TFF PHARMACEUTICALS

Better Delivery, Better Therapy:
Powerful Drug Delivery Solutions

Science Day | June 15, 2021 | **Nasdaq: TFFP**

Safe Harbor Statement

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This document contains forward-looking statements concerning TFF Pharmaceuticals, Inc. ("TFF", the "Company," "we," "us," and "our"). The words "believe," "may," "will," "potentially," "estimate," "continue," "anticipate," "intend," "could," "would," "project," "plan," "expect" and similar expressions that convey uncertainty of future events or outcomes are intended to identify forward-looking statements. These forward- looking statements include, but are not limited to, statements concerning the following:

- our future financial and operating results;
- our intentions, expectations and beliefs regarding anticipated growth, market penetration and trends in our business;
- the timing and success of our plan of commercialization;
- our ability to successfully develop and clinically test our product candidates; and
- our ability to file for FDA approval of our product candidates through the 505(b)(2) regulatory pathway.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially. Among those factors are: (i) no drug product incorporating the TFF platform has received FDA pre-market approval or otherwise been incorporated into a commercial drug product, (ii) the Company has no current agreements or understandings with any large pharmaceutical companies for the development of a drug product incorporating the TFF Platform and (iii) those other risks disclosed in the section "Risk Factors" included in the Company's 2020 Annual Report on Form 10-K filed March 10, 2021 with the SEC. TFF Pharmaceuticals cautions readers not to place undue reliance on any forward-looking statements. TFF Pharmaceuticals does not undertake, and specifically disclaims, any obligation to update or revise such statements to reflect new circumstances or unanticipated events as they occur, except as required by law.

This document contains only basic information concerning TFF. Because it is a summary it does not contain all of the information you should consider before investing. Please refer to our reports and registration statements on file with the SEC for more comprehensive information concerning TFF Pharmaceuticals.

Agenda

Glenn Mattes TFF Pharmaceuticals President & CEO	• Overview of TFF Pharma and pipeline • Speaker introduction
Deborah Jo Levine, M.D. UT Health San Antonio	• Lung transplantation: current procedure and treatment with tacrolimus and other therapies • Current shortcomings of therapies and current unmet medical need • Therapeutic potential of inhaled tacrolimus in lung transplantation
Kartik Chandran, Ph.D. Albert Einstein College of Medicine	• Using rVSV to treat COVID-19 • Application of TFF platform technology to multiple rVSV potential candidates
Ted Ross, Ph.D. University of Georgia	• Universal influenza vaccine • Application of TFF platform technology to a universal influenza vaccine
Question & Answer Session	• Following KOL presentations • Moderated by Corey Davis, Ph.D., Managing Director, LifeSci Advisors, LLC

Two-pronged Strategy
For Leveraging TFF Formulations
and Maximizing Value

TFF PHARMACEUTICALS

TFF Business Model

In-house Development

Identify opportunities that address significant unmet medical need, and/or lower risk clinical pathway via 505(b)(2):

- TFF Voriconazole (VIC) for IPA/ABPA
- **TFF Tacrolimus (TAC) for lung transplant and severe asthma**
- TFF Niclosamide for COVID-19 in early formulation development

Pharma Licensing Platform

Pursue R&D collaborations to provide direct-to-lung, intranasal, topical and intra-ocular delivery for oncology, COPD, PAH, CF, biologics, and combinations in multiple therapeutic indications

- **Academic vaccine partnerships – University of Georgia, Albert Einstein College of Medicine**
- National priority biodefence vaccines and countermeasures – USAMRIID, DARPA, and LEIDOS
- Monoclonal antibodies for COVID-19 – Augmenta Bioworks
- Bacteriophage-based biotherapeutic – Felix Biotechnology
- Cannabis market opportunity – PLUS Products

2021 Clinical Catalysts: Including NICLO and AUGMENTA

✓ Q1	TAC: 6-month tox completed, Phase 1 SAD dosing complete NICLO: Pre-IND submission, oral tox study start
✓ Q2	VORI: 13-week tox complete, reactive airway study topline data TAC: Phase 1 dosing complete/topline data NICLO: Inhaled tox study start, oral tox complete
Q3	AUGMENTA: Efficacy study VORI: 26-week GLP tox starts, EOP1 meeting AUGMENTA: Tox starts NICLO: Phase 1 (O and I) first dosing
Q4	VORI: Phase 2 first dosing TAC: Phase 1b/2a first dosing NICLO: Phase 1 (O and I) dosing complete

TFF PHARMACEUTICALS

Deborah Jo Levine, M.D. – UT Health San Antonio

Deborah Jo Levine, M.D. is Professor and Director of Inpatient and Outpatient Lung Transplantation, and Director of Pulmonary Hypertension Center with the UT Health San Antonio Long School of Medicine, where she regularly follows over 200 patients. Dr. Levine's research interests include antibody-mediated rejection in lung transplantation, critical care medicine, end-stage lung disease, interventional pulmonology, lung transplantation, organ donor management in the ICU, pulmonary disease, and pulmonary hypertension. She is Board Certified in critical care and internal medicine, and completed a fellowship in interventional pulmonology. Dr. Levine received her B.S. in Physiology from the University of California, and an M.S. in Pharmacology and Toxicology and M.D. degree from the University of Arizona College of Medicine.

Kartik Chandran, Ph.D. – Albert Einstein School of Medicine

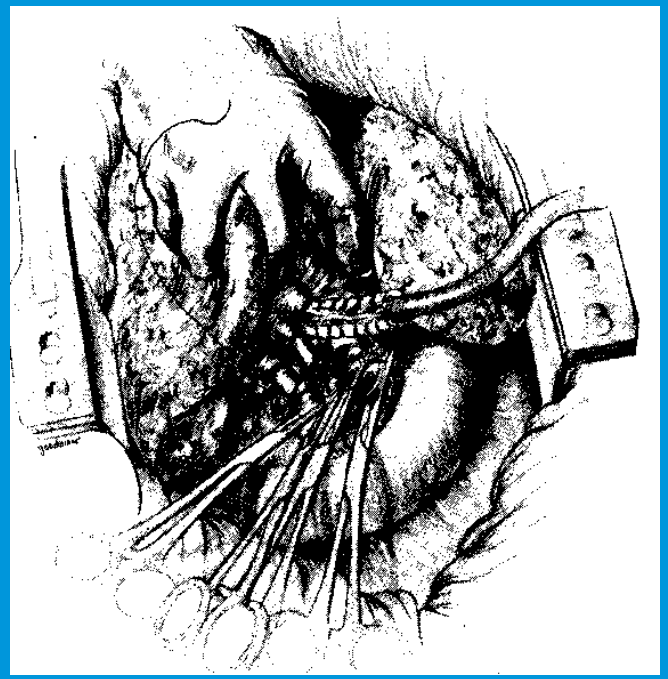
Kartik Chandran, Ph.D. is the Principal Investigator at The Chandran Lab, Professor of Medicine and Immunology, and The Harold and Muriel Block Faculty Scholar in Virology at the Albert Einstein School of Medicine. Dr. Chandran's research interests include merging viruses, Ebola and Marburg viruses, bunyaviruses, hantaviruses, viral entry into cells, structure and function of viral fusion glycoproteins, virus-host interactions, viral genetics, and the development of novel antiviral therapeutics. More specifically, his work at The Chandran Lab focuses on understanding the complex relationship between virus and cell and developing novel antiviral treatments directed against filoviruses, such as Ebola virus and Marburg virus, and hantaviruses, such as Sin Nombre virus and Hantaan virus. Dr. Chandran and his colleagues frequently partner with academia, industry, and government also focus on translational research to accelerate the development of novel small molecule and antibody-based therapeutics that leverage the basic knowledge on viral invasion. Most recently, the Chandran Lab is developing research tools to discover and optimize therapeutics against COVID-19 and is also directly involved in the development of convalescent plasma and human monoclonal antibody-based therapeutics to prevent and treat COVID-19.

Ted M. Ross, Ph.D. – University of Georgia

Ted M. Ross, Ph.D. is the Director of the Center for Vaccines and Immunology and Georgia Research Alliance Eminent Scholar and Professor of Infectious Diseases at the University of Georgia. Dr. Ross earned his undergraduate and graduate studies in Zoology and Microbiology at the University of Arkansas and he received a Doctorate in Microbiology and Immunology from Vanderbilt University in 1996. He was awarded the inaugural Sidney P. Colowick Award in Outstanding Graduate Research while at Vanderbilt. Dr. Ross performed post-doctoral fellowships at Duke University on HIV biology of viral entry and at Emory University on vaccine development for HIV and influenza viruses. He then started his own laboratory as Principal Investigator at East Carolina University and in 2003 moved the laboratory to the University of Pittsburgh in the Departments of Medicine-Infectious Diseases, Microbiology and Molecular Genetics, and as a founding member of the Center for Vaccine Research where he served the University for 10 years. In 2015, he joined the faculty at the University of Georgia. Dr. Ross explores new vaccine technologies intended to protect against all strains of influenza – an endeavor that could potentially eliminate the need for seasonal flu shots. Dr. Ross and his colleagues are applying similar strategies to fight other serious viruses such as, Dengue, Zika, Ebola, Chikungunya, and HIV Type-1 viruses.

Dr. Ross has published more than 130 papers and book chapters on infectious disease and vaccine development. He has been an invited speaker at more than 130 national and international conferences and participates in several vaccine working groups, including at the U.S. NIH, U.S. Centers for Disease Control and Prevention and the World Health Organization. He is an editorial 100 board member of Vaccine. He previously served as Editor-in-Chief of the journal Current HIV Research. In addition, he has been an ad-hoc reviewer on NIH study sections and a reviewer for 24 different journals.

Dr. Ross served as the Treasurer and Secretary of International Society for Vaccines from 2012-2017 and now is the current President-Elect (elected 2018) and has served as the Co-Chair of the 8th and 9th Vaccine and ISV Congress in Philadelphia (8th) and Seoul (9th).



Lung Transplantation

Deborah Jo Levine MD FCCP
University of Texas Health
San Antonio

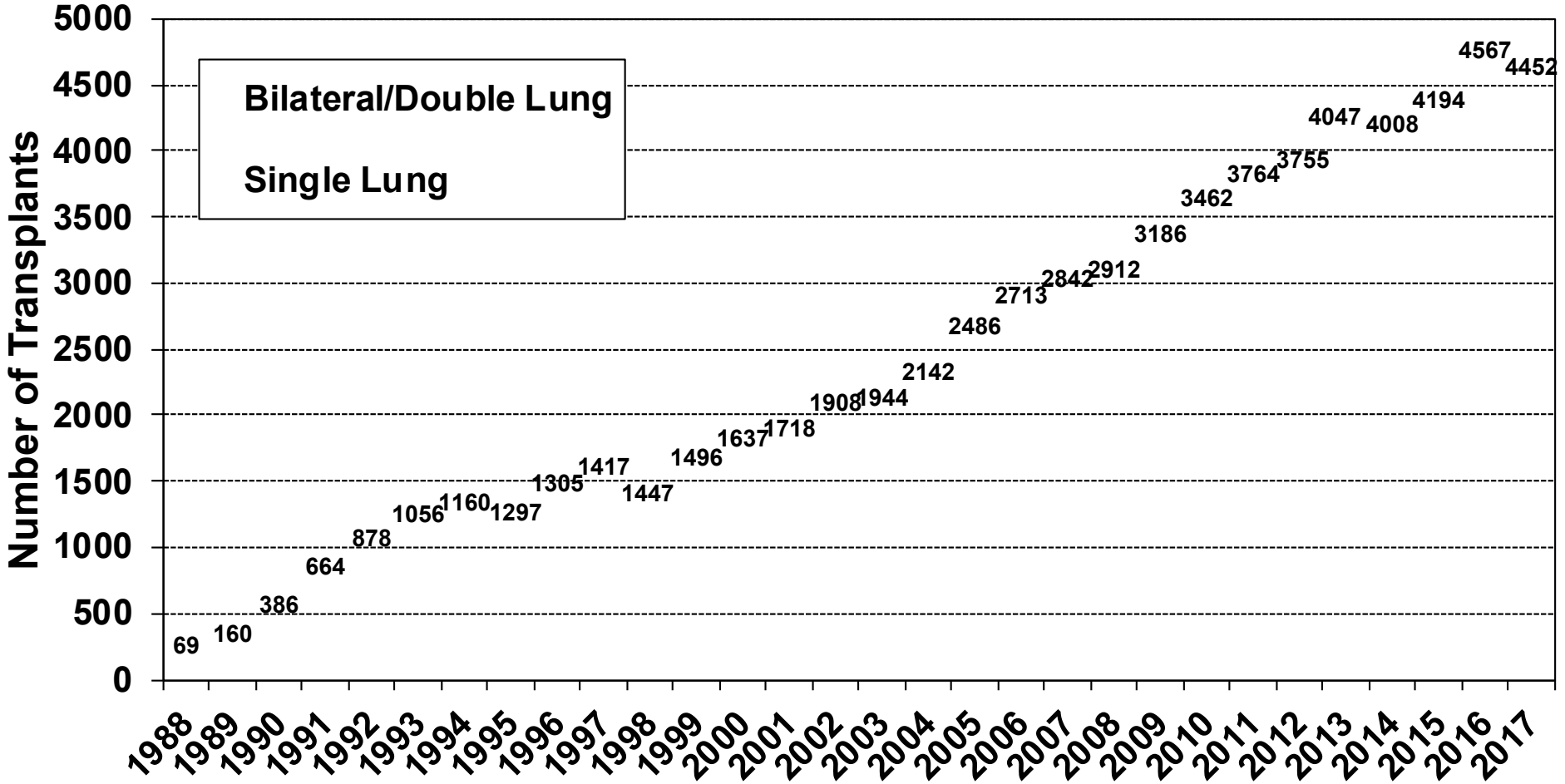
Reasons for Lung Transplant

Lung Transplantation (LT) continues to be the best therapy for some patients with end-stage lung disease for which other medical or surgical therapy is not available.

Underlying Diseases

- Restrictive Lung Disease
  - Idiopathic Pulmonary Fibrosis (IPF)
  - Interstitial Lung Disease (ILD)
- Obstructive Lung Disease
  - Chronic Obstructive Pulmonary Disease (COPD)
- Cystic Fibrosis and other suppurative lung disease
- Pulmonary Vascular Disease
  - Pulmonary Arterial Hypertension (PAH)

Annual Lung Transplants Performed

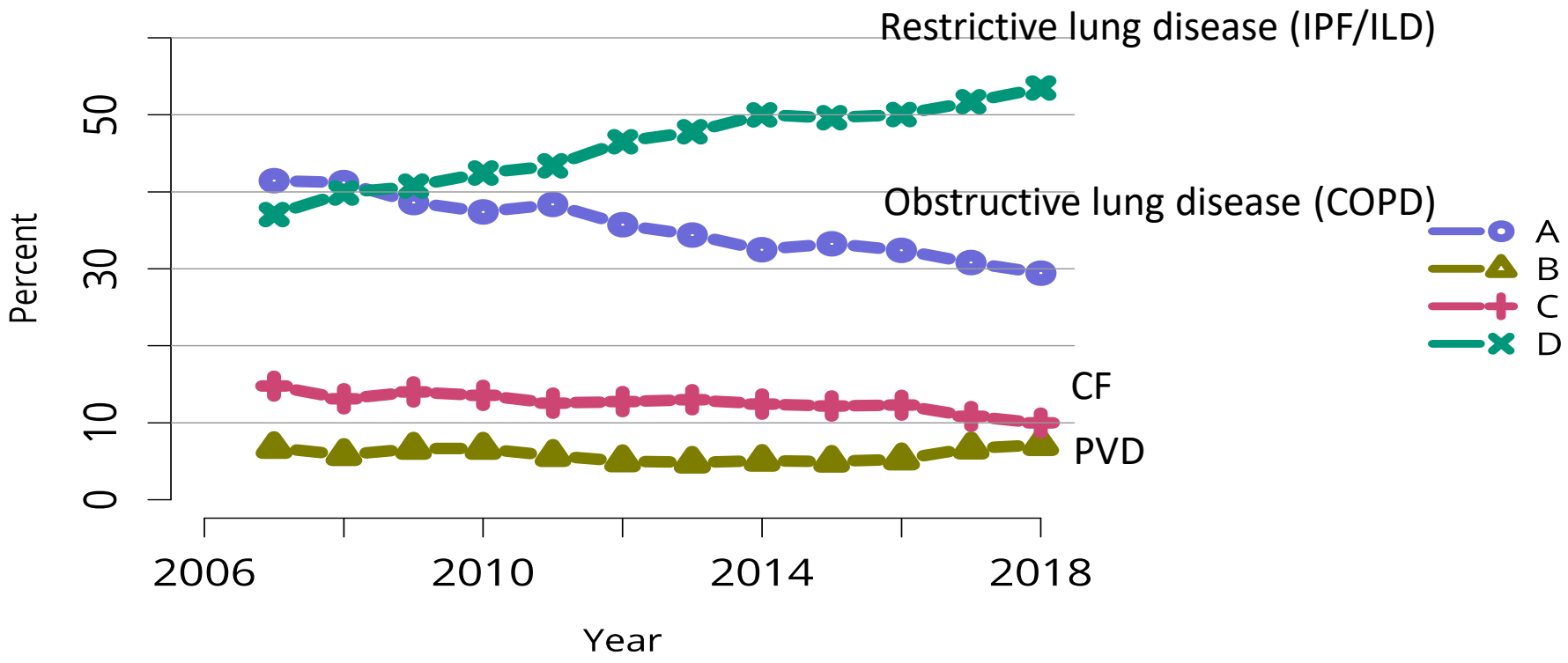


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

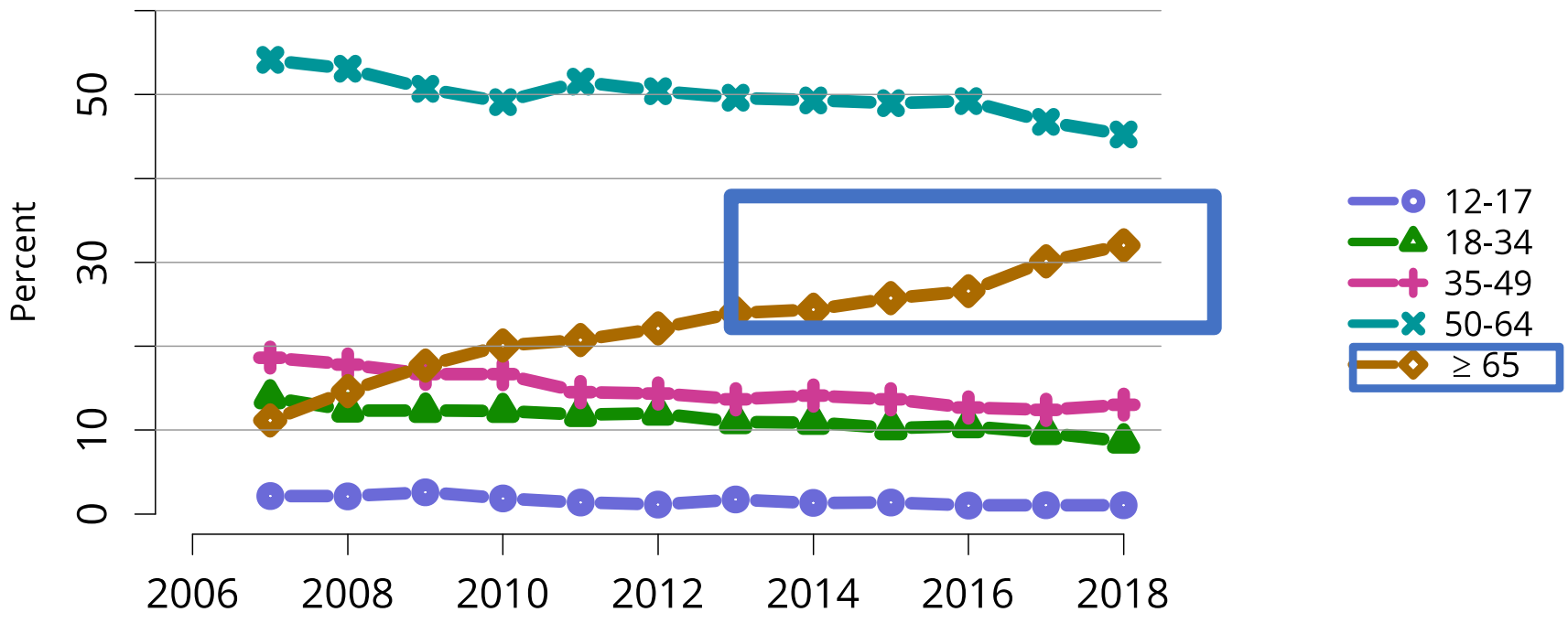
JHLT. 2019 Oct; 38(10): 1015-1066

NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.

