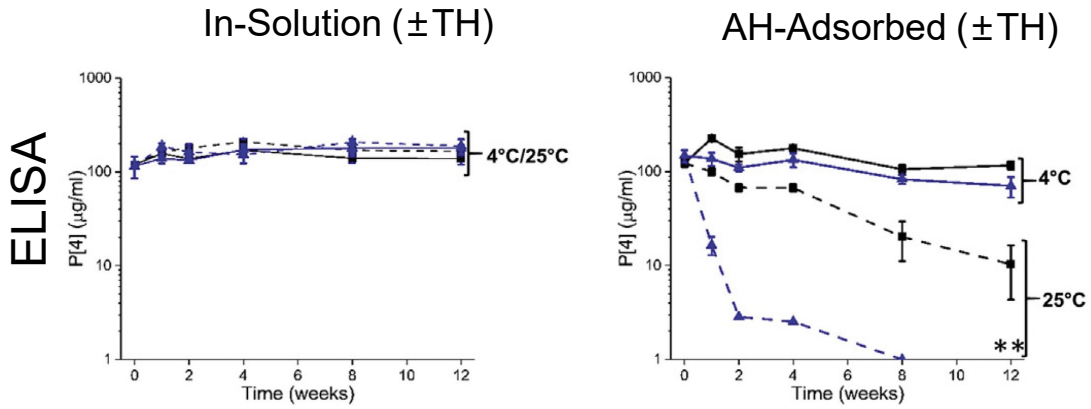
Adapted from: Lee *et al*, 2010 "Single versus Multi-Dose Vaccine Vials: An Economic Computational Model"

t-NRRV Vaccine Formulation Challenges using Alhydrogel Adjuvant and Preservatives

Alhydrogel improves immunogenicity but decreases storage stability at elevated temps

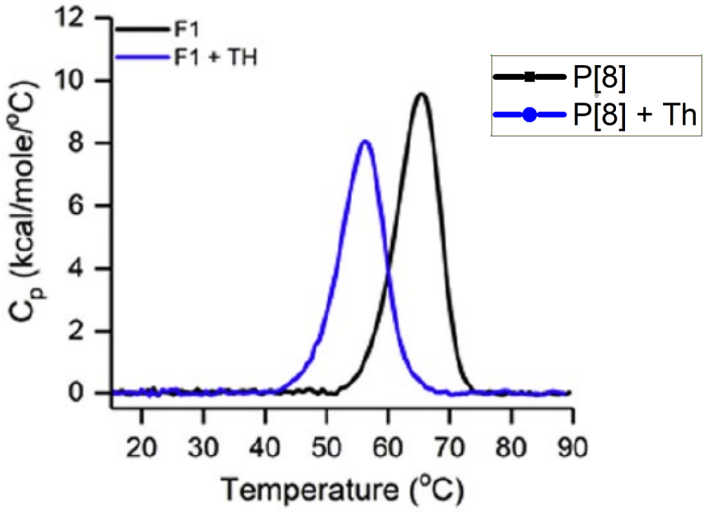
- Alhydrogel enhances immunogenicity of P2-VP8 compared to unadjuvanted in guinea pigs
- P2-VP8 adsorbs to Alhydrogel

Human Vaccines & Immuno 16 1957 (2020) (PATH)

