
FOURTEENTH INTERNATIONAL
ROTAVIRUS SYMPOSIUM
MARCH 14–16 2023 BALI INDONESIA
Learn more on www.sabin.org

Inactivated Rotavirus Vaccine (IRV) Development: An Update

Baoming Jiang

Division of Viral Diseases

CDC

bxj4@cdc.gov

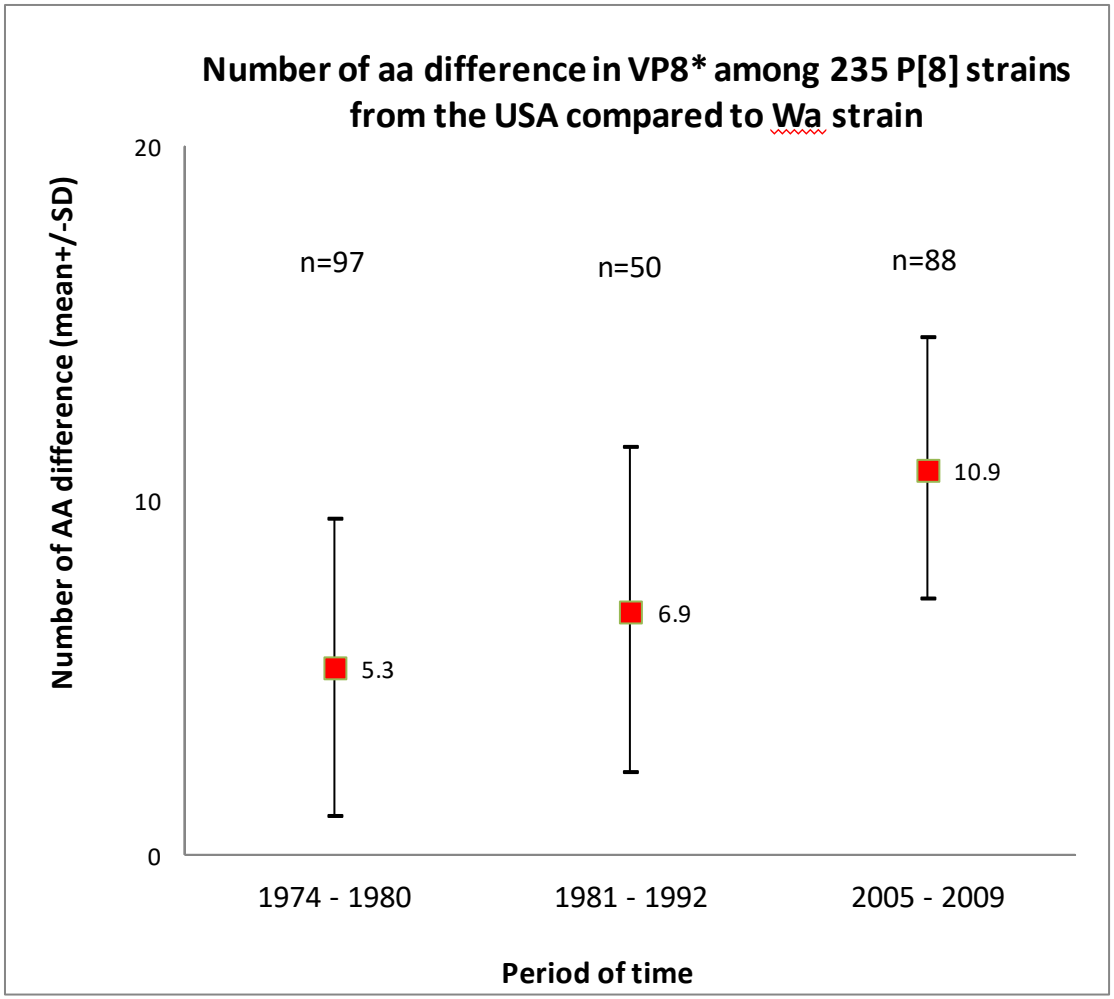