Distribution of candidates aged 12 years or older actively waiting for lung transplant by diagnosis group

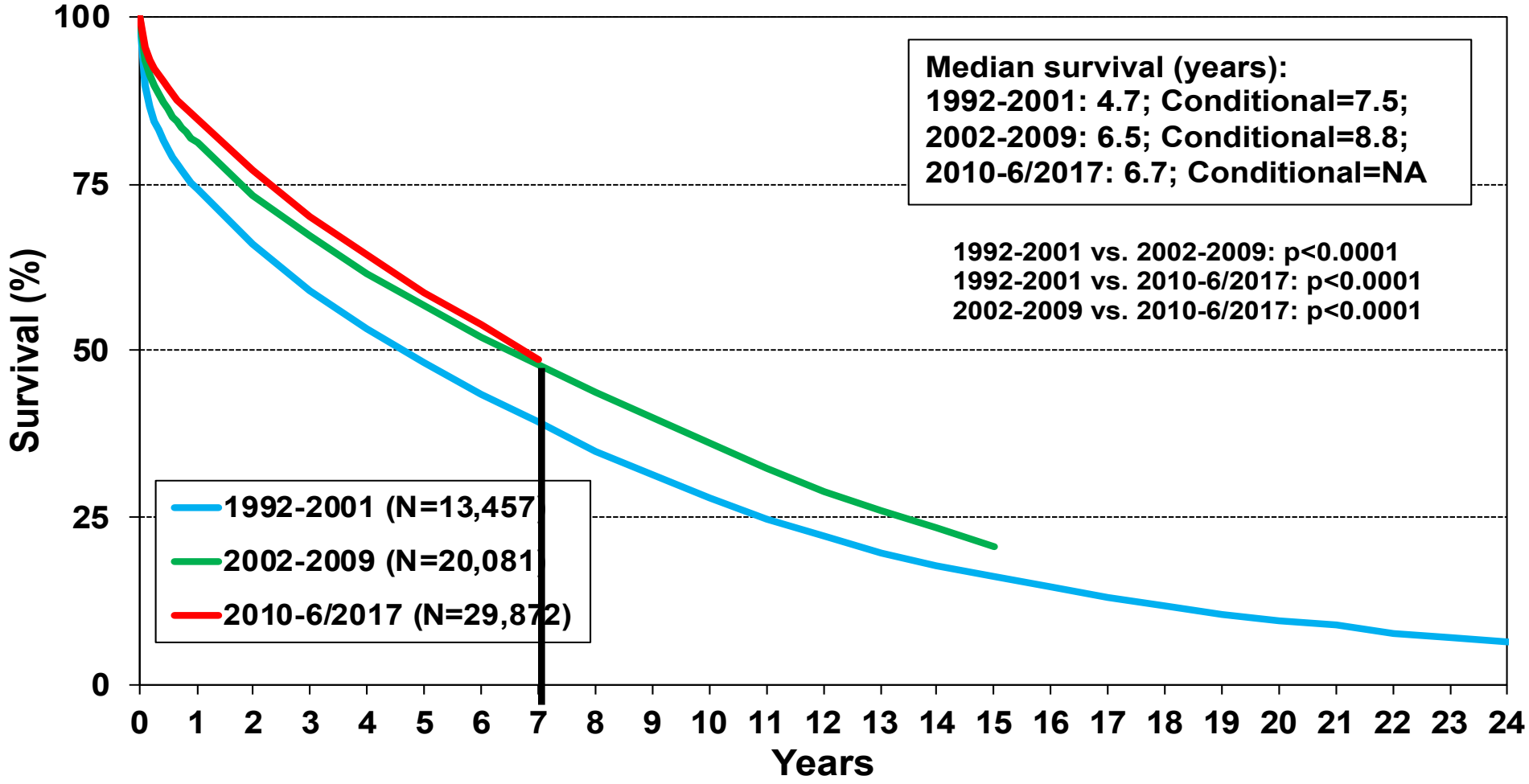


Distribution of candidates aged 12 years or older actively waiting for lung transplantation



SRTR 2020

Adult Lung Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1992 – June 2017)

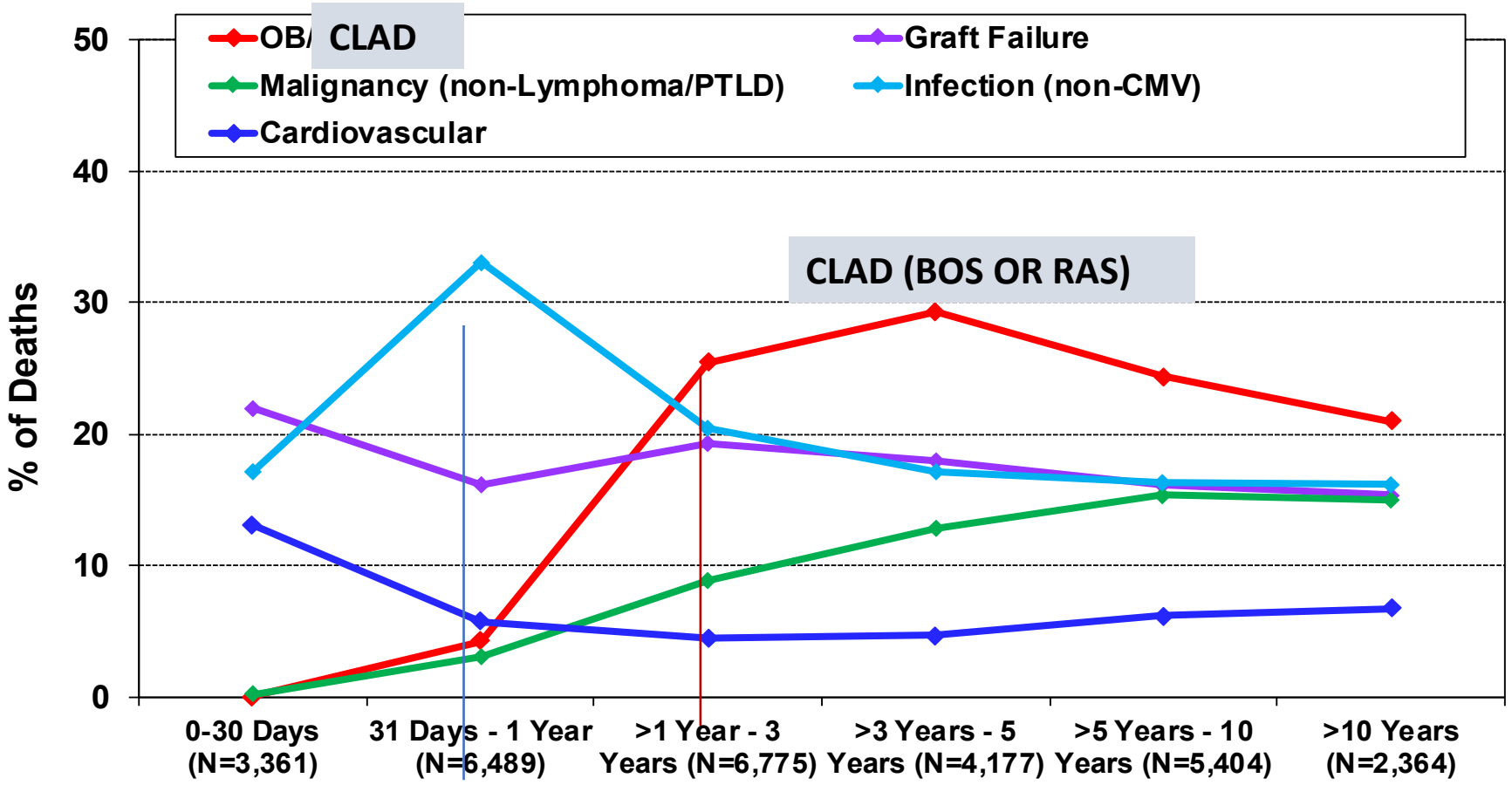


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2019
JHLT. 2019 Oct; 38(10): 1015-1066

Adult Lung Transplants

Relative Incidence of Leading Causes of Death

(Deaths: January 1995 – June 2018)



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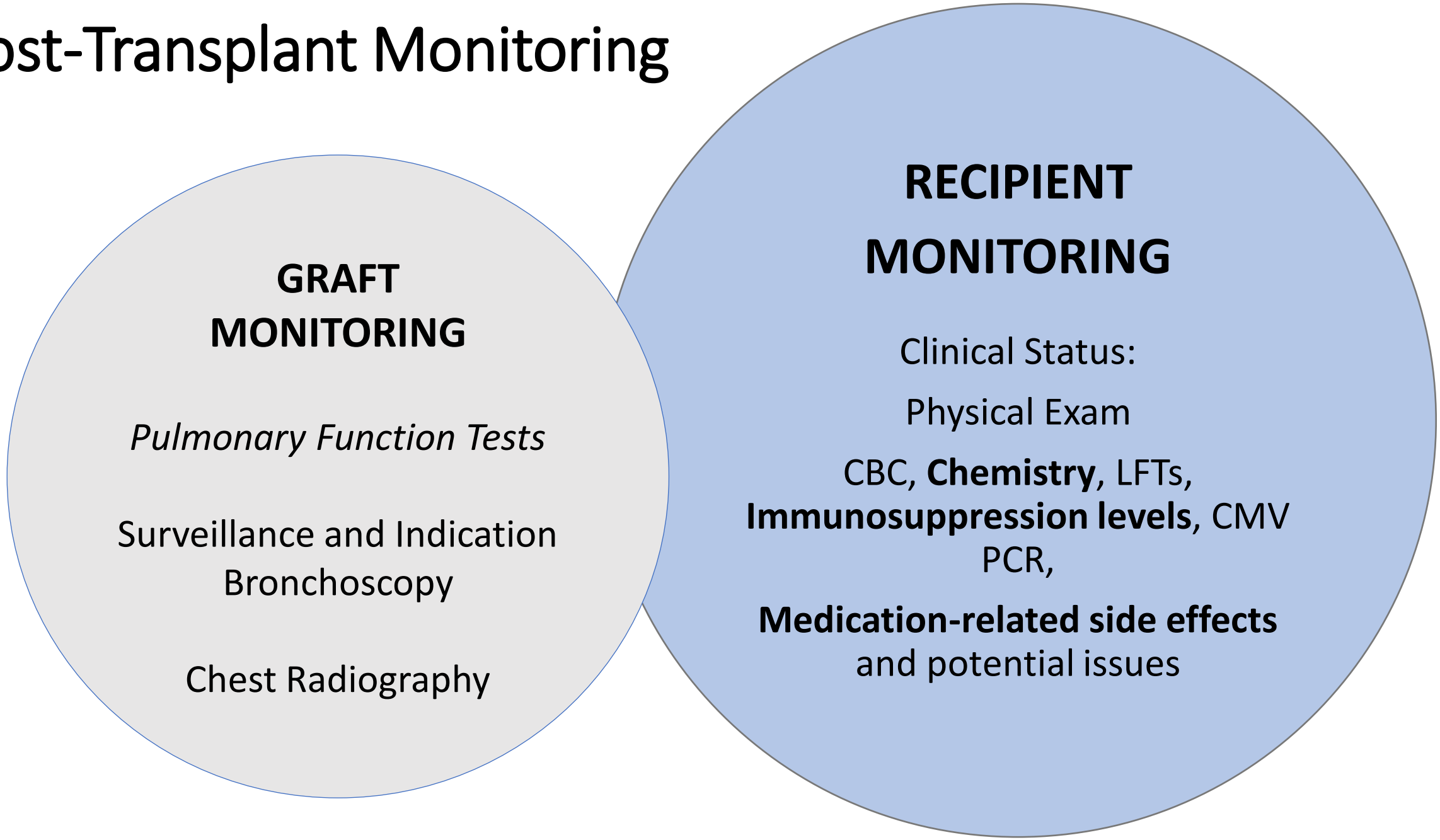
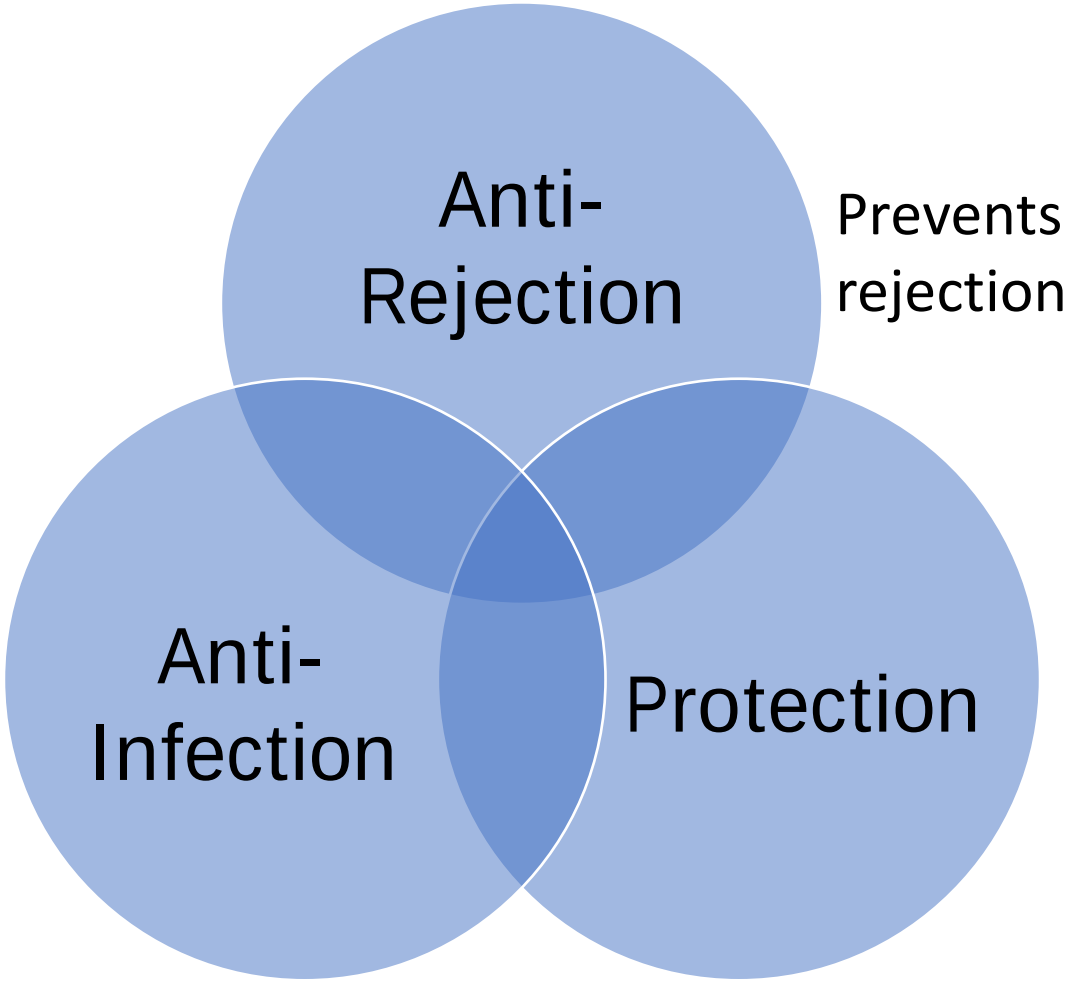
Post-Transplant Monitoring



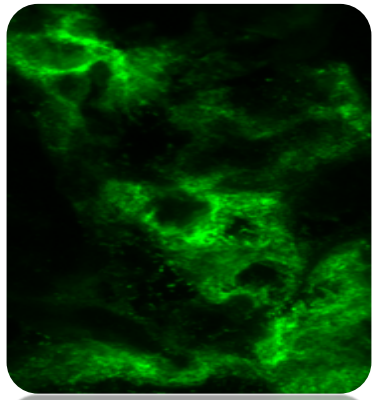
Categories of Medications Used in Transplant Patients

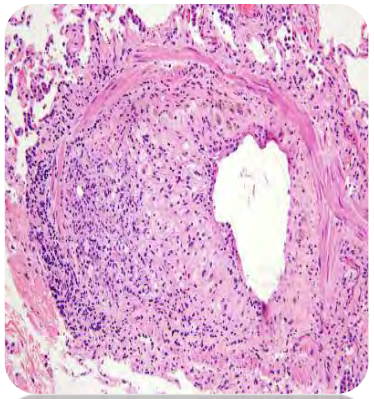


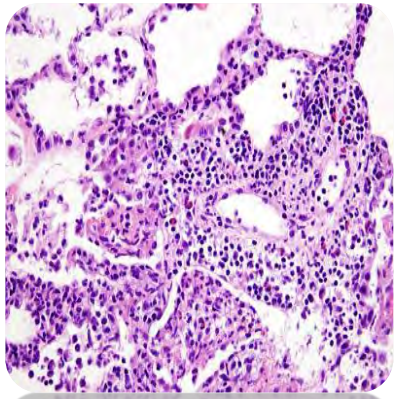
Prevents host rejection of organ

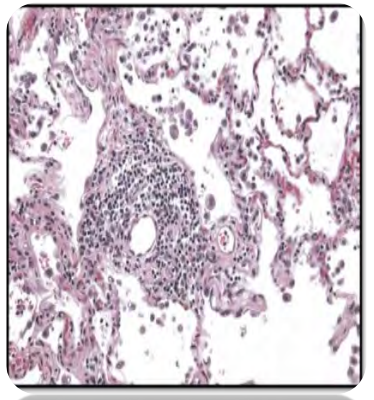
Anti-rejection drugs increase susceptibility to infection

Protect other organs from damage









Lung Allograft Rejection

Acute Cellular Rejection (ACR)

Acute Antibody Mediated Rejection (AMR)

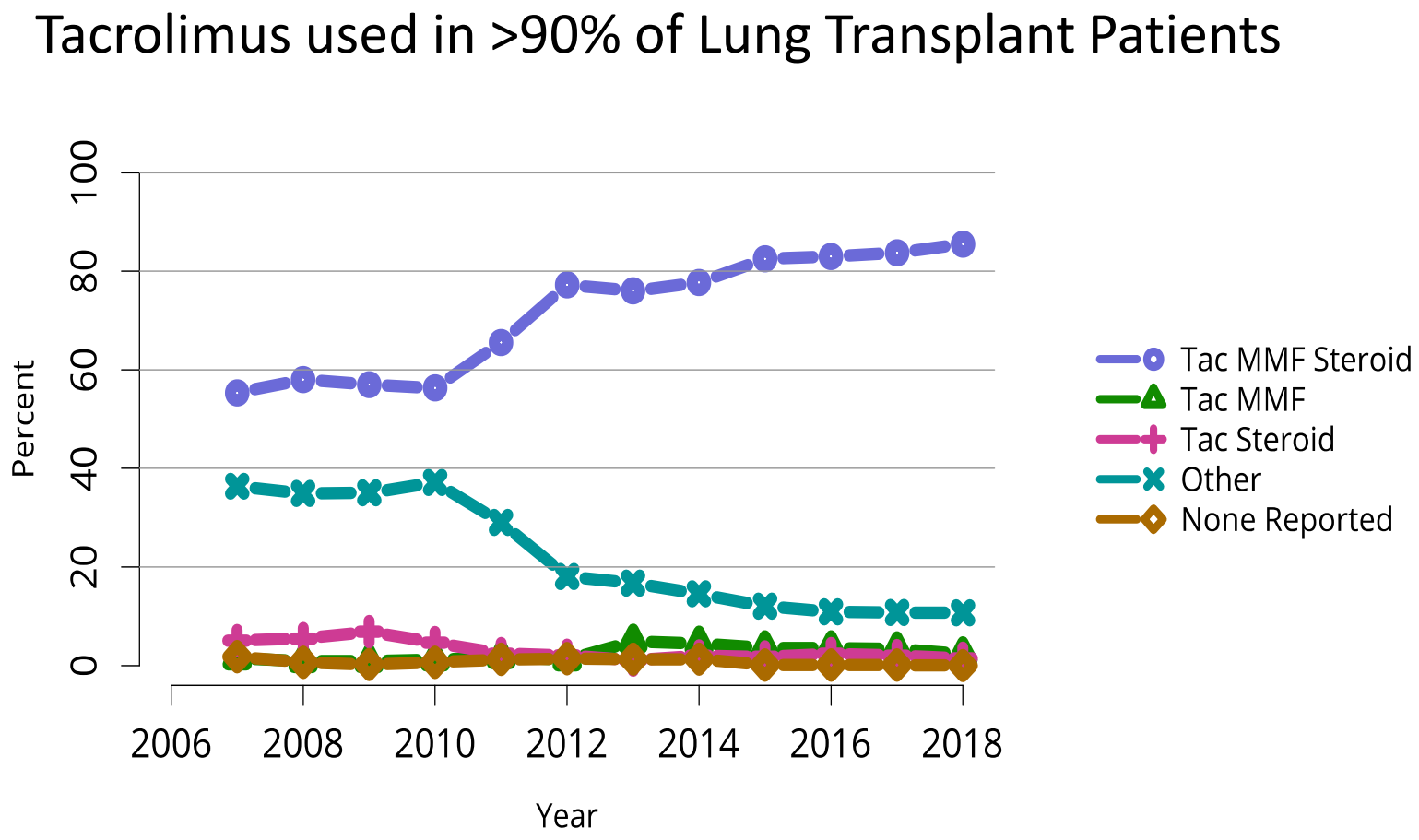
Chronic Lung Allograft Dysfunction (CLAD)
Bronchiolitis obliterans Syndrome (BOS)
Restrictive Allograft Syndrome (RAS)