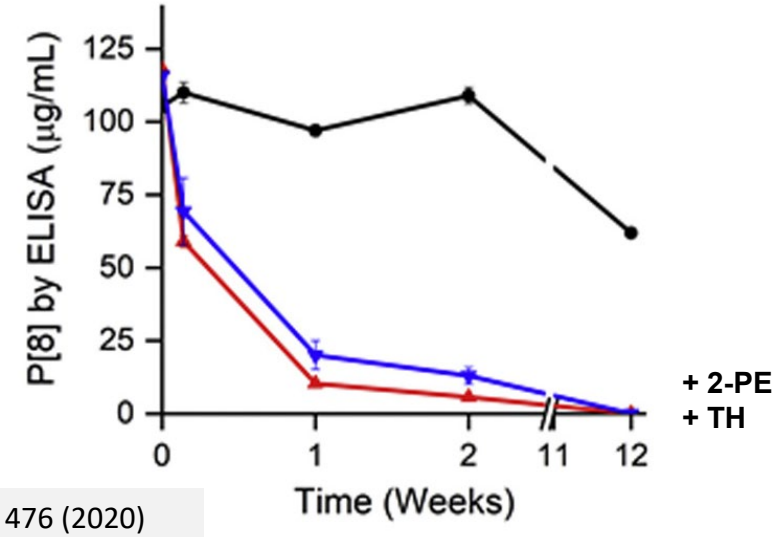


Sawant *et al.*, *J Pharm Sci* 110 1867 (2021)

Common Vaccine Preservatives Destabilize AH-adsorbed NRRV Antigens



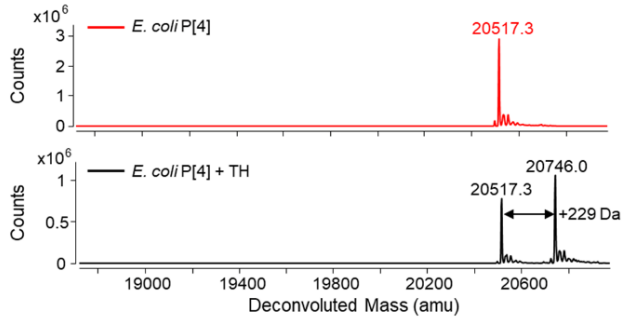
Accelerated Stability of AH-adsorbed P[8] (37˚C)



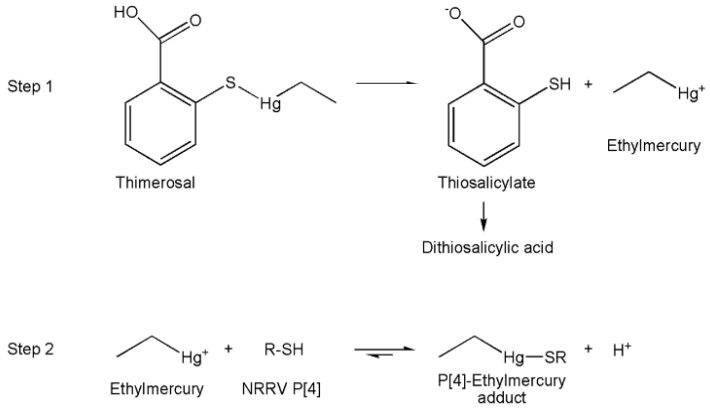
Agarwal *et al.*, *J Pharm Sci* 109 476 (2020)

Mechanistic understanding of thimerosal interaction with NRRV antigens using HX-MS