Preventing Rejection: Maintenance Immunosuppression

- Calcineurin inhibitors
  - Tacrolimus
  - Cyclosporine
- Corticosteroids
  - Methylprednisolone
  - Prednisone
  - Prednisolone

- DNA synthesis inhibitors
  - Mycophenolate mofetil
  - Azathioprine
- mTOR inhibitors
  - Sirolimus (Rapamune®)
- Others: Belatacept, etc

Immunosuppression regimen use in transplant recipients



Tacrolimus adverse effects

- Lymphoma and Other Malignancies
- Serious Infections
- New Onset Diabetes After Transplant
- **Nephrotoxicity**
- Neurotoxicity
- Hyperkalemia
- Hypertension
- Anaphylactic Reactions with PROGRAF Injection
- Myocardial Hypertrophy
- Pure Red Cell Aplasia

Adult Lung transplants
Cumulative Morbidity Rates in Survivors within 1 and 5 Years
(Transplants: January 1994 – June 2016)

Outcome	Within 1 Year	Total number with known response	Within 5 Years	Total number with known response
Severe Renal Dysfunction*	8.4%	(N = 787)	20.9%	(N = 277)
Creatinine > 2.5 mg/dl (221 µmol/L)	*5.3%*		*13.0%*	
Chronic Dialysis	*2.8%*		*5.8%*	
Renal Transplant	*0.3%*		*2.2%*	
Diabetes	17.6%	(N = 790)	31.6%	(N = 272)
Bronchiolitis Obliterans Syndrome	14.7%	(N = 748)	49.1%	(N = 228)

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*** Severe renal dysfunction = Creatinine > 2.5 mg/dl (221 µmol/L), dialysis or renal transplant**

Risk factors for Acute Kidney Injury

Pre-transplant

- Higher lung allocation score
- Pulmonary Hypertension
- LT for diagnoses other than COPD
- Re-transplant
- Older patients
- Higher baseline creatinine, proteinuria, AKI episodes
- Connective tissue disease
- Cystic fibrosis
- Pre-transplant ECMO or mechanical ventilation

Post- transplant

- Hypotension/hemodynamic insufficiency
- Prolonged duration of cardiopulmonary bypass
- Duration of mechanical ventilation/ECMO
- Medications: Calcineurin Inhibitors (**Tacrolimus, cyclosporine**), antibiotics, antifungals, antivirals, radiographic contrast, diuretics
- DM
- Sepsis

Drug-drug interactions (DDI) with Tacrolimus

- <u>CYP3A4 enzyme inhibitors:</u>
- Increase calcineurin inhibitor levels *(increased toxicity)*
  - Macrolides, **Azole Antifungals,** Calcium channel blockers, Grapefruit juice

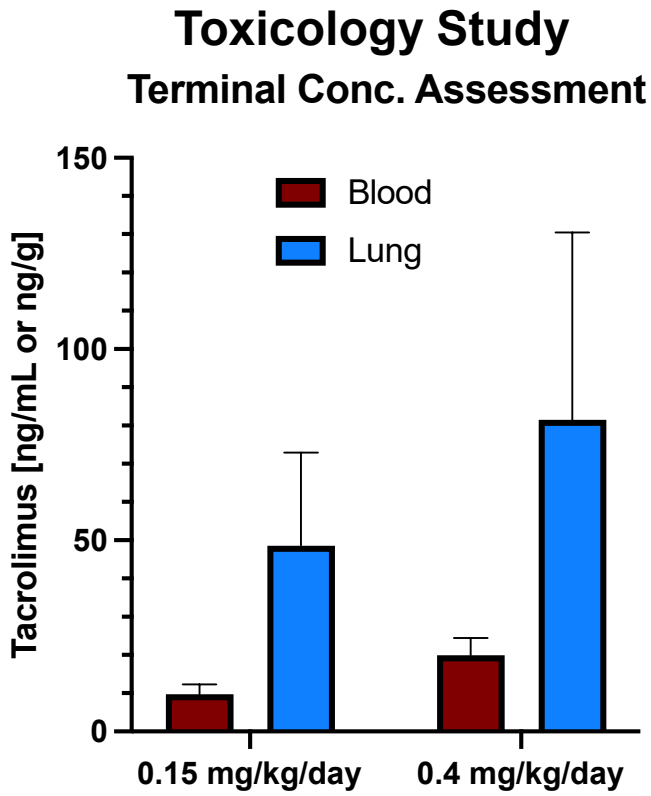
- <u>CYP3A4 enzyme inducers:</u>
- Decrease calcineurin inhibitor levels *(decreased efficacy)*
  - Rifampin, Carbamazepine, phenobarbital, phenytoin
  - St. John's wort

- Statins: Increased statin levels with CY3A4

TFF's Tacrolimus Product Development

Potential Advantages of TFF Tacrolimus Powder

- **May improve compliance with reduced GI adverse events.**
- **May provide higher PK trough concentrations at lower dose.**
- **May indicate that once a day dosing is a feasible dosing strategy with lower drug burden.**
- **May be 3-fold higher in absorption by the inhaled route compared to oral administration.**
- **Drug levels in Lung Tissue greater than blood for improved tissue immunosuppression with less systemic exposure (toxicology study results support this concept) ---------->**



Tacrolimus Inhalation Powder

Phase I HNV Study Design

Part A: SAD

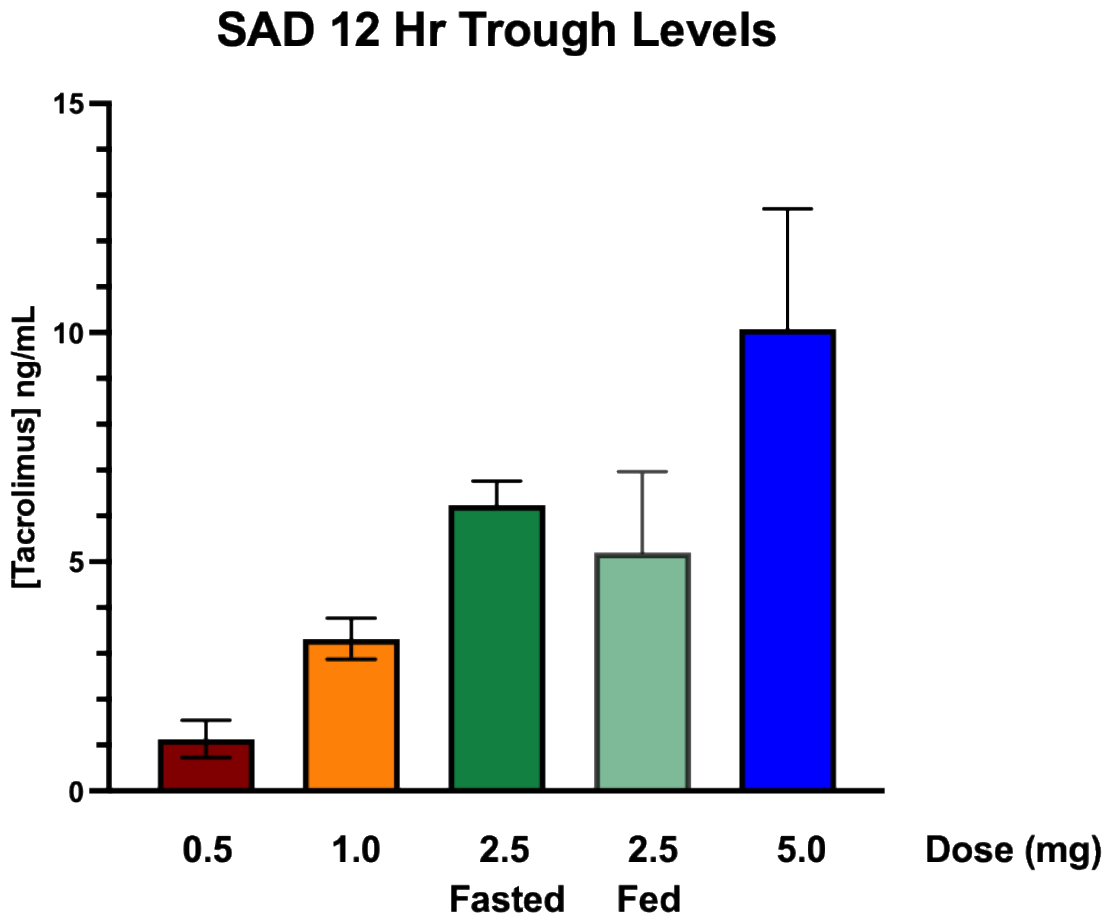
- Normal volunteers
- Single inhaled dose
- 6+2 volunteers per cohort
- 5 escalating dose levels (0.5, 1.0, 2.5, 5.0, and 10.0 mg)
- Endpoints:
  - Blood exposure
  - Tolerability
  - Effects of a high fat meal on blood exposure
  - Effect on IL-2 and IL-6 biomarkers

Part B: MAD

- Normal volunteers
- Inhaled dosing 2x/day – 7 Days
- 8 volunteers per cohort
- 3 dose levels (BID: 1.0, 0.5mg QD: TBD)
- Endpoints:
  - Blood exposure (Day 1 & 7)
  - Tolerability
  - Effect on IL-2 and IL-6 biomarkers

Tacrolimus Phase 1 – Therapeutic Drug Levels

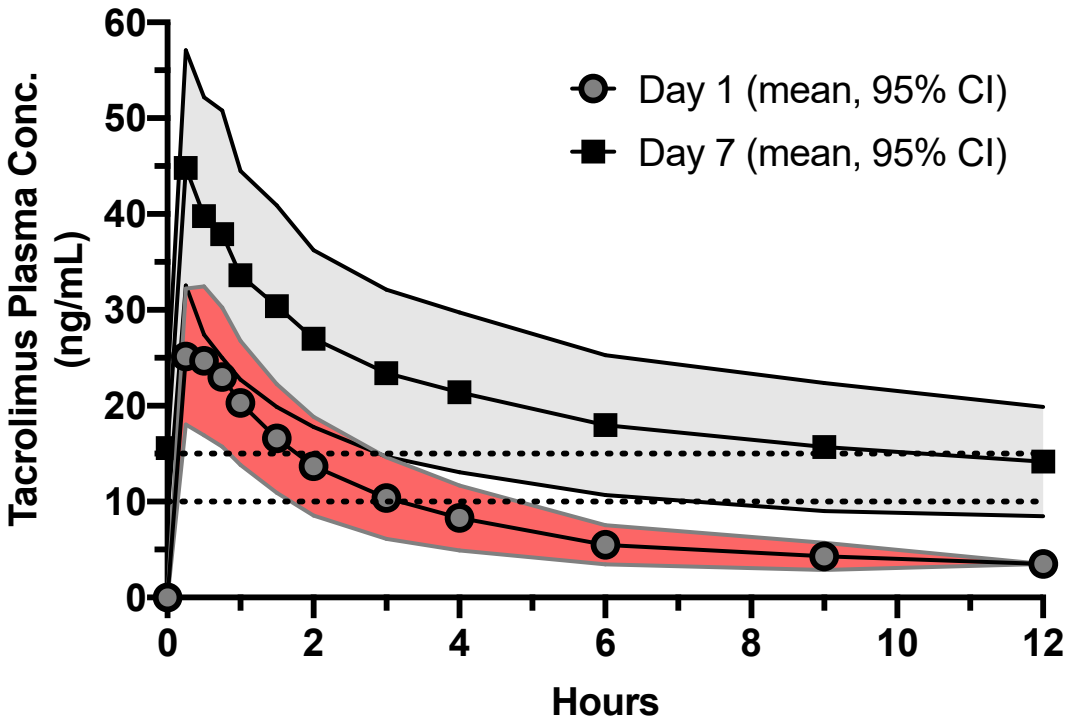
- Blood levels measured 12 hr after dose administration
- Target dose levels for lung transplant patients



Tacrolimus Development: Phase 1 Repeat Dose PK Profile

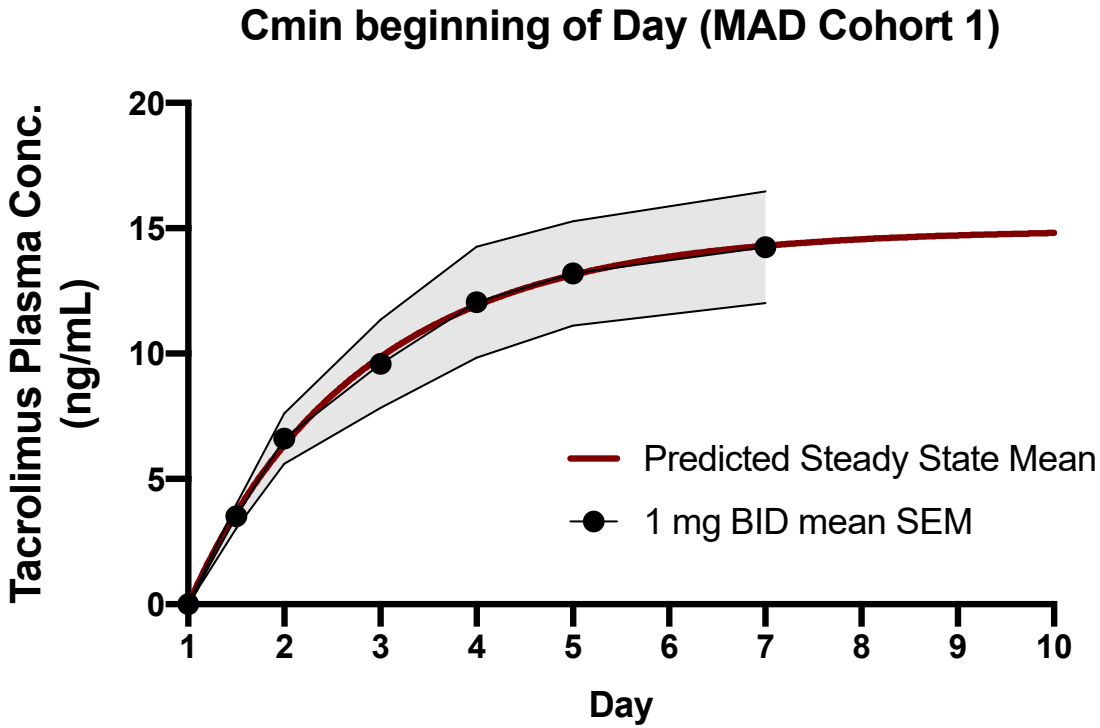
Tacrolimus Plasma Exposure after Inhalation of a 1 mg dose BID

Day 1 and Day 7 (TFF-T1-001)



N=6 subjects/ time point
Mean (95% CI) for Day 1 and Day 7 (BID)
Target Cmin range presented at 10 – 15 ng/mL

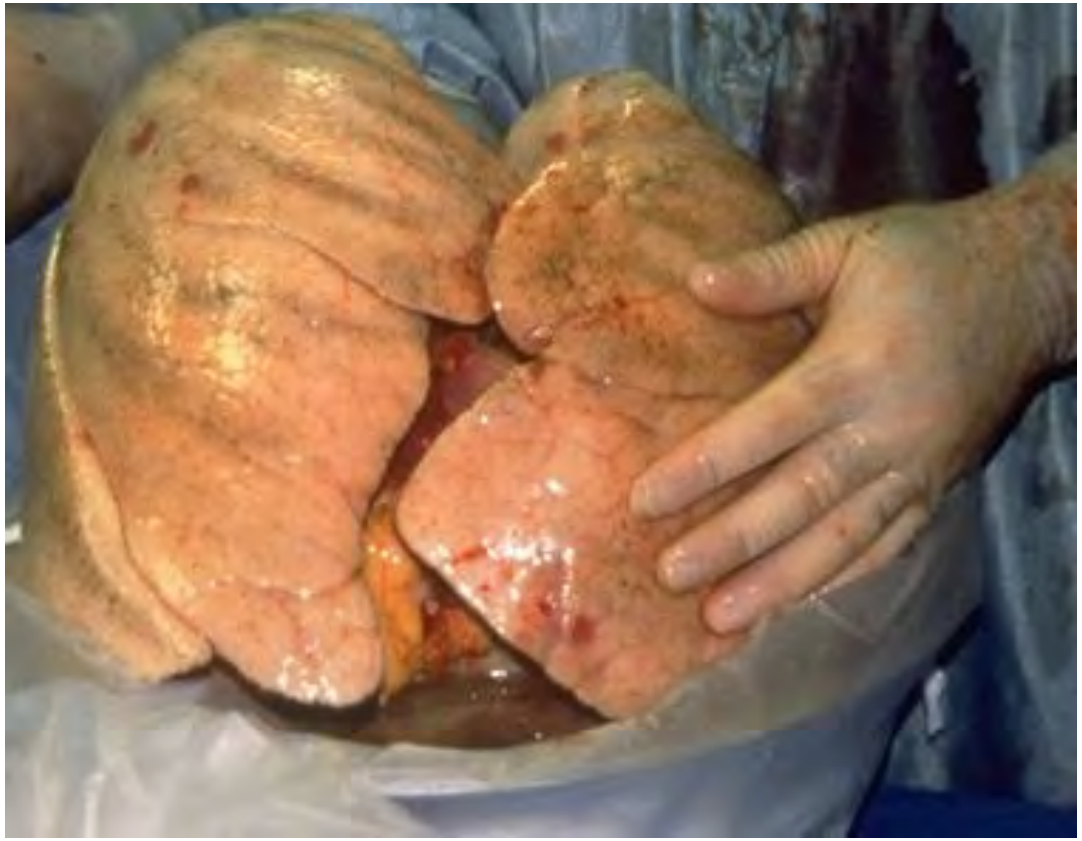
Tacrolimus Plasma Exposure C_{min} through Day 7 (TFF-T1-001)



Whole blood C12h median conc. – 9.5 ng/mL

Tacrolimus Inhalation Powder Potential

- Less susceptible to drug-drug interactions
- May provide higher trough concentrations at lower total dose
- Provide more drug in the lung with lower blood concentration to enhance efficacy while reducing adverse effects on kidney, pancreas and other organ systems.