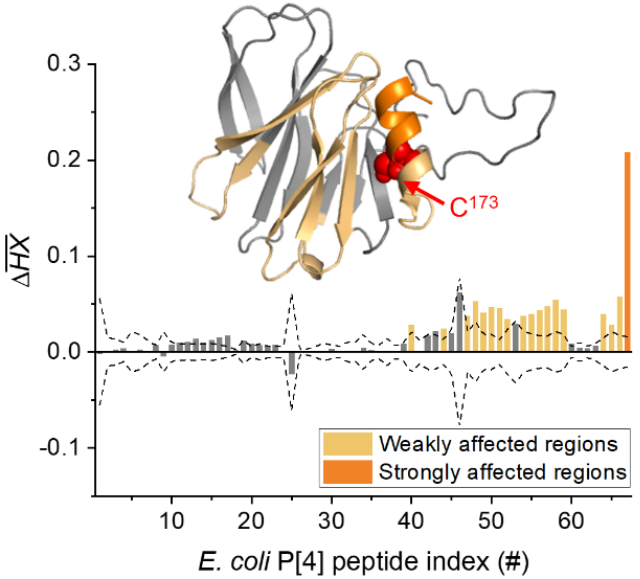
Intact MS



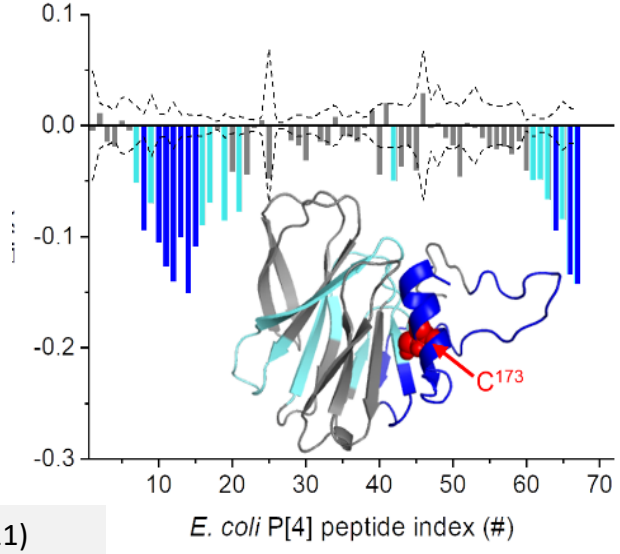
Proposed Mechanism



Thimerosal byproduct interacts with free SH group in P[4] antigen via partially reversible coordinate Hg-S bond



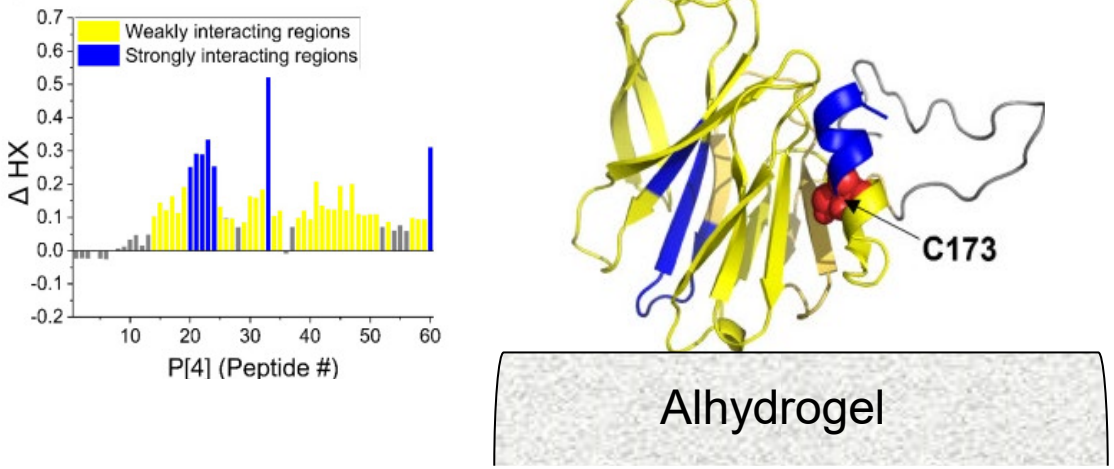
HX-MS analysis shows thimerosal interaction effects local flexibility of native P[4] antigen in region of free Cys residue



HX-MS epitope mapping shows conformational mAb binds to P[4] antigen in region of free Cys residue

Kaur and Jiang *et al.*, *J Pharm Sci* 110 1054 (2021)

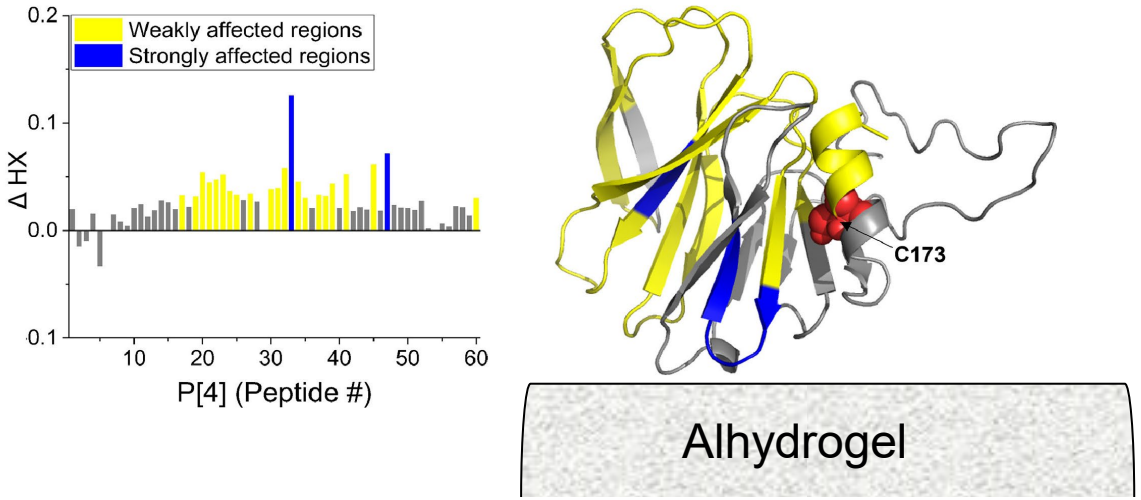
HX-MS as New Analytical Tool to Probe Antigen Stability on Surface of Alhydrogel



AH-adsorbed P[4] with TH

after 4 weeks at 4 ℃ (vs. time zero)

- Detect same TH induced destabilization sites on P[4]
- Additional sites of destabilized identified on P[4] upon AH-adsorption and storage



AH-adsorbed P[4] (no TH)

after 4 weeks at 25 ℃ (vs. 4 ℃)

- No effect at the TH induced destabilization sites on P[4]
- Additional sites of destabilized identified on P[4] upon AH-adsorption and 25°C storage

Sawant *et al.*, *J Pharm Sci* 111 970 (2022)

Current Status of t-NRRV Vaccine Candidate and Formulations

Completed Ph 2 clinical trials in South Africa

Lancet 20(5):851-863 (2020)

Safety and immunogenicity of a parenteral trivalent P2-VP8 subunit rotavirus vaccine: a multisite, randomised, double-blind, placebo-controlled trial

Ongoing Phase 3 clinical trials in Africa

https://clinicaltrials.gov/ct2/show/NCT04010448

A Phase 3 Double-blind, Randomized, Active Comparator-controlled, Group-sequential, Multinational Trial to Assess the Safety, Immunogenicity and Efficacy of a Trivalent Rotavirus P2-VP8 Subunit Vaccine in Prevention of Severe Rotavirus Gastroenteritis in Healthy Infants

Current Formulation (in Ph 2 and 3 clinical trials)

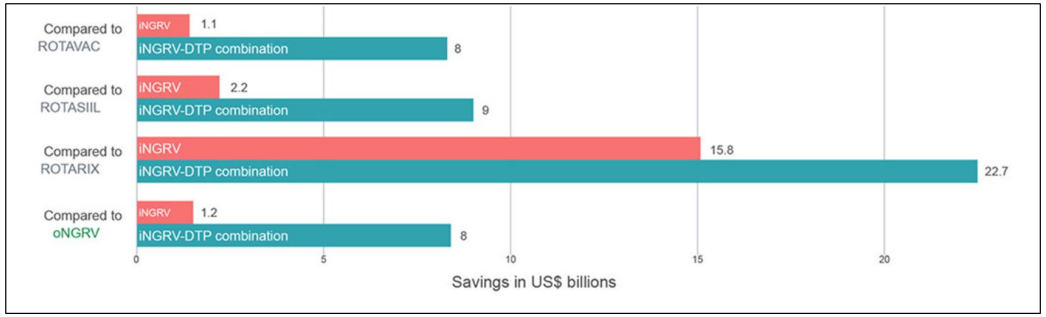
- Stand-alone t-NRRV formulated with Alhydrogel
- Single-dose formulation without preservatives (two-doses per container)

?

Ongoing formulation development work:

- Identify multidose formulations of NRRV
- Assess compatibility of NRRV with pediatric pentavalent combination vaccines

Significant cost savings of combination vaccine over stand alone t-NRRV



2022 *Human Vaccine and Immuno*-epub

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NRRV Vaccine Dev
NRRV (Low Cost Mfg)

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NRRV Vaccine Dev

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