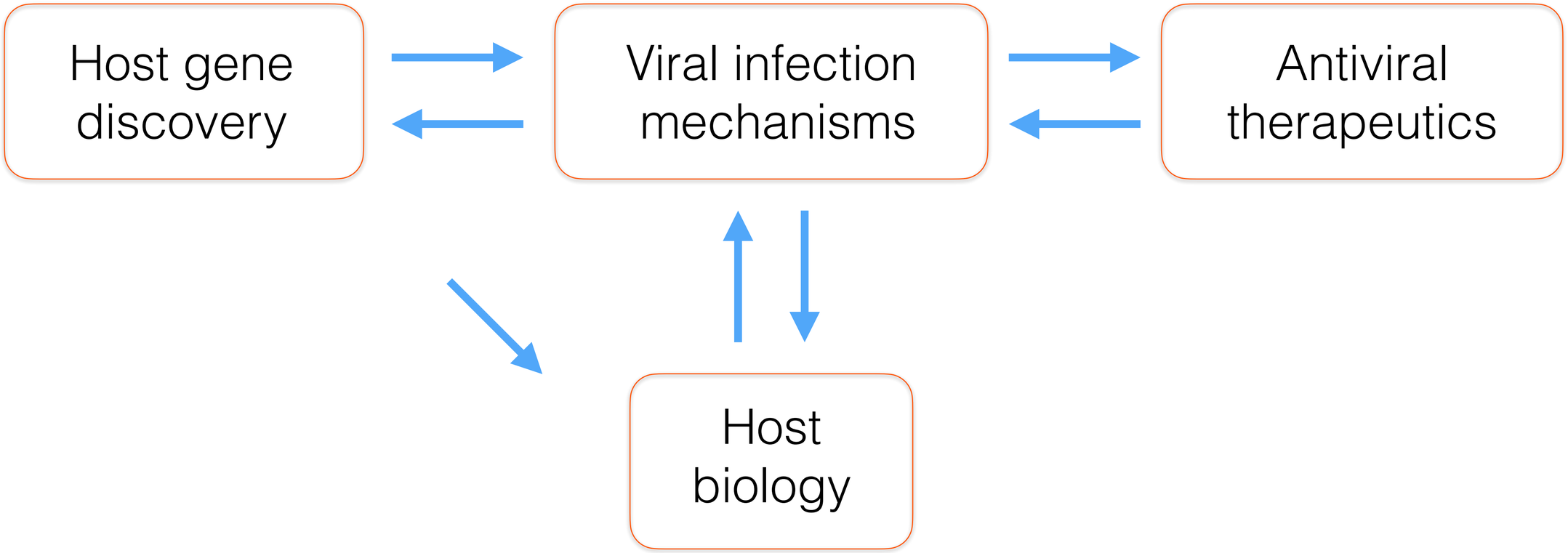



Recombinant vesicular stomatitis virus-based systems to dissect and disable emerging viruses

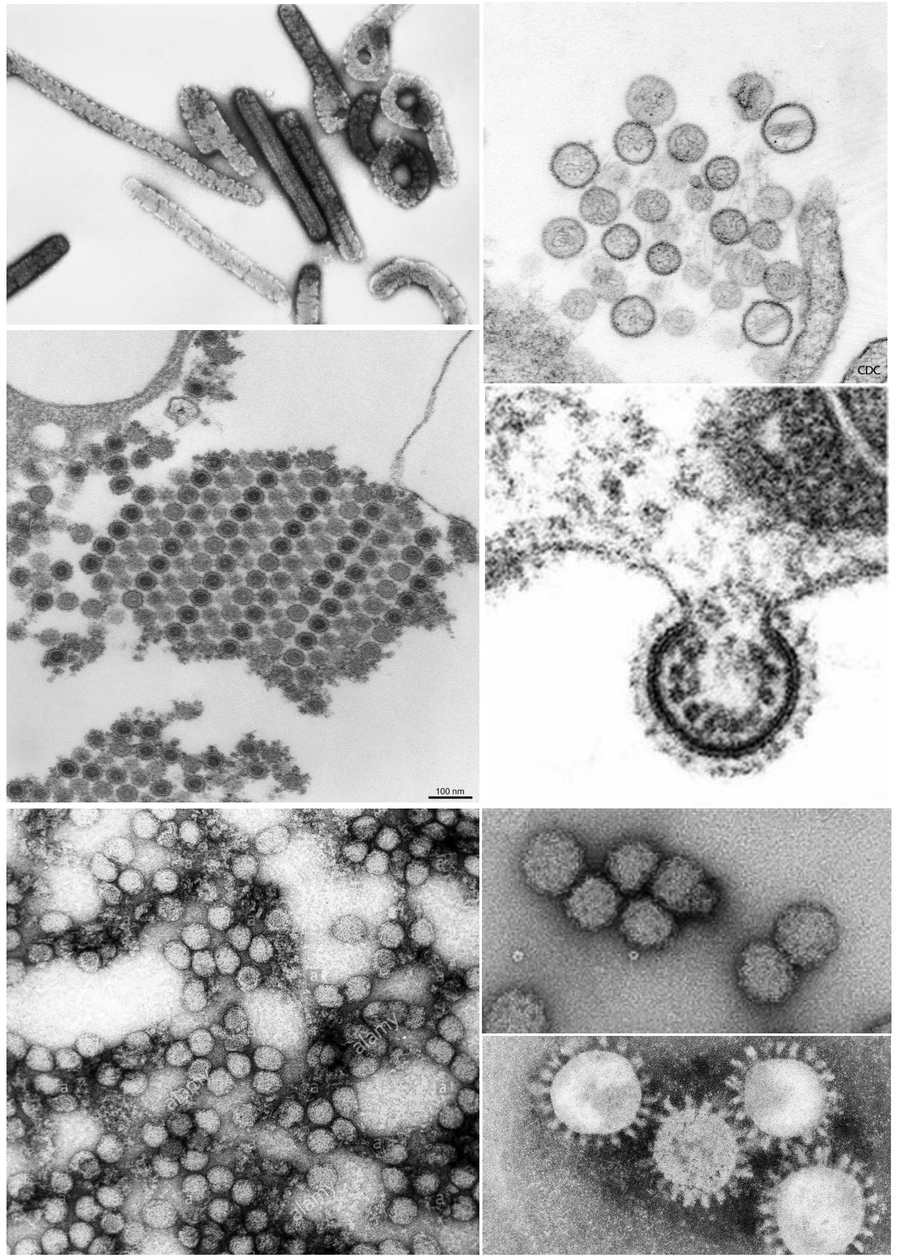
Kartik Chandran

Department of Microbiology & Immunology
Albert Einstein College of Medicine


The Chandran Lab's approach



Viruses we study



Filoviruses | Ebola & Marburg viruses

Hantaviruses | Sin Nombre virus, Andes virus, Puumula virus, Dobrava virus, Hantaan virus, Seoul virus

Nairoviruses | Crimean-Congo hemorrhagic fever virus

Coronaviruses | SARS-CoV-2 and other ‘pre-emergent’ betacoronaviruses

Pneumoviruses | Human respiratory syncytial virus

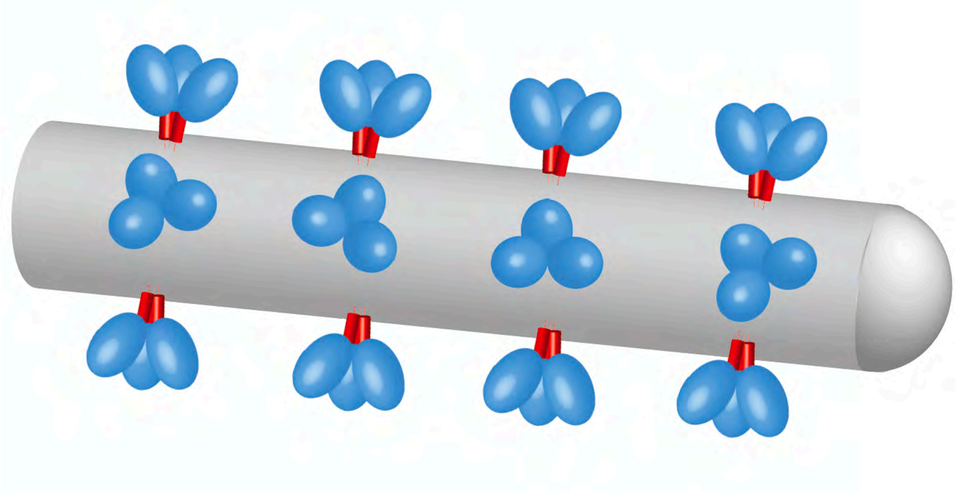
Alphaviruses | Eastern, Western, and Venezuelan encephalitis viruses

Flaviviruses | Yellow fever virus. Powassan virus, West Nile virus

Poxviruses | Vaccinia virus

How can we investigate high biocontainment (BSL-3 and BSL-4) viral pathogens safely and efficiently ?

We exploit the modular nature of the viral entry apparatus …



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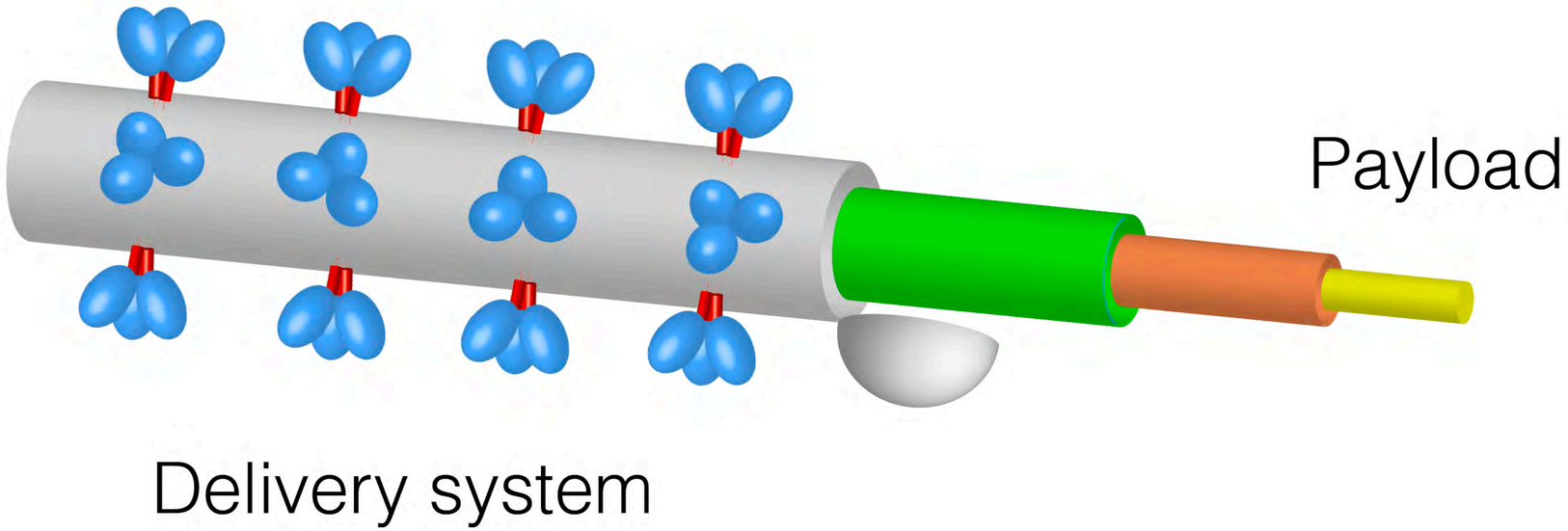

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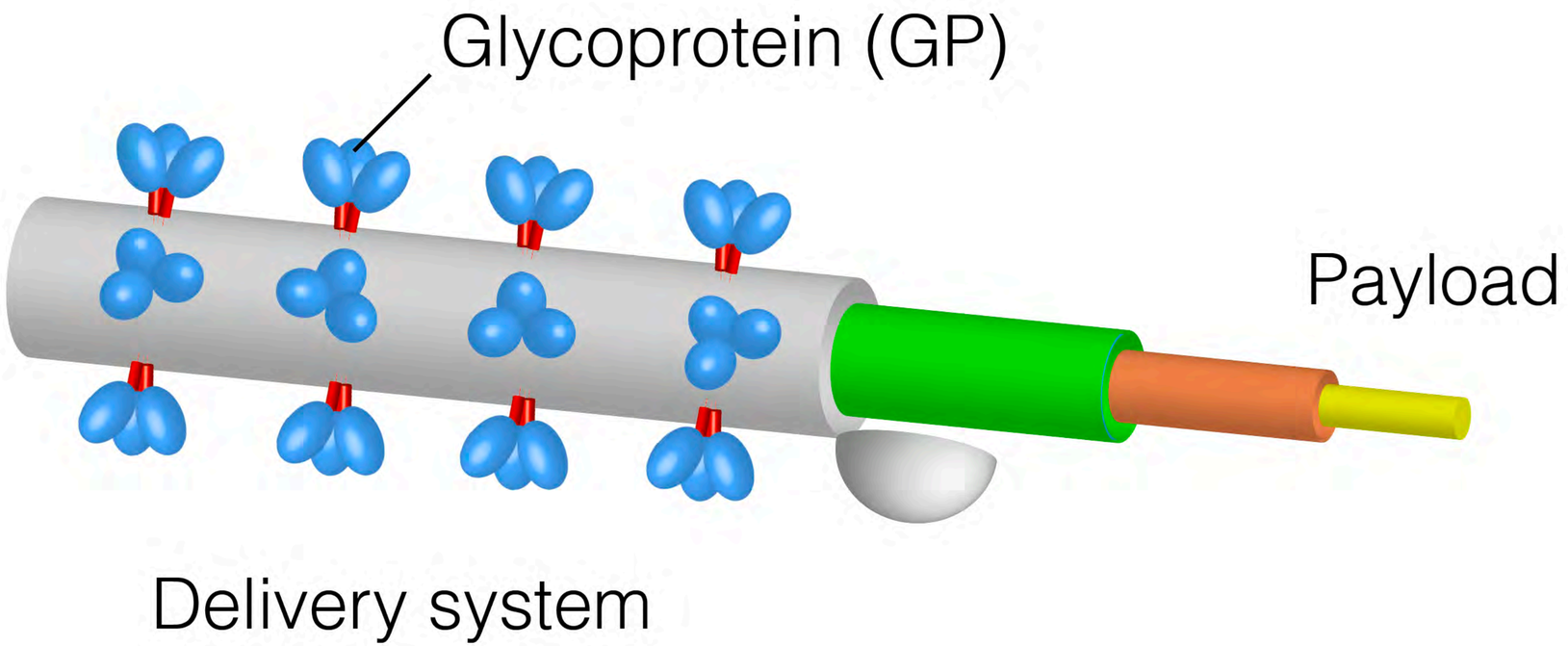
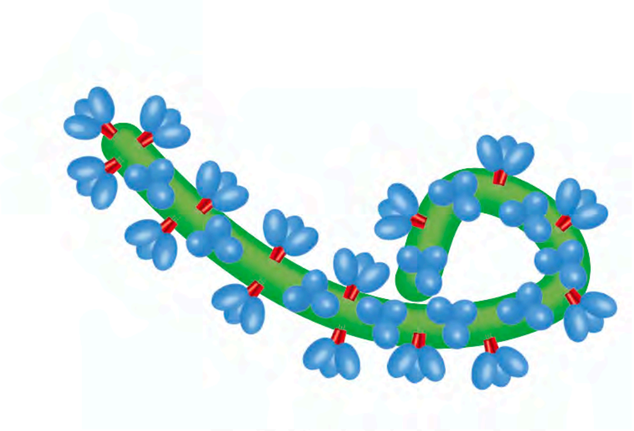


… to genetically and functionally transplant it onto an innocuous virus, vesicular stomatitis virus (VSV)



Ebola virus

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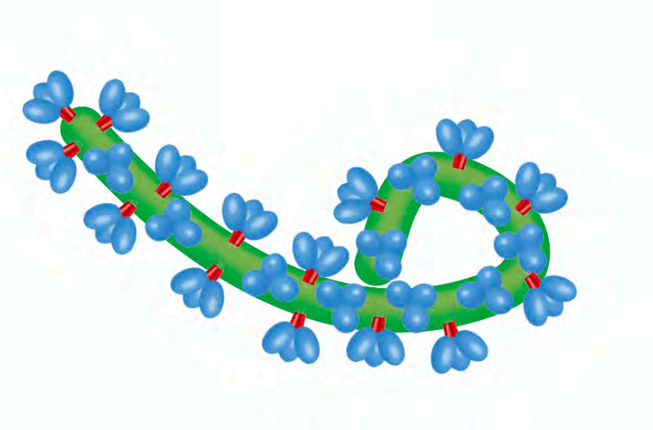
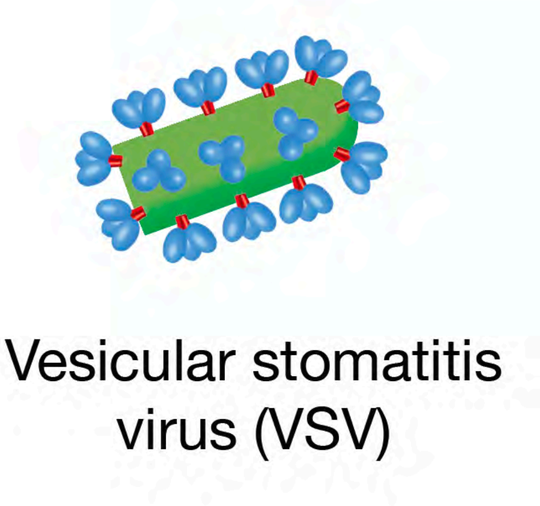
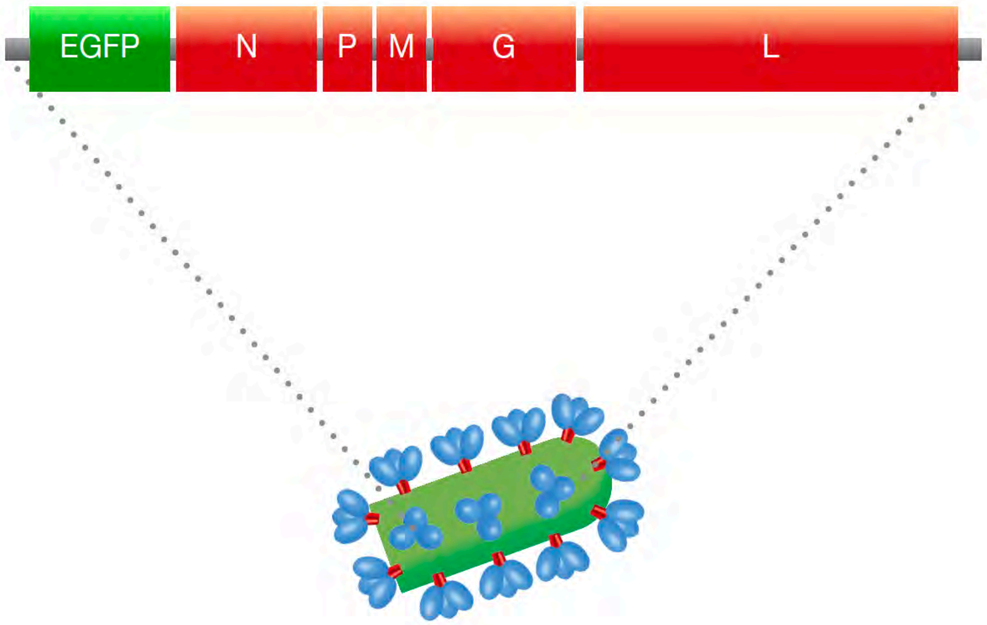


Ebola virus

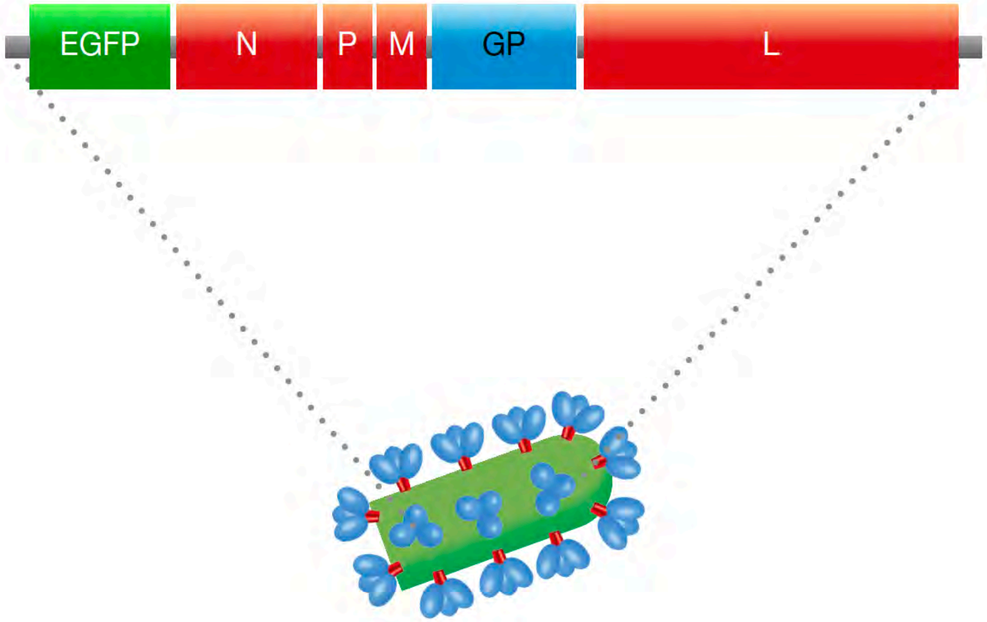


Vesicular stomatitis virus (VSV)

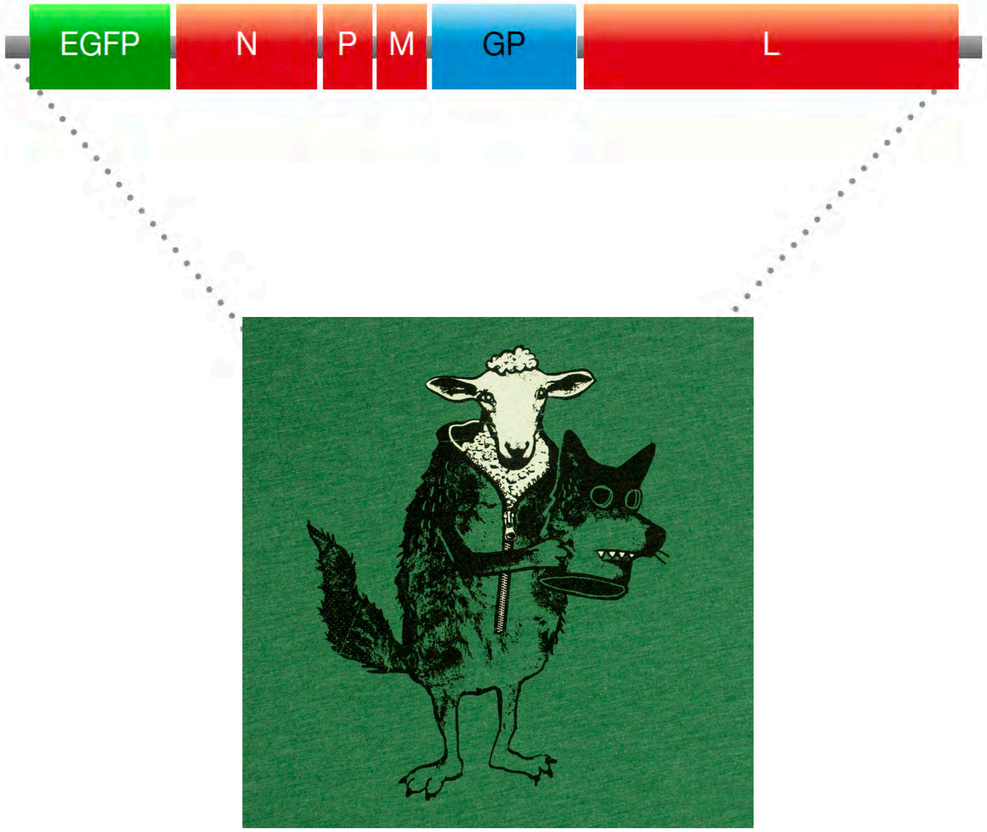
… to genetically and functionally transplant it onto an innocuous virus, vesicular stomatitis virus (VSV)



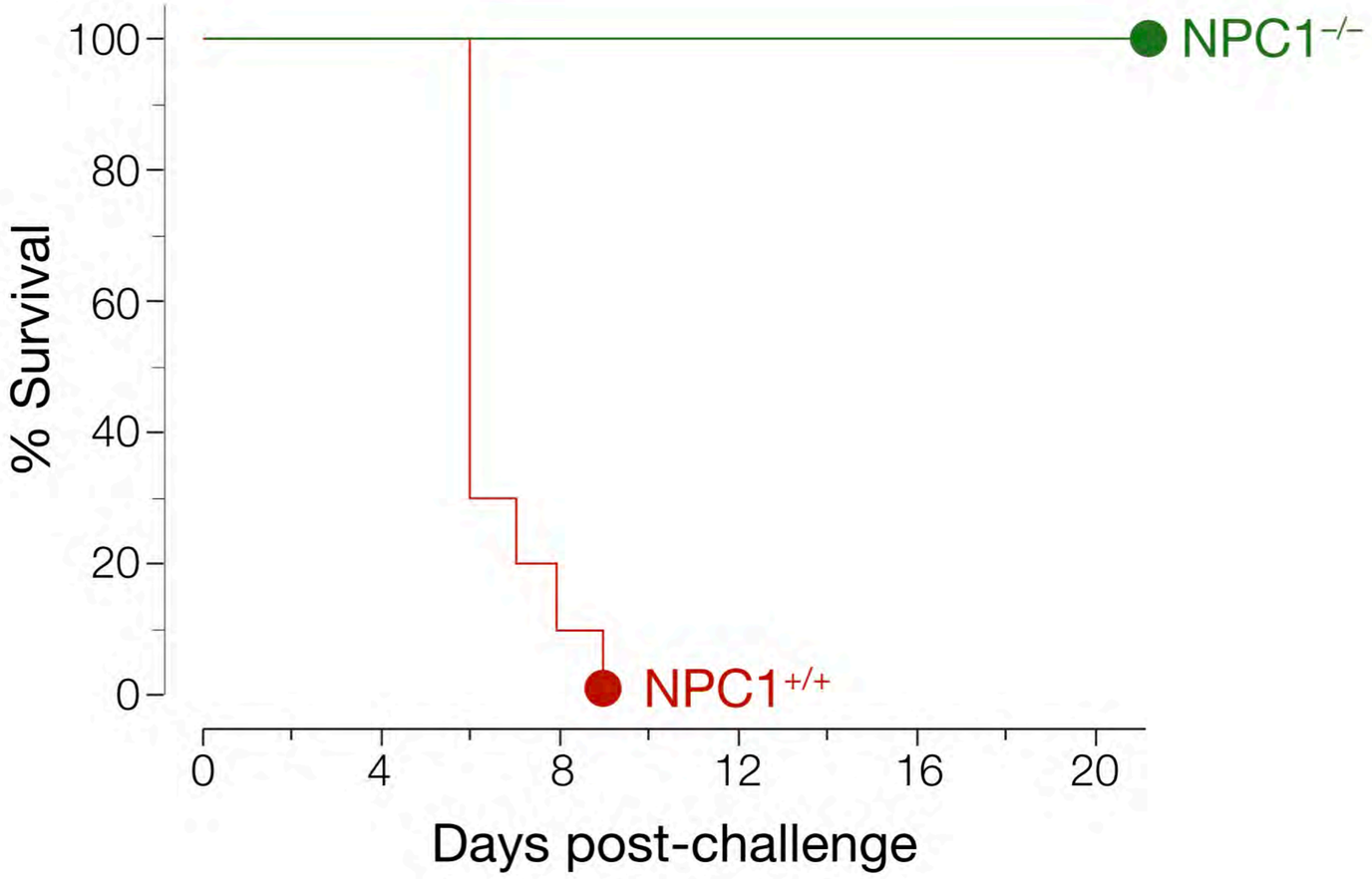
… to genetically and functionally transplant it onto an innocuous virus, vesicular stomatitis virus (VSV)

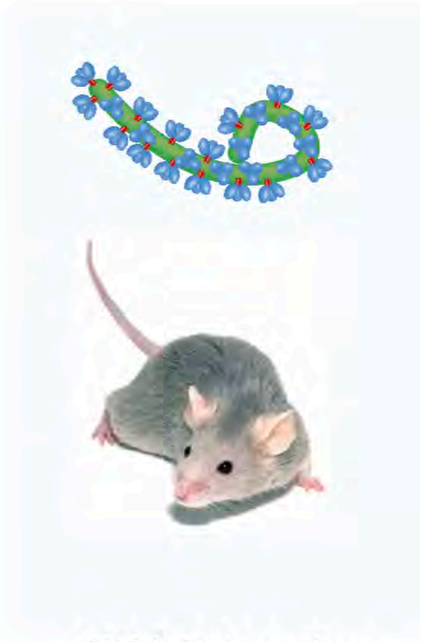


… to genetically and functionally transplant it onto an innocuous virus, vesicular stomatitis virus (VSV)



rVSVs afforded genetic screens to identify the filovirus receptor, NPC1…



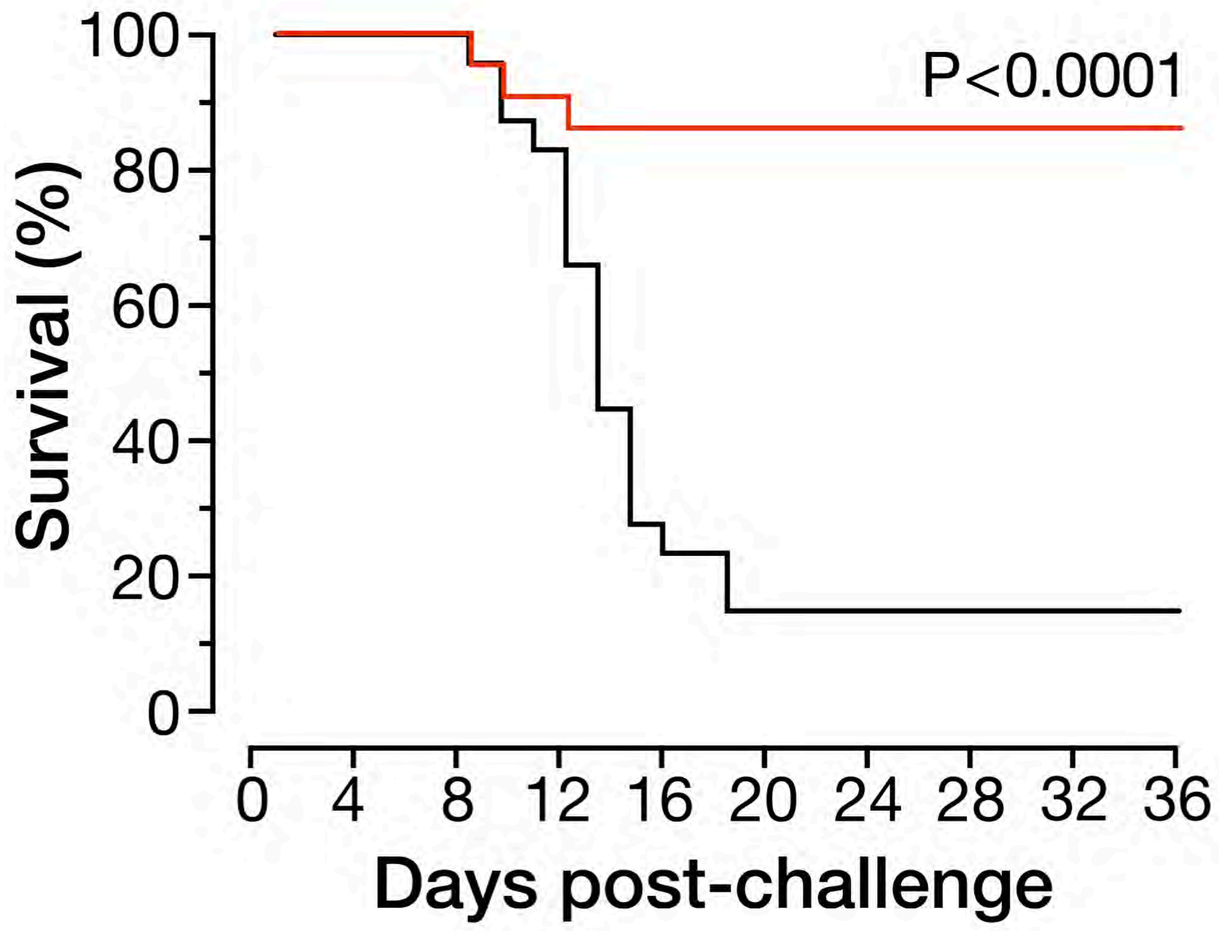


BALB/c mice
(n=19–28)

100 pfu i.p.

Carette *et al.*, Nature 2011

… and the hantavirus receptor, PCDH1



ANDV
2000 pfu i.n.

Syrian hamsters:

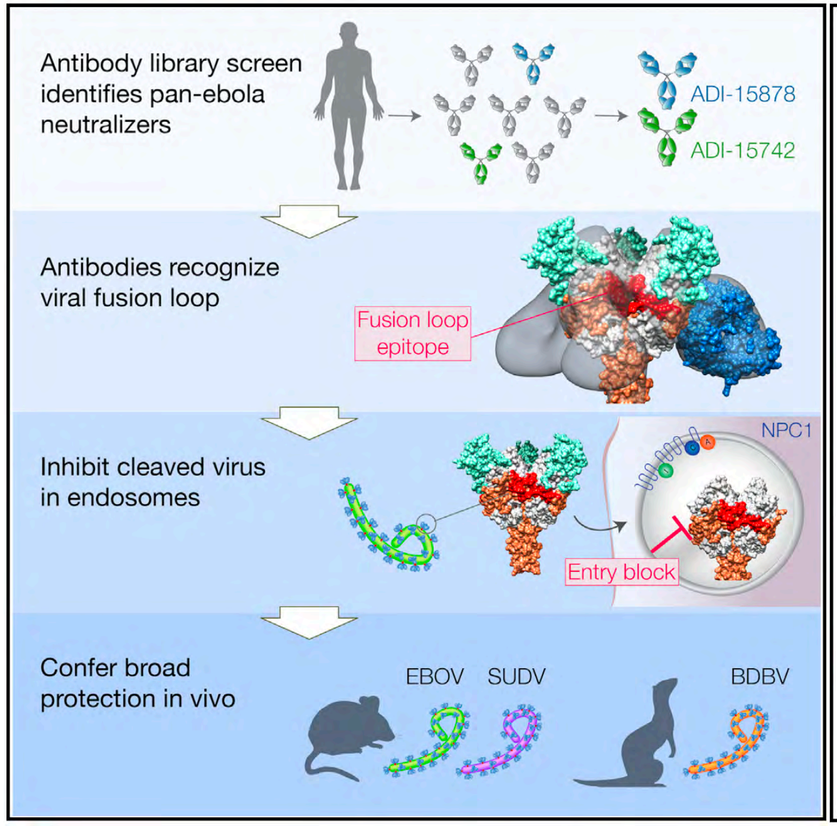
— *PCDH1*–WT (n=23)

— *PCDH1*–KO (n=21)

Jangra *et al.*, Nature 2018

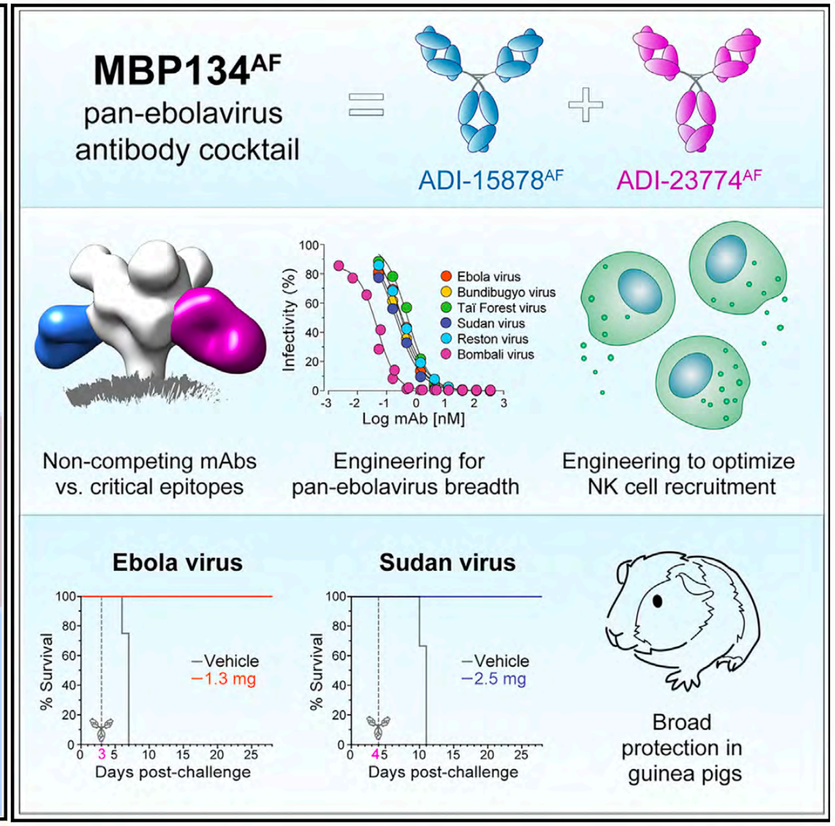
rVSVs have allowed us to rapidly identify and down-select therapeutic mAbs

Graphical Abstract



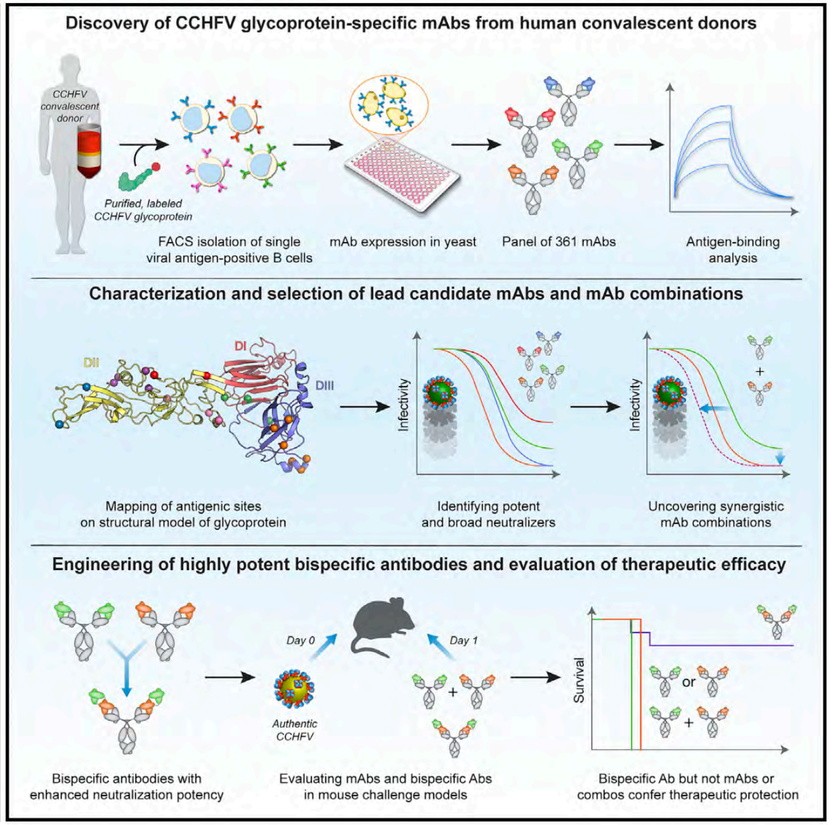
Wec, Cell 2017

Graphical Abstract



Wec, Cell Host & Microbe 2019

Graphical abstract

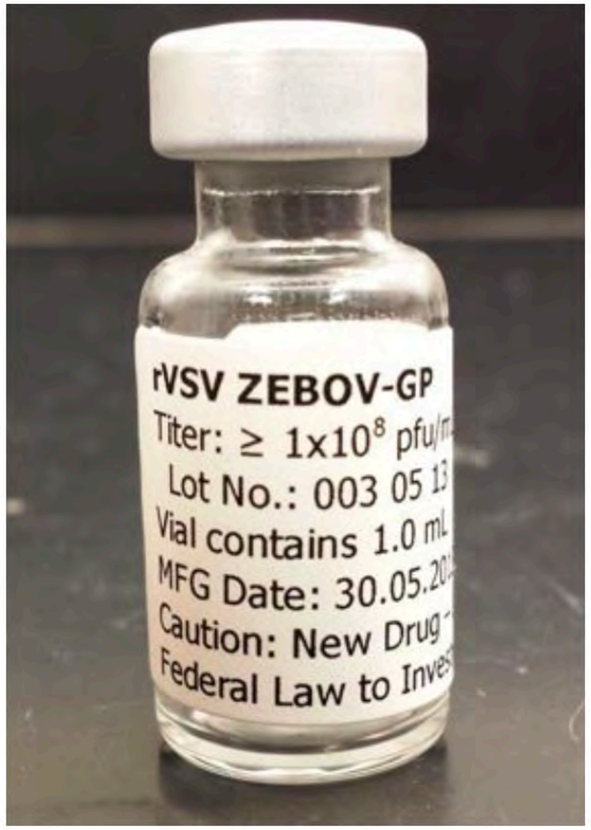


Fels, Cell 2021

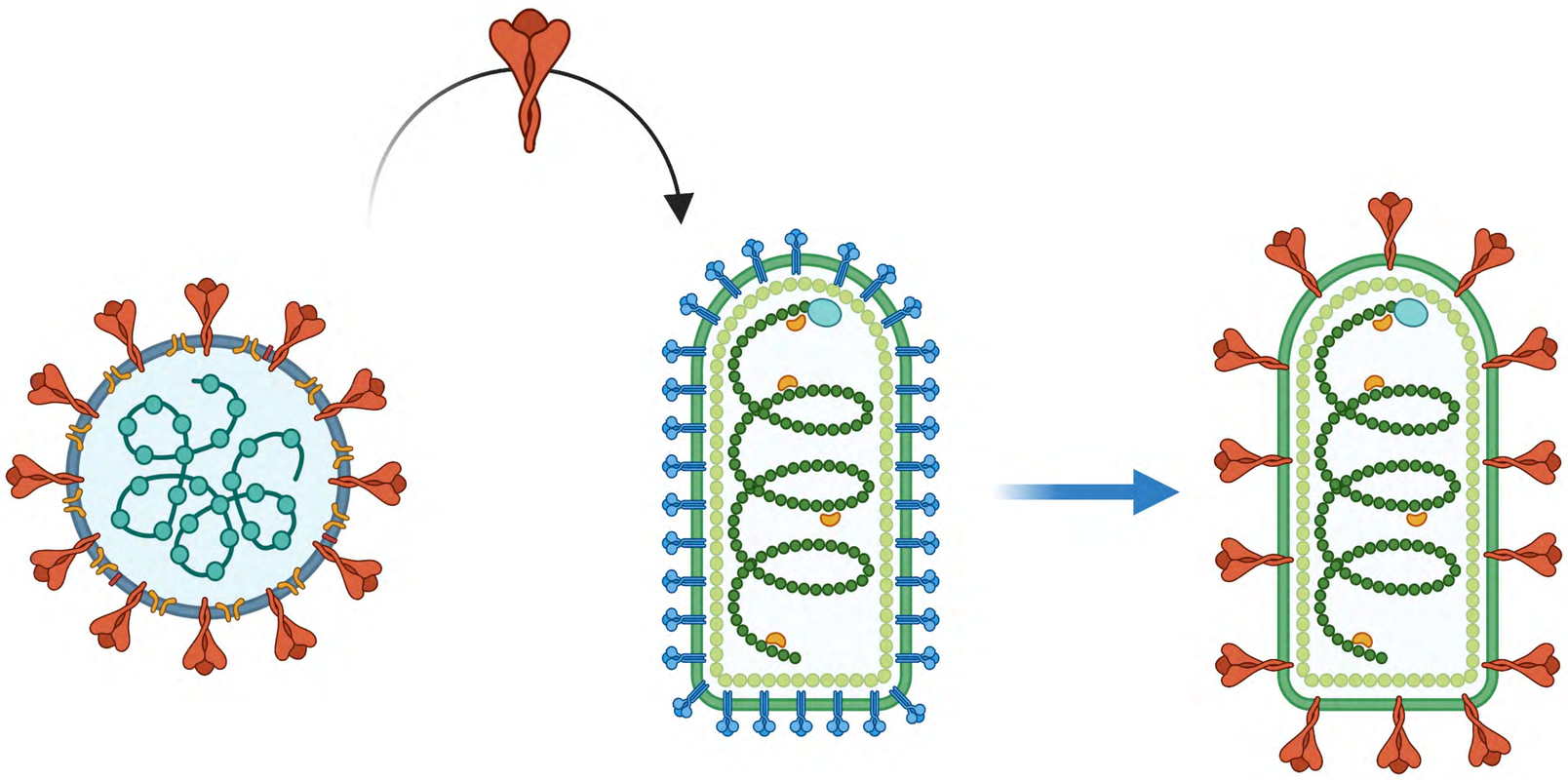
Pan-ebolavirus mAbs

CCHFV mAbs

rVSVs also provide excellent vaccine candidates



Developing a SARS-CoV-2 specific rVSV

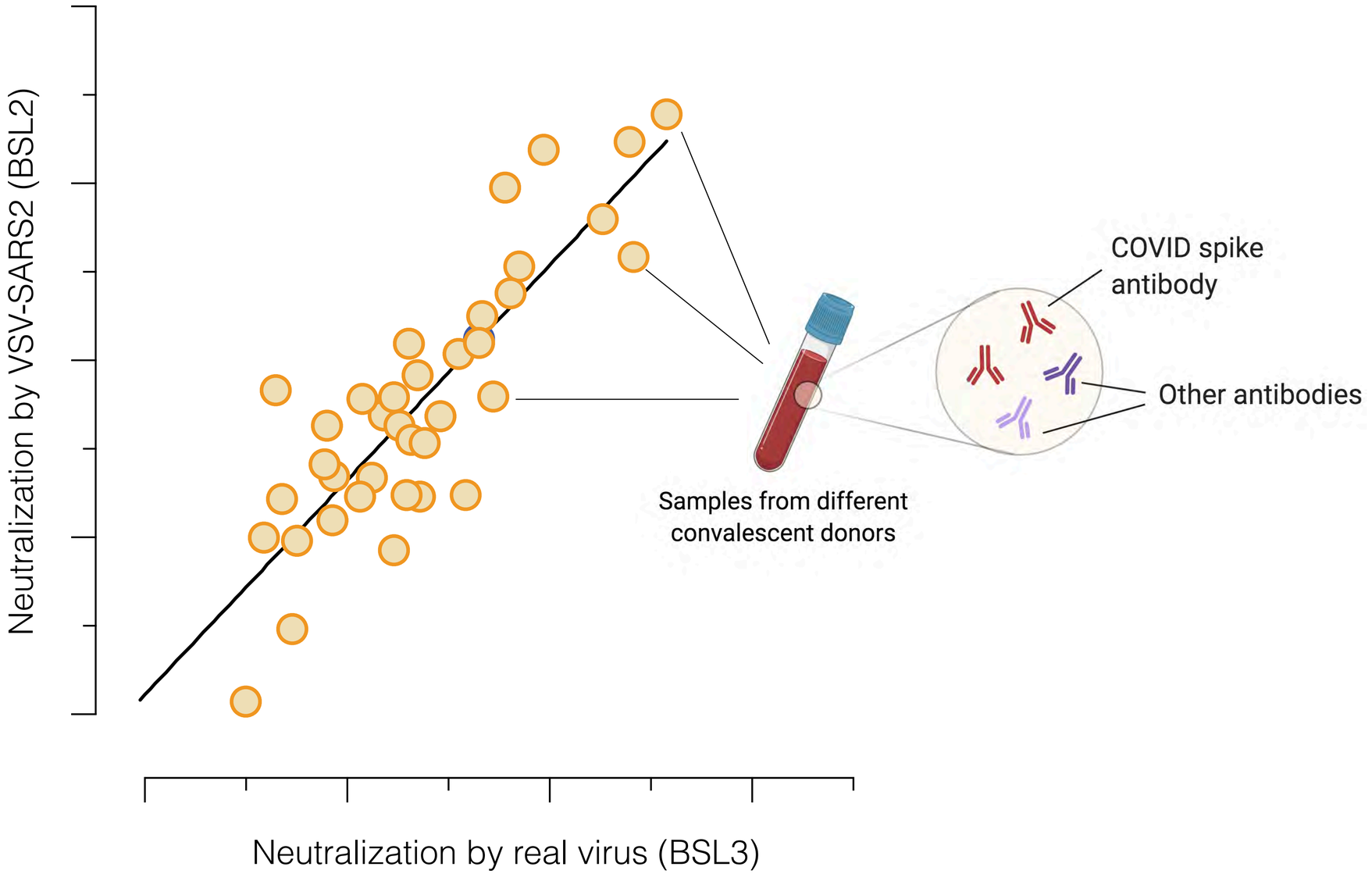


SARS-CoV-2

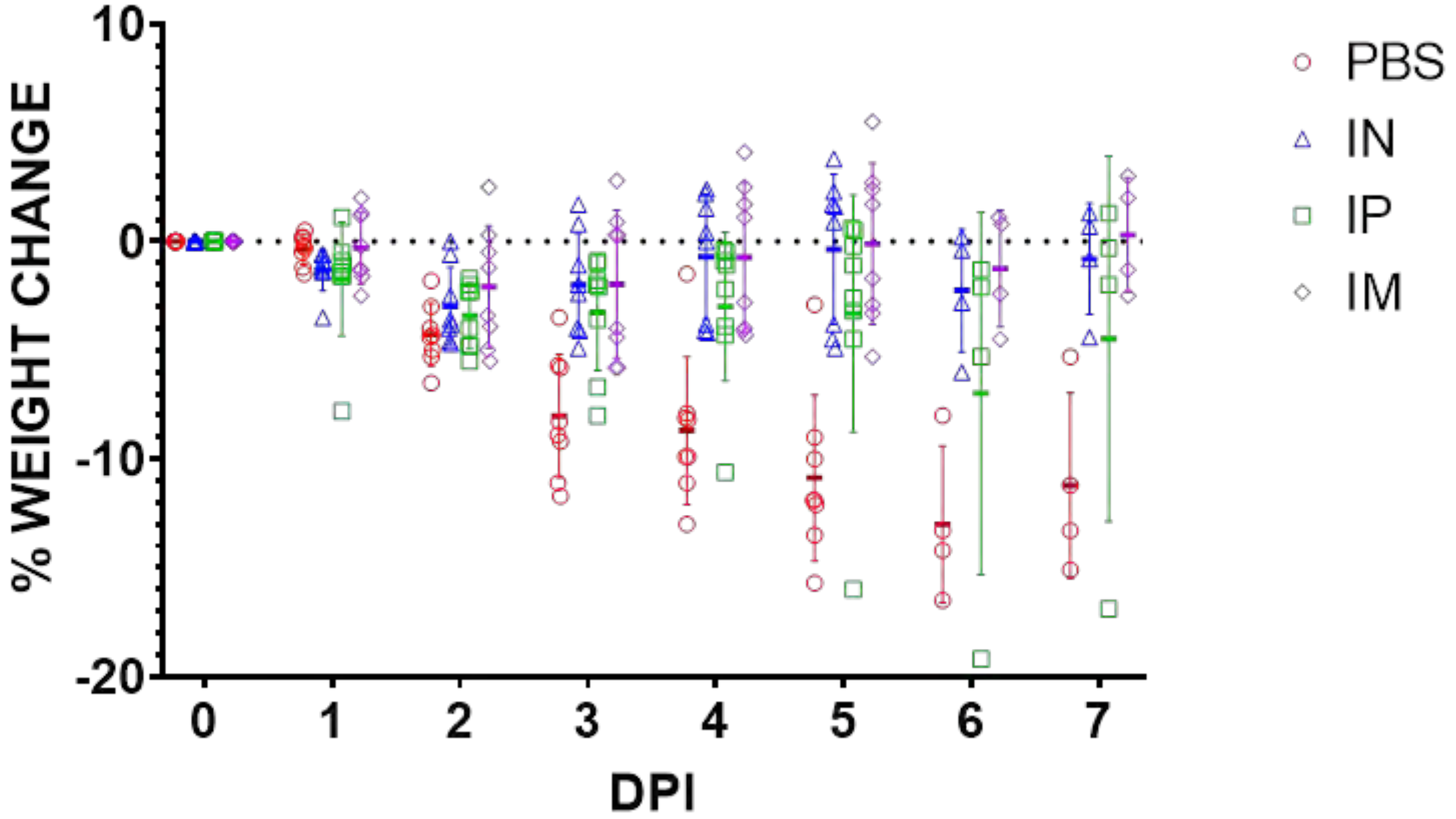
Vesicular stomatitis virus (VSV)

VSV-SARS-CoV-2

rVSV-SARS2 recapitulates key SARS2 properties



rVSV-SARS2 protects hamsters from SARS2 challenge via multiple routes



Developing rVSV-SARS2 as a thin-film freeze-dried formulation

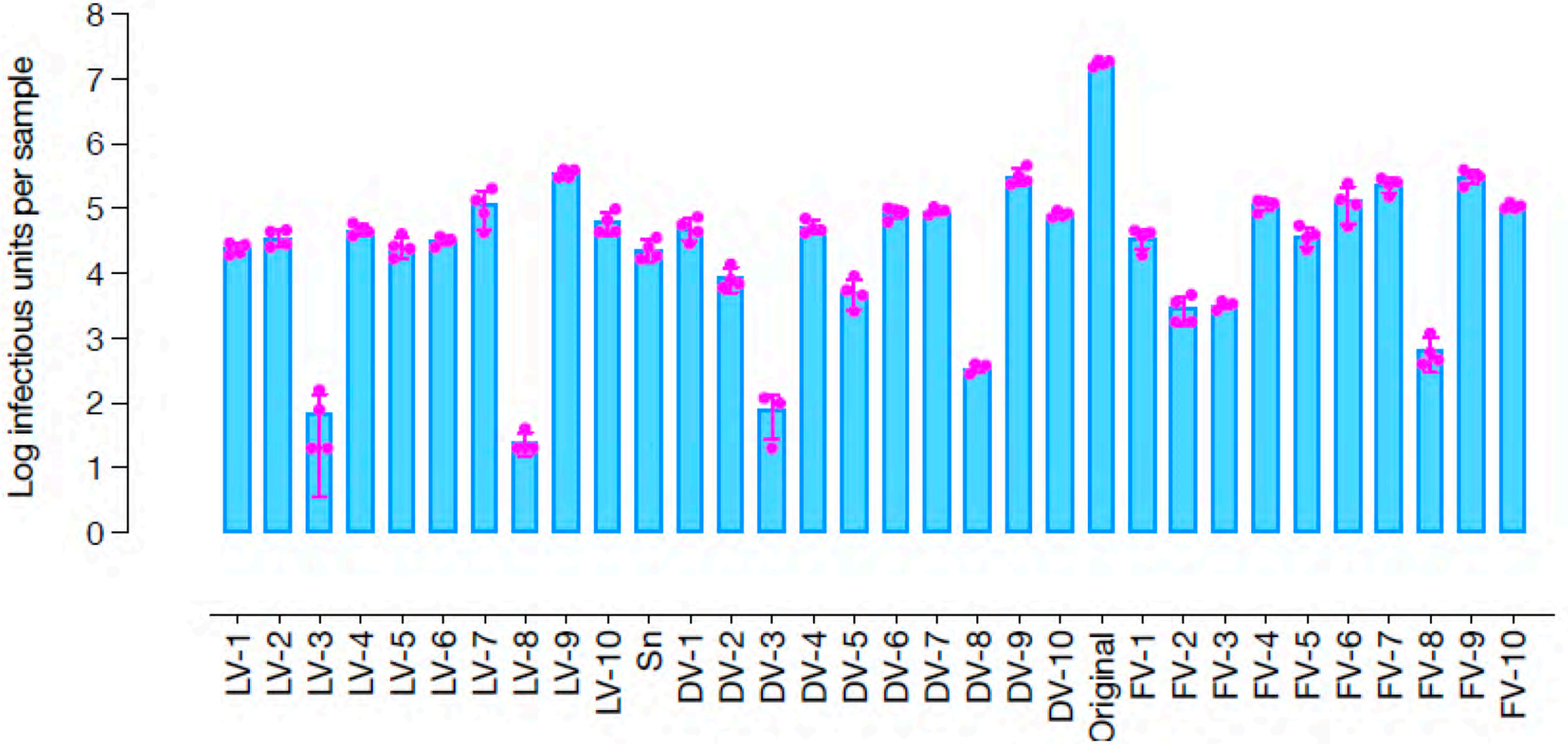
- Collaboration with TFFP, UT-Austin, and USAMRIID
- TFF formulation could potentially overcome logistical issues related to cold-chain and vaccine expiration, especially in low- and medium-income countries
- Direct inhalation delivery of vaccine could afford more rapid delivery to sites of action and greater efficacy
- This work is likely ‘platformable.’ Benefits could extend well beyond SARS2 to thermostable vaccine candidates against many other enveloped viruses
- To date, we have generated more than 60 rVSVs bearing spikes from many virus families
- **Challenge:** will fragile membrane-enveloped VSV particles survive freeze-drying and retain infectivity, biological activity?

TFF PHARMACEUTICALS

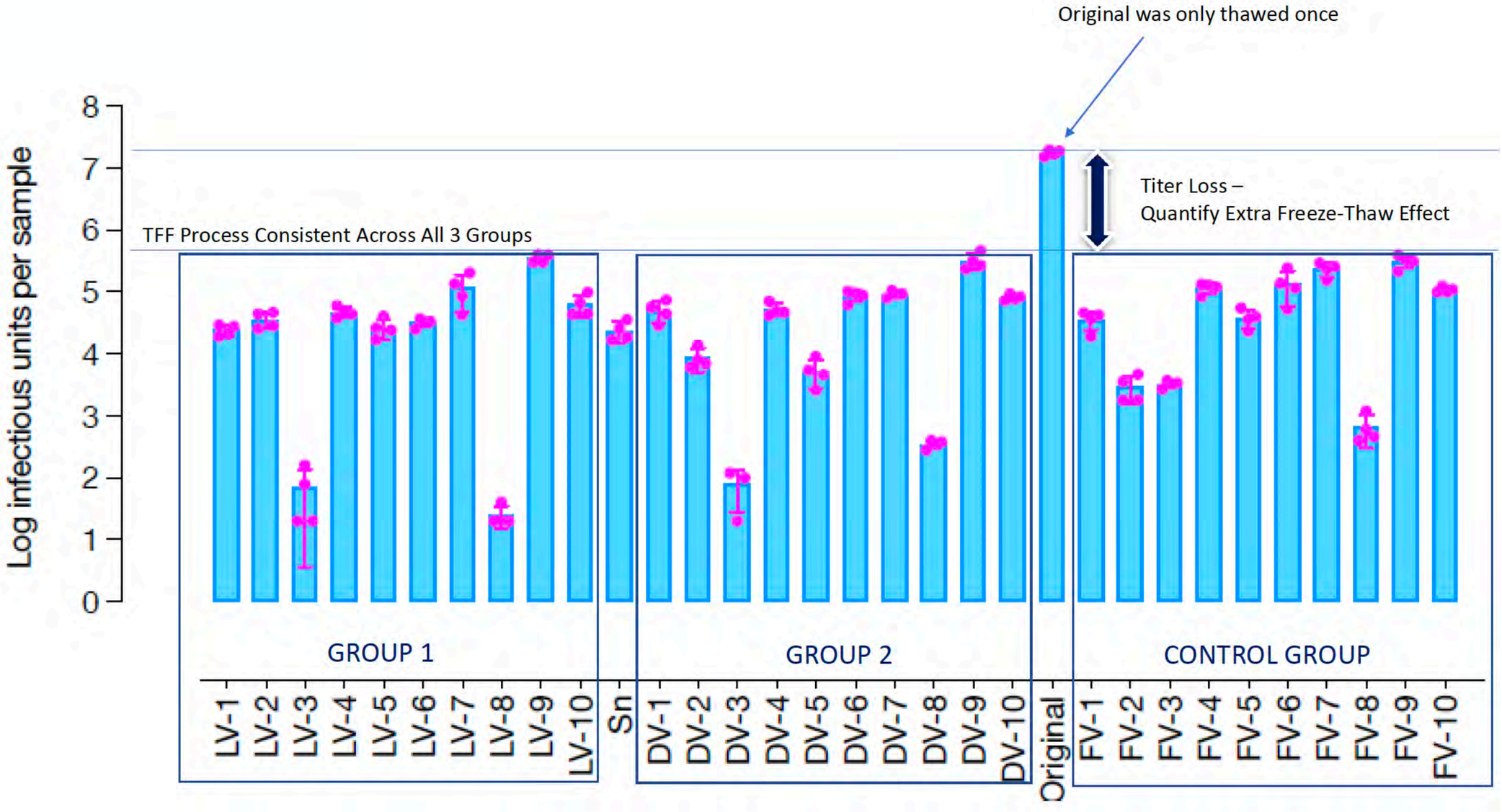
The University of Texas at Austin College of Pharmacy

USAMRIID
United States Army Medical Research Institute of Infectious Diseases
Biodefense solutions to protect our nation

Evaluating a panel of formulations for rVSV-SARS2 survivability



Many conditions are compatible with high levels of rVSV-SARS2 infectivity



Upcoming:

Evaluate an initial set of formulations for protective efficacy against SARS2 in the hamster challenge model (USAMRIID)

Continue to iteratively optimize candidate formulations (Einstein and TFF/UT-Austin)

Acknowledgments

Kartik Chandran | **Einstein**
Rohit Jangra
Denise Haslwanter
Maria Eugenia Dieterle

Zhengrong Cui | **UT-Austin**

Chris Cano | **TFF Pharma**

John Dye | **USAMRIID**

TFF Pharma Science Day

Ted M. Ross
Center for Vaccines and Immunology
Department of Infectious Diseases
University of Georgia
Athens, Georgia, USA

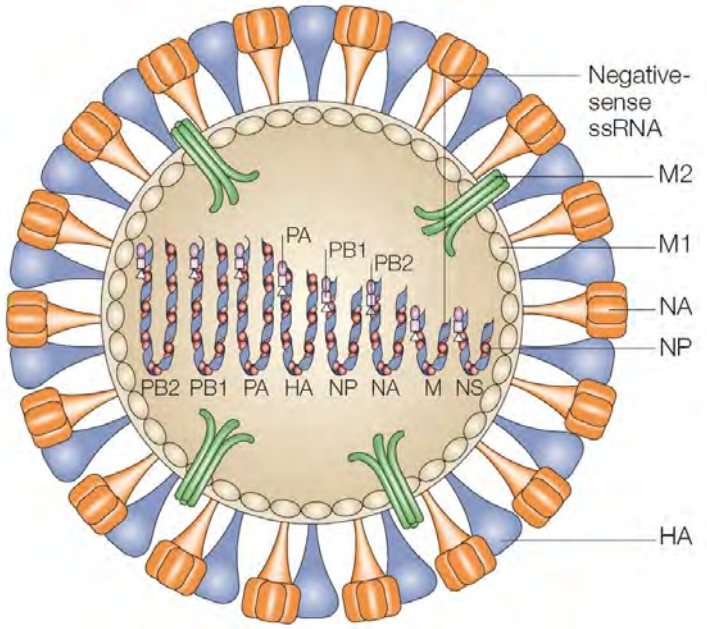
Next Generation Universal Influenza Virus Vaccines

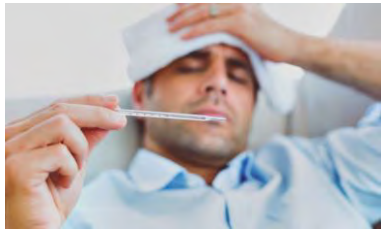
June 15, 2021

UNIVERSITY OF GEORGIA

The Influenza Virus

- Viral family Orthomyxoviridae
  - Enveloped viruses
  - 8 segmented negative-sense genome
  - Predominant glycoproteins HA and NA
- Primarily infect humans, birds, & pigs
  - Type B and C only infect humans
- Symptoms include fever, cough, sore throat, runny nose, muscle aches, headaches, & fatigue
  - Vomiting and diarrhea in severe cases
- CDC estimates that virus caused 13-15 million symptomatic illnesses from 10/1/2018 – 2/2/2019
  - Current VE of 22%





Transmission of Respiratory Viruses

Transmission pathways[1,2]

References:

1. CDC. Influenza: In: Atkinson W, et al, eds. *Epidemiology and Prevention of Vaccine-preventable Diseases.* 12th edition. Washington, DC: Public Health Foundation; 2011:151-171.
2. American Academy of Pediatrics (AAP). Influenza: In: *Red Book: 2012 Report of the Committee on Infectious Diseases.* 29th edition. Elk Grove Village, IL: AAP; 2012:439-453.

Collaborative Influenza Vaccine Innovation Centers (CIVIC)

Center for Influenza Vaccine Research for High Risk Populations (CIVR-HRP)

1. Provide comprehensive assessment of broadly-protective influenza vaccine candidates
2. Integrate this assessment with fundamental research on protective host responses
3. Provide insight into the mechanisms that drive vaccine effectiveness

The CIVR-HRP forms a collaborative network of primary investigators around a comprehensive research program that centers on identifying broadly protective influenza vaccines for all populations, ***with a focus on our most vulnerable populations***.

Vaccine Centers
CIVIC A

UNIVERSITY OF GEORGIA

Principal Investigators: Ted M. Ross, Ph.D. (at the University of Georgia),
and Stacey Schultz-Cherry, Ph.D. (at St. Jude Children's Research Hospital)

Mount Sinai

Principal Investigators: Florian Krammer, Ph.D. (at the Icahn School of Medicine at Mount Sinai), and Rafi Ahmed, Ph.D. (at Emory University)

Duke UNIVERSITY

Principal Investigator: Michael Moody, M.D.

Vaccine Manufacturing and Toxicology Core
CIVIC B

Duke UNIVERSITY

Principal Investigator: Matthew Johnson, Ph.D.

Clinical Core
CIVIC C

UNIVERSITY of MARYLAND SCHOOL OF MEDICINE
CENTER FOR VACCINE DEVELOPMENT AND GLOBAL HEALTH

Principal Investigator: Kathleen Neuzil, M.D., M.P.H.

Duke University School of Medicine

Principal Investigator: Emmanuel Walter, M.D., M.P.H.

CIVICs Statistical, Data Management, and Coordination Center

Digital Infuzion, Inc., Gaithersburg, Maryland
Principal Investigator: Stephan Bour, Ph.D.

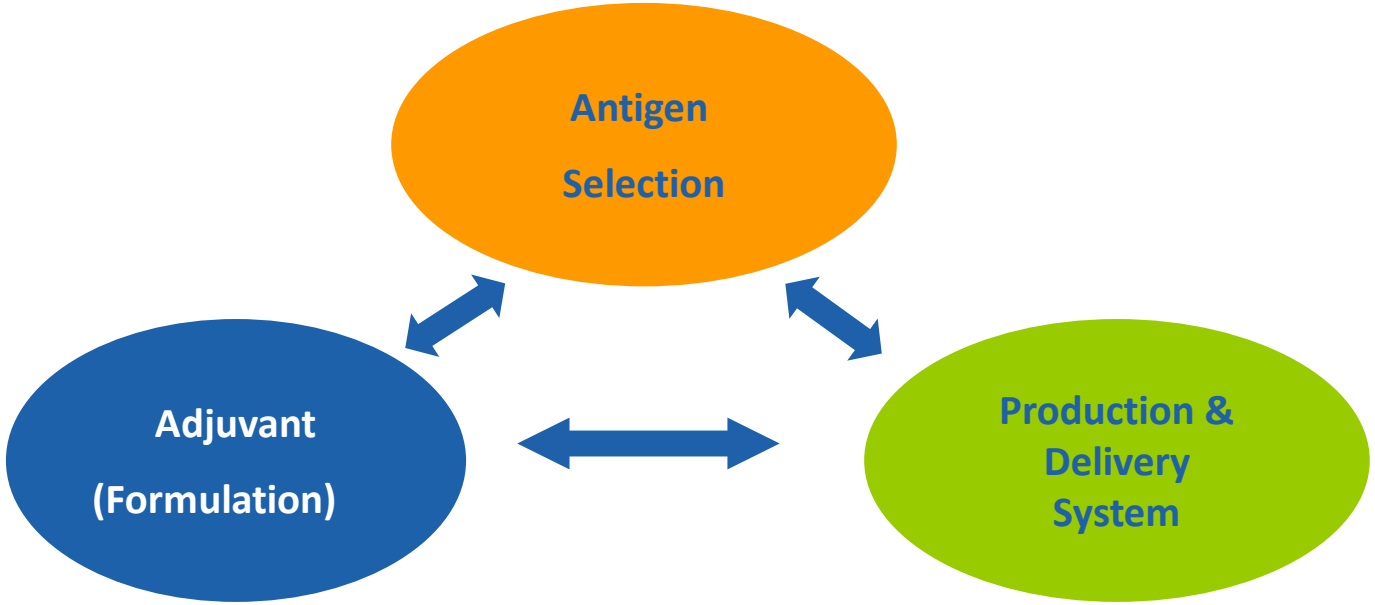
7 Year Timeline (2019-2026)

Program Hypothesis

Universal influenza vaccines can be rationally engineered to elicit broadly cross-neutralizing epitopes

Universal antigens can be used in pre-immune hosts to re-focus the immune response, preferentially recalling broadly neutralizing antibodies that provides **breadth** against multiple strains within a subtype

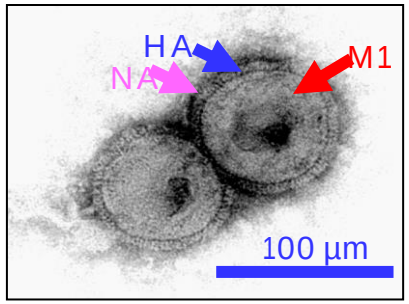
Universal antigens can also be delivered with appropriate technologies to stimulate **durable** and long-lasting immunity



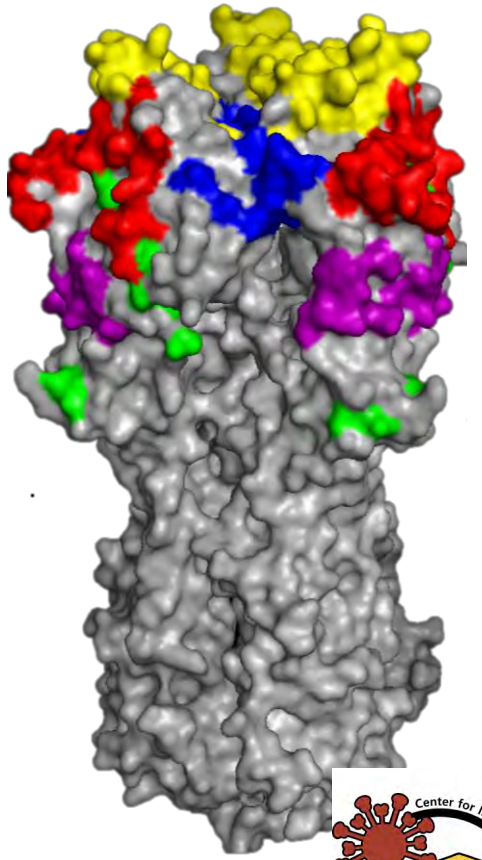
COBRA Approach for Developing Broadly Reactive Vaccines

- Computationally Optimized Broadly Reactive Antigen (COBRA)
  - Layered consensus building approach
  - Utilizes sequence data from flu surveillance databases
    - GISAID, FLUDB
    - Allow viral evolution to dictate antigen design

- Capable of eliciting potent, broadly reactive HA-specific antibody responses
  - Effective against seasonal and pandemic strains
    - H5, H3, and H1 subtypes
    - Mice, ferrets, non-human primates
      - **Carter, Ross, et al., 2016, J. Virol.**
      - **Giles, Ross, et al., 2012, J. Infect. Dis.**
      - **Giles & Ross, 2011, Vaccine**
      - **Allen, Ross, et al 2018. J. Virol.**
      - **Sautto, Ross, et al. 2019. J. Immunol.**
      - **Sautto GA, et al. 2018. ImmunoHorizons.**
      - **Huang et al. 2020. J. Virol.**



H5 Human COBRA 2 VLPs

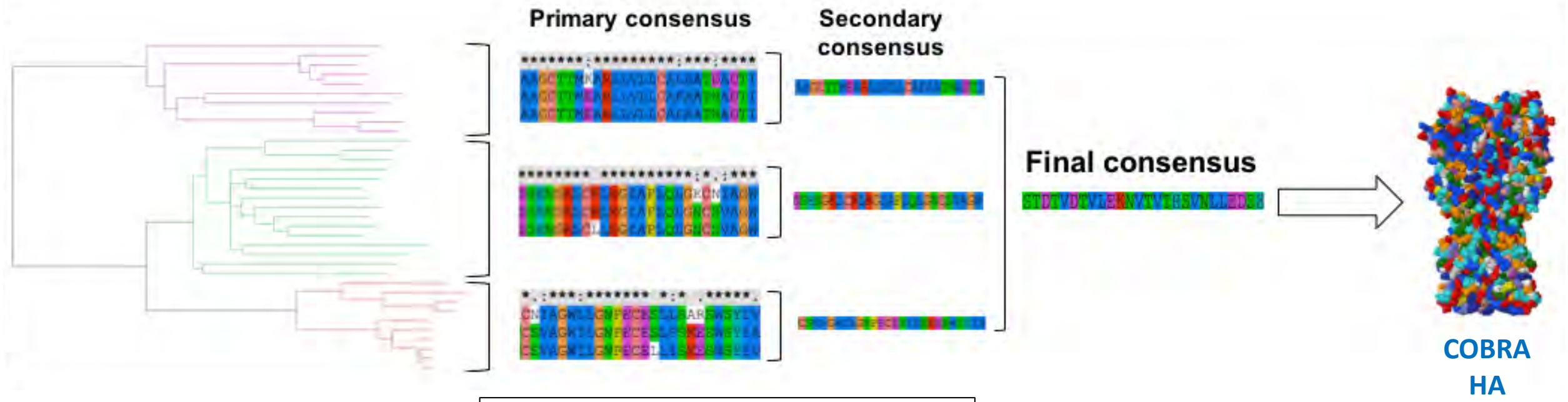


T-7 H3 COBRA

CIVICs Collaborative Influenza Vaccine Innovation Centers

Center for Influenza Vaccine Research for High Risk Populations

Computationally Optimized Broadly Reactive Antigens (COBRA)



Wong *et al.*, 2017. *JVI*	**H3N2**
Carter *et al.*, 2016. *JVI*	**H1N1**
Giles *et al.*, 2011. *Vaccine*	**H5N1**
Reneer *et al.* 2020. *JVI*	**H2N2**

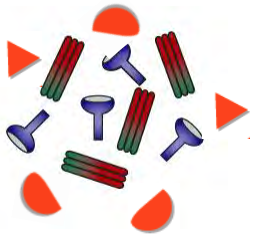
Adapted from Sautto *et al.*, 2018. *Virol. J.*

CIVICs
Collaborative Influenza Vaccine Innovation Centers

Center for Influenza Vaccine Research for High Risk Populations

Versatility of COBRA-based vaccine platform

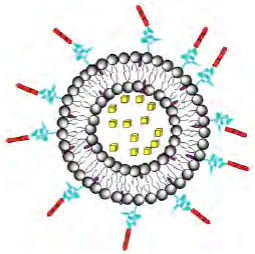
Virus-like particles (VLP)
Carter *et al.,* 2016. *J. Virol.*



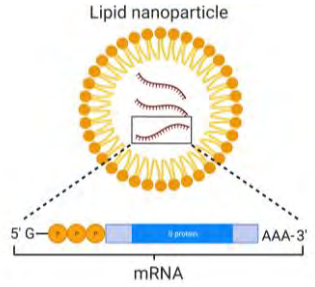
Split vaccine
Allen *et al.,* 2018. *PLoS One*

Influenza live viruses
Sautto *et al.,* 2018. *ImmunoHorizons*

HA recombinant proteins
Huang Y. *et al.*, 2019. *J. Virol.*



HA-ferritin nanoparticles
Darricarrère *et al.,* 2018. *J. Virol.*



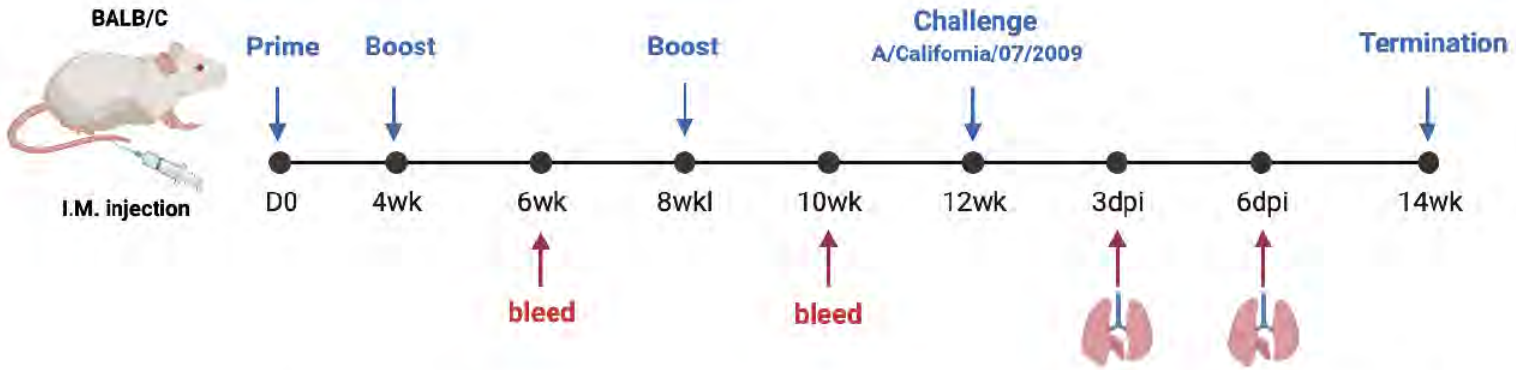
mRNA LNP
Ross et al. 2021. In progress

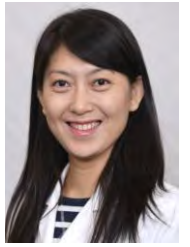
CIVICs
Collaborative Influenza Vaccine Innovation Centers

Center for Influenza Vaccine Research
for High Risk Populations

Soluble rHA

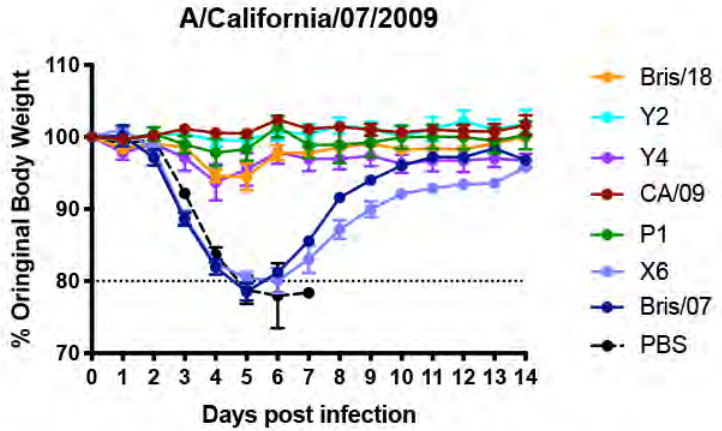
A.





Ying Huang (UGA)

B.



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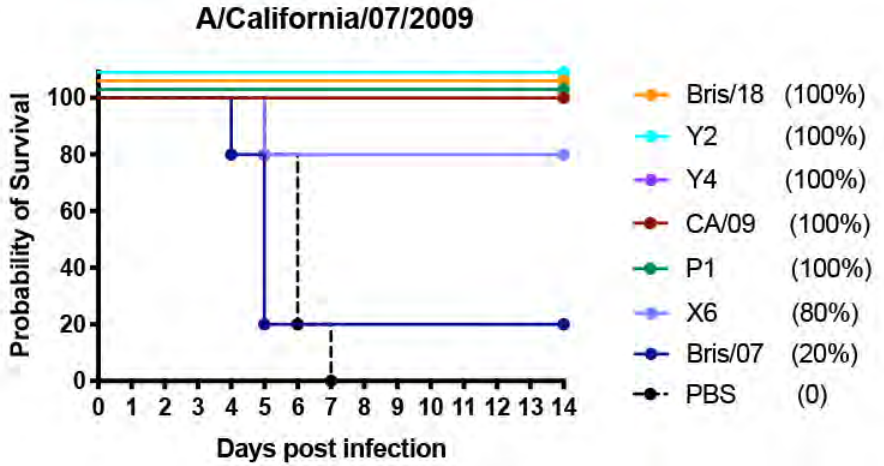

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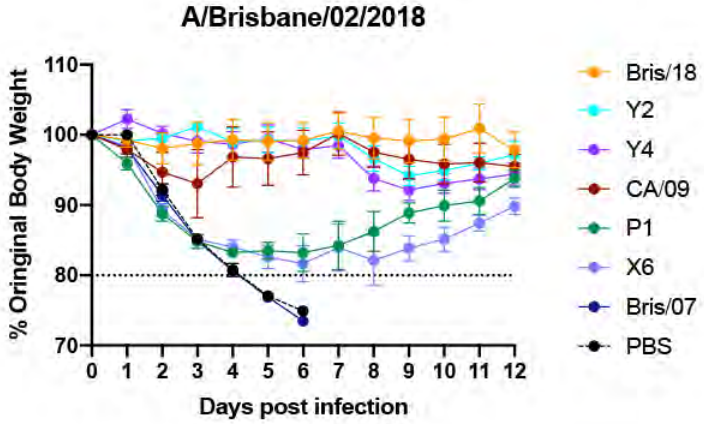
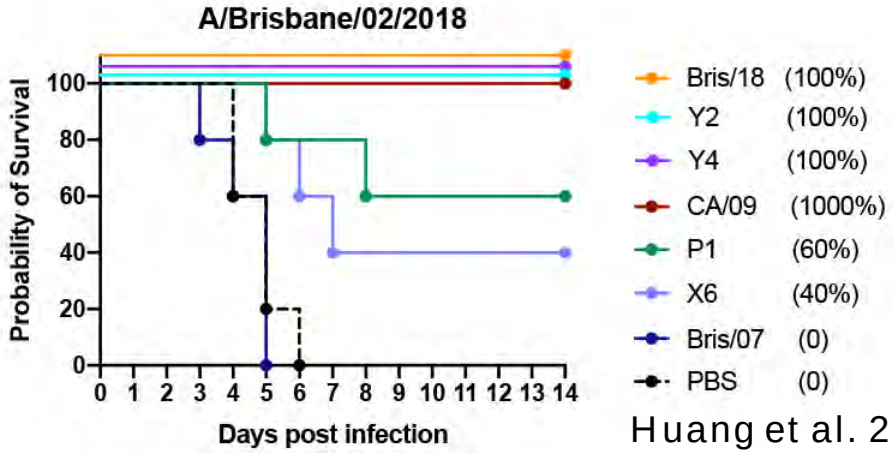


E.



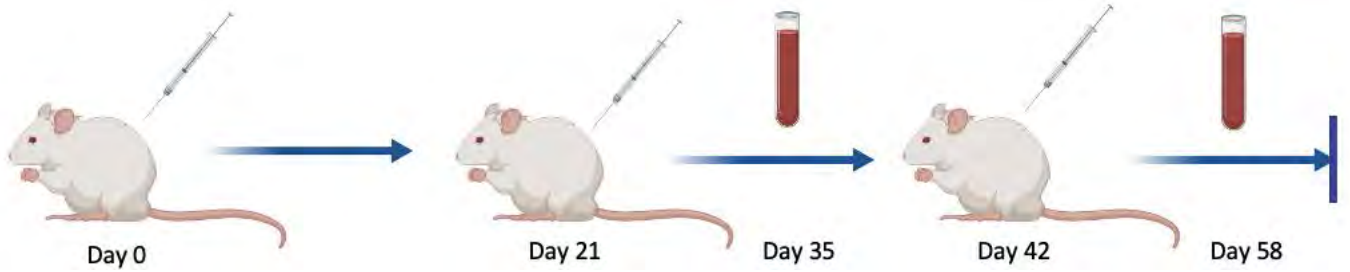
Huang et al. 2021. in prep.

Next Generation H3 COBRA HA Antigens

James Allen (UGA)

D0	D21	D35	D42	D58
Vaccinate	**Vaccinate**	**Bleed**	**Vaccinate**	**Bleed**
TJ-5 (H3)	TJ-5 (H3)		TJ-5 (H3)	
J4 (H3)	J4 (H3)		J4 (H3)	
NG-2 (H3)	NG-2 (H3)		NG-2 (H3)	
Sing/16	Sing/16		Sing/16	
Kansas/17	Kansas/17		Kansas/17	
Switz/17	Switz/17		Switz/17	
South Australia/19	South Australia/19		South Australia/19	

Vaccine	Design Timeframe
TJ-5	2008-2012
J4	2013-2015
NG-2	2016-2018

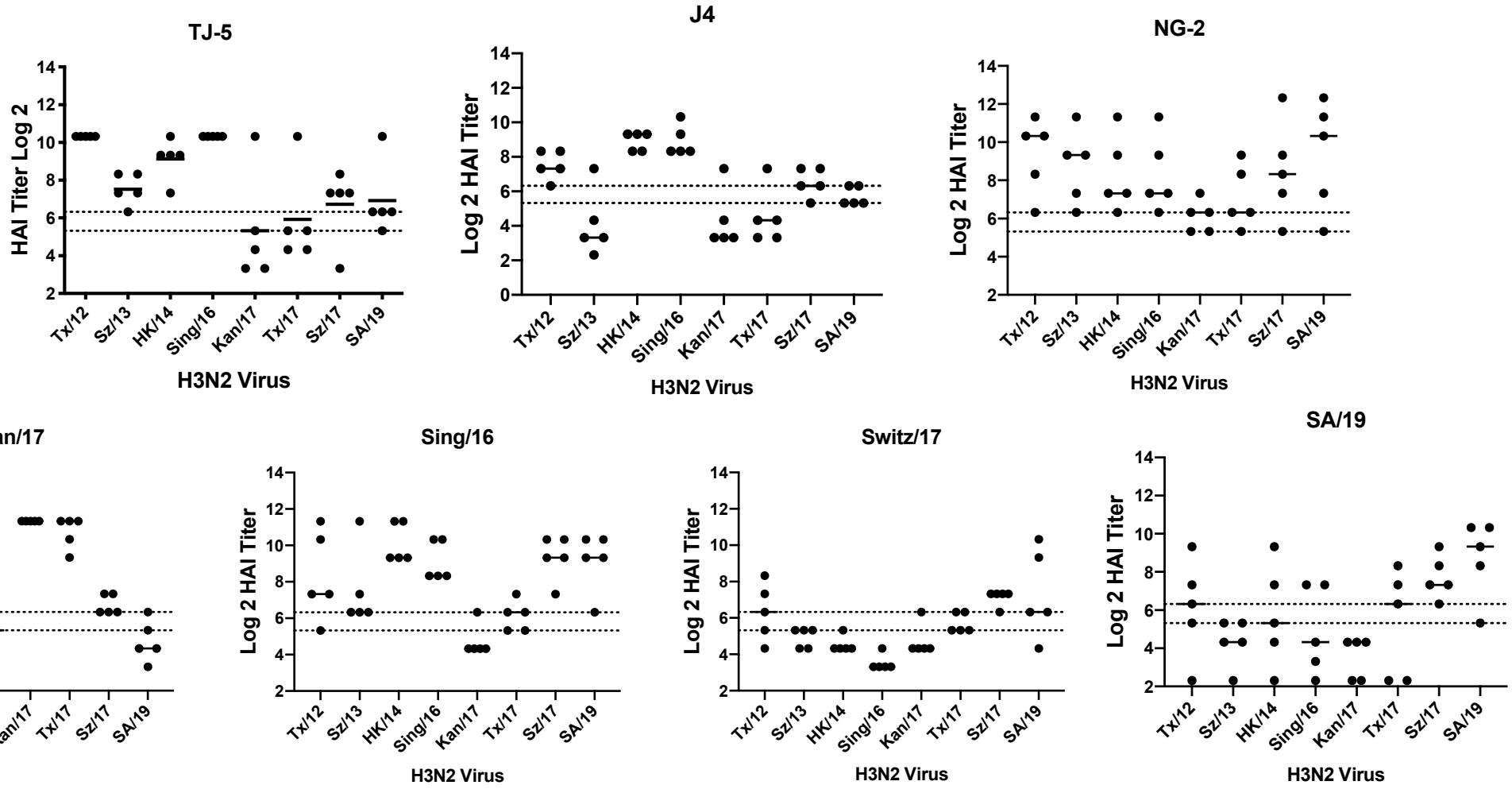


Balb/c mice (N=5) vaccinated 3x with 3ug rHA mixed 1:1 with Addavax (oil-in-water emulsion) adjuvant

Allen et al., 2021. revision.

Vaccine	Design Timeframe
TJ-5	2008-2012
J4	2013-2015
NG-2	2016-2018

H3 COBRA in Naive Mice



Allen et al., 2021. revision.

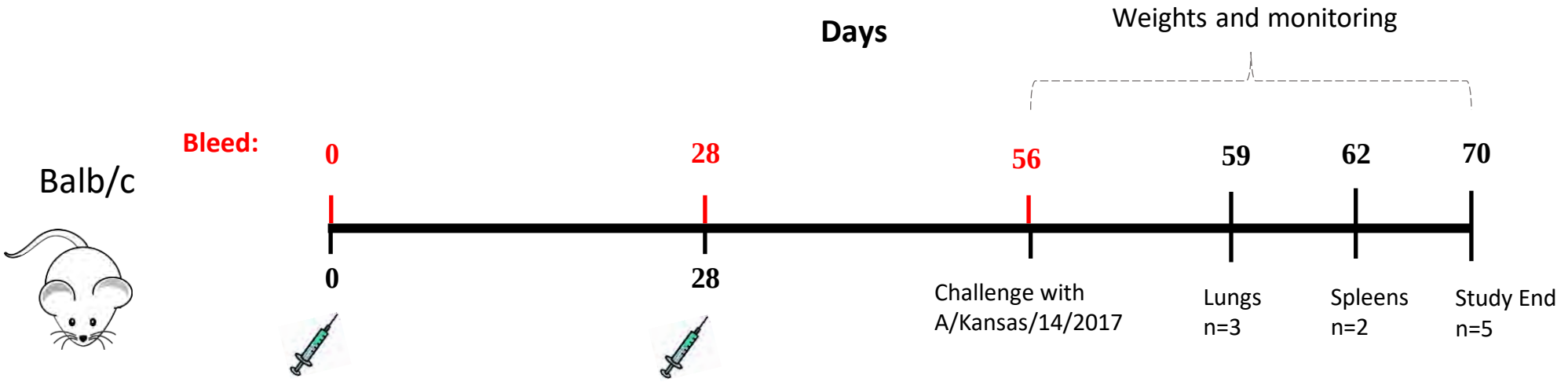
TFF HA Vaccine Study

Naoko
Uno
(UGA)

- **Objective:** Test immunogenicity and efficacy of universal HA vaccines following thin film freezing (TFF) process.
- **Rationale:** TFF process allows protein vaccines to be more stable and long-lasting than in liquid solution.
- **Hypothesis:** TFF HA vaccination will elicit similar breadth of neutralizing antibodies against Influenza virus compared to HA in solution vaccination

Uno et al. 2021. in prep.

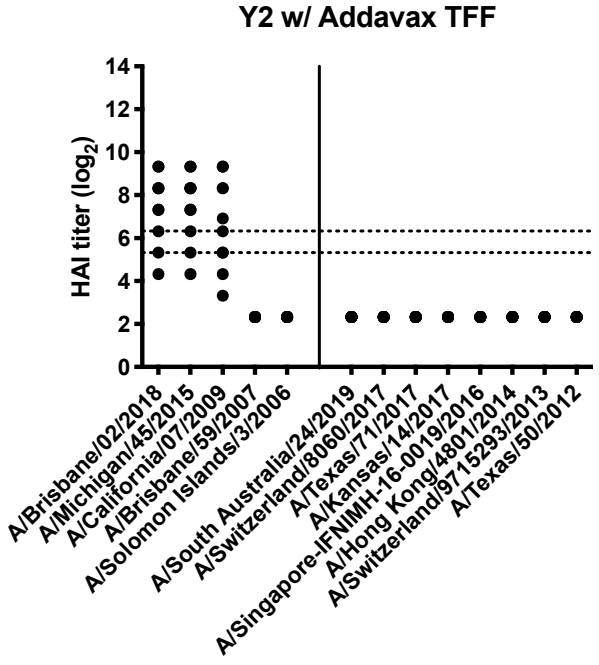
Timeline for vaccinations and bleeds



- HAI on day 56 serum
- Quantify viral titer in lungs
- Influenza-specific B cell response

Group	N	Vaccine (3ug)	Adjuvant	TFF method?
1	10	Y2	Addavax	YES
2	10	J4	Addavax	YES
3	10	Y2+J4	Addavax	YES
4	10	Y2+J4+TJ5	Addavax	YES
5	10	Adjuvant Only	Addavax in solution	YES
6	10	Y2+J4+TJ5	Addavax in solution	YES/No
7	10	Y2 in solution	Addavax in solution	No
8	10	Mock	No	No

Uno et al. 2021. in prep.


Y2 w/ Addavax TFF
HAI titer (log2)
0
2
4
6
8
10
12
14
A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
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A/Switzerland/9715293/2013
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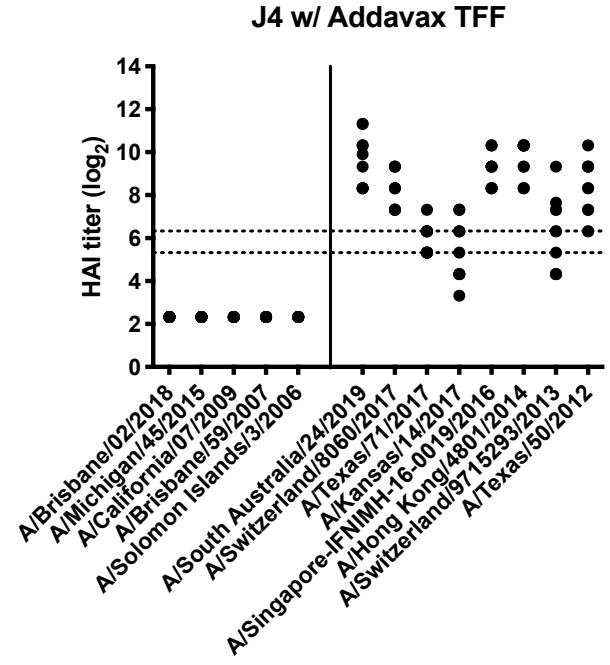
J4 w/ Addavax TFF
HAI titer (log2)
0
2
4
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14
A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
A/Kansas/14/2017
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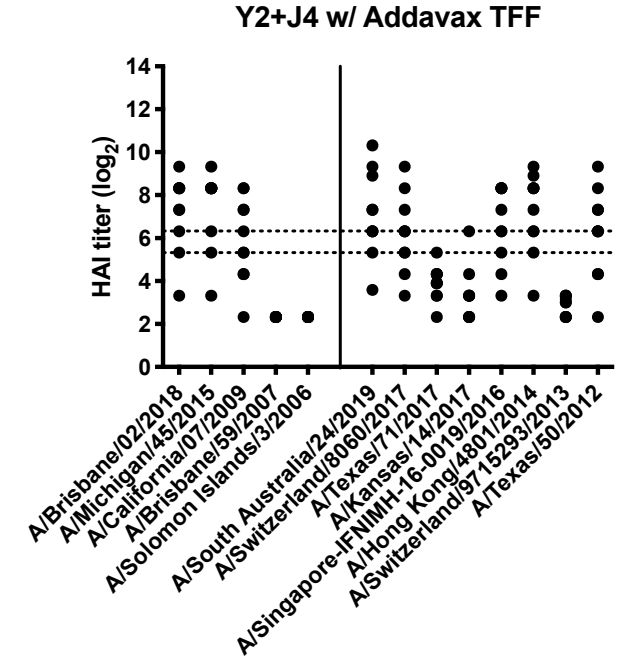
Y2+J4 w/ Addavax TFF
HAI titer (log2)
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A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
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A/Switzerland/9715293/2013
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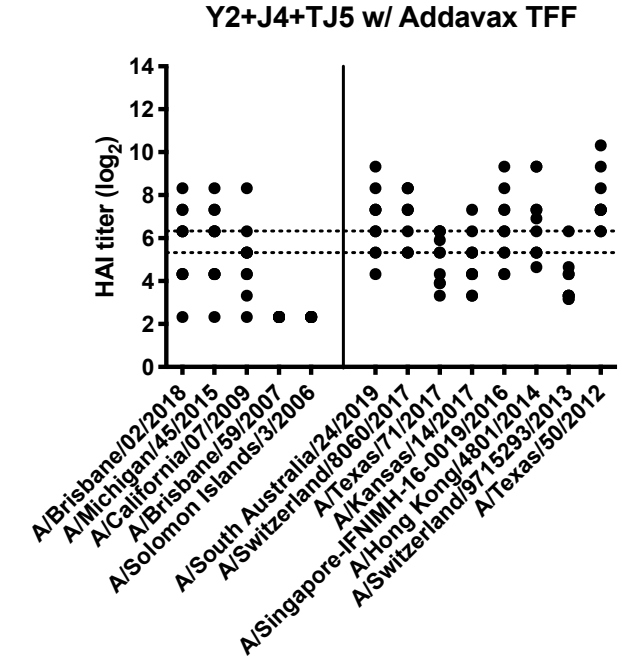
Y2+J4+TJ5 w/ Addavax TFF
HAI titer (log2)
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14
A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
A/Kansas/14/2017
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A/Switzerland/9715293/2013
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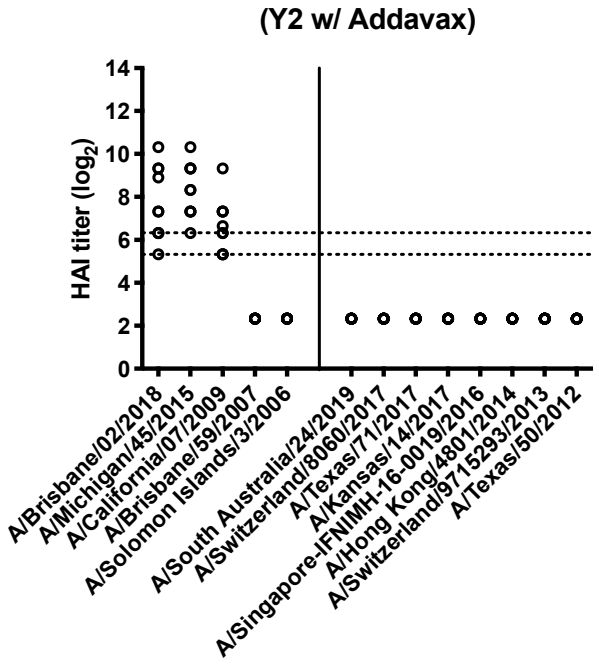
(Y2 w/ Addavax)
HAI titer (log2)
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A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
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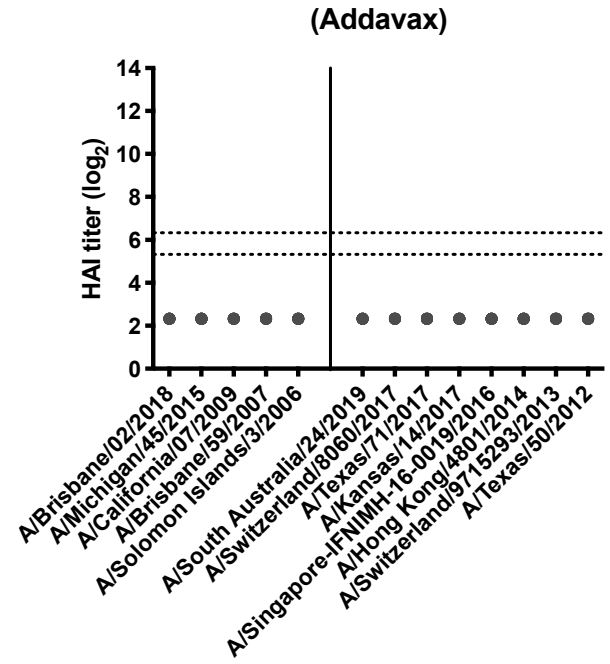
(Addavax)
HAI titer (log2)
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A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
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A/South Australia/24/2019
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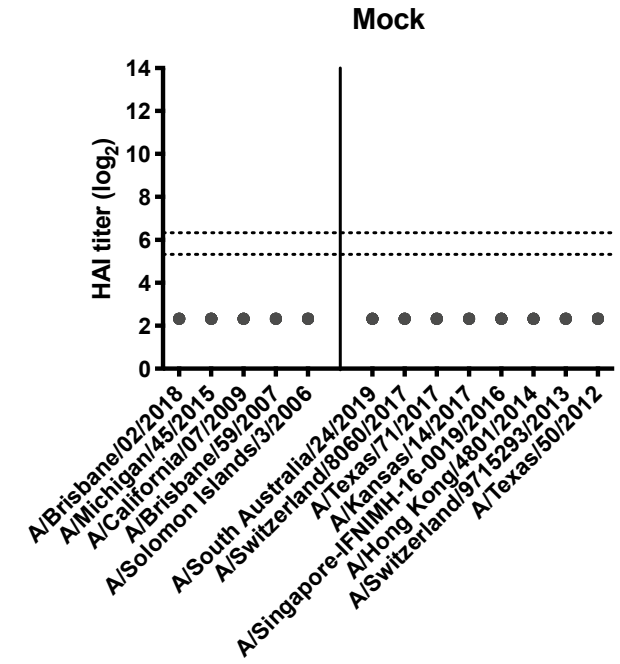
A/Switzerland/9715293/2013
A/Texas/50/2012


Mock
HAI titer (log2)
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A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
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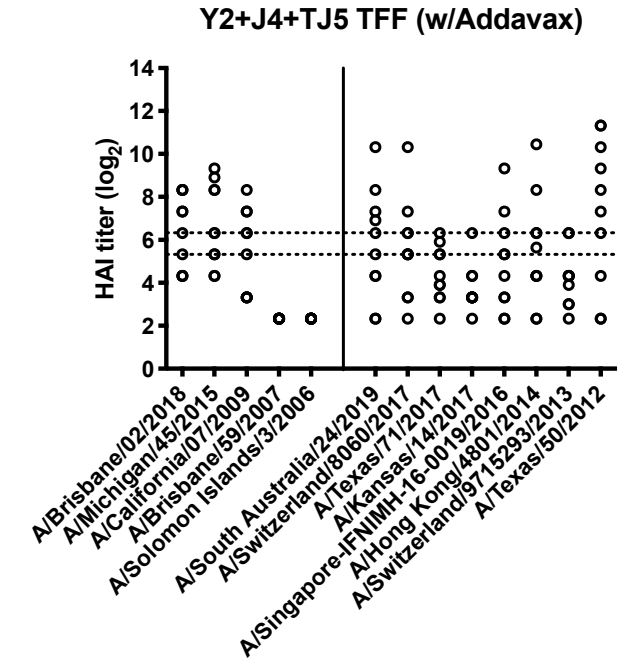
Y2+J4+TJ5 TFF (w/Addavax)
HAI titer (log2)
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A/Brisbane/02/2018
A/Michigan/45/2015
A/California/07/2009
A/Brisbane/59/2007
A/Solomon Islands/3/2006
A/South Australia/24/2019
A/Switzerland/8060/2017
A/Texas/71/2017
A/Kansas/14/2017
A/Singapore-IFNIMH-16-0019/2016
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A/Texas/50/2012

TFF HA Vaccine Study

- Conclusions:
  - TFF process did not decrease effectiveness of HA vaccines in HAIs

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