14th International Rotavirus Symposium

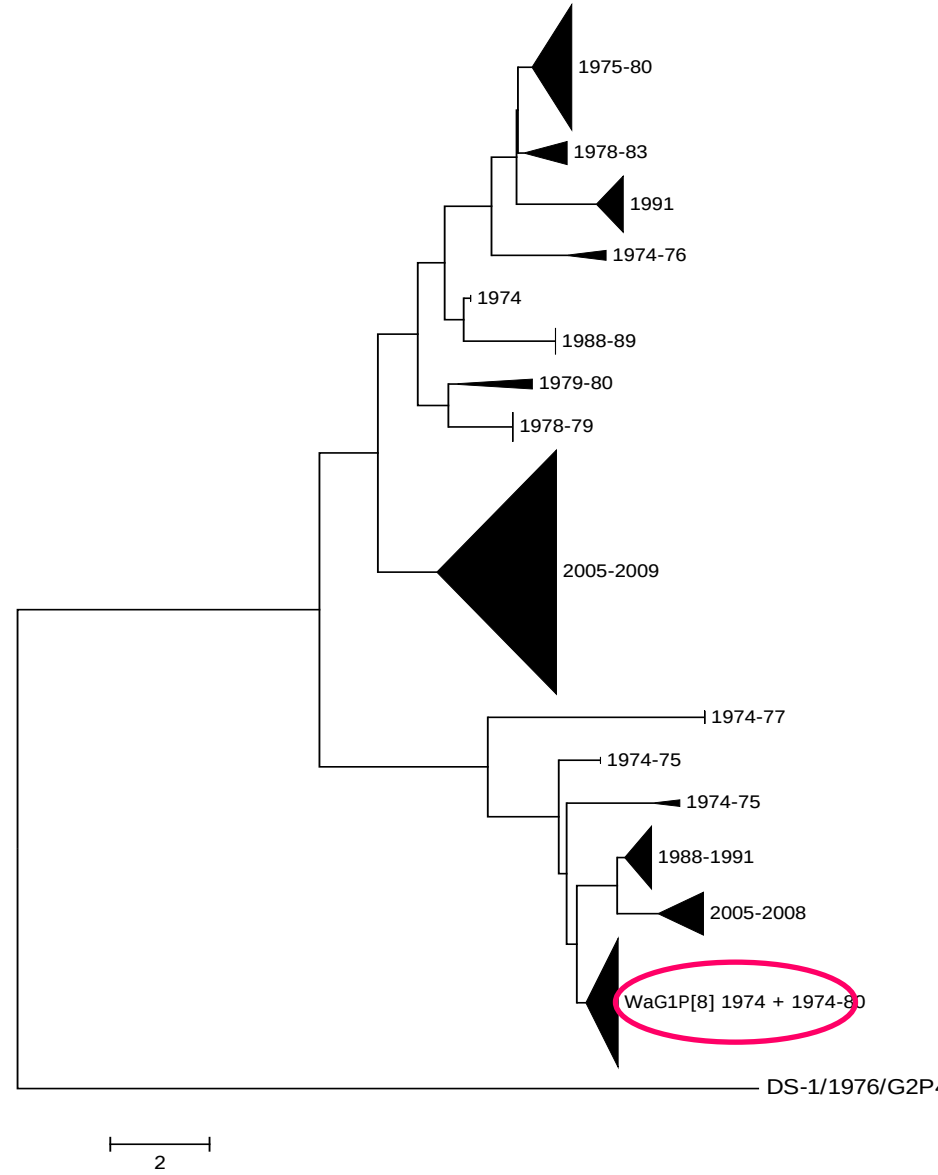
Bali, Indonesia

March 16, 2023

CDC
Centers for Disease Control and Prevention

VP8* of RV strains is highly variable and has a high mutation rate





Jiang, 11th Int RV Sym, 2014; Velasquez & Jiang, Human Vaccines 2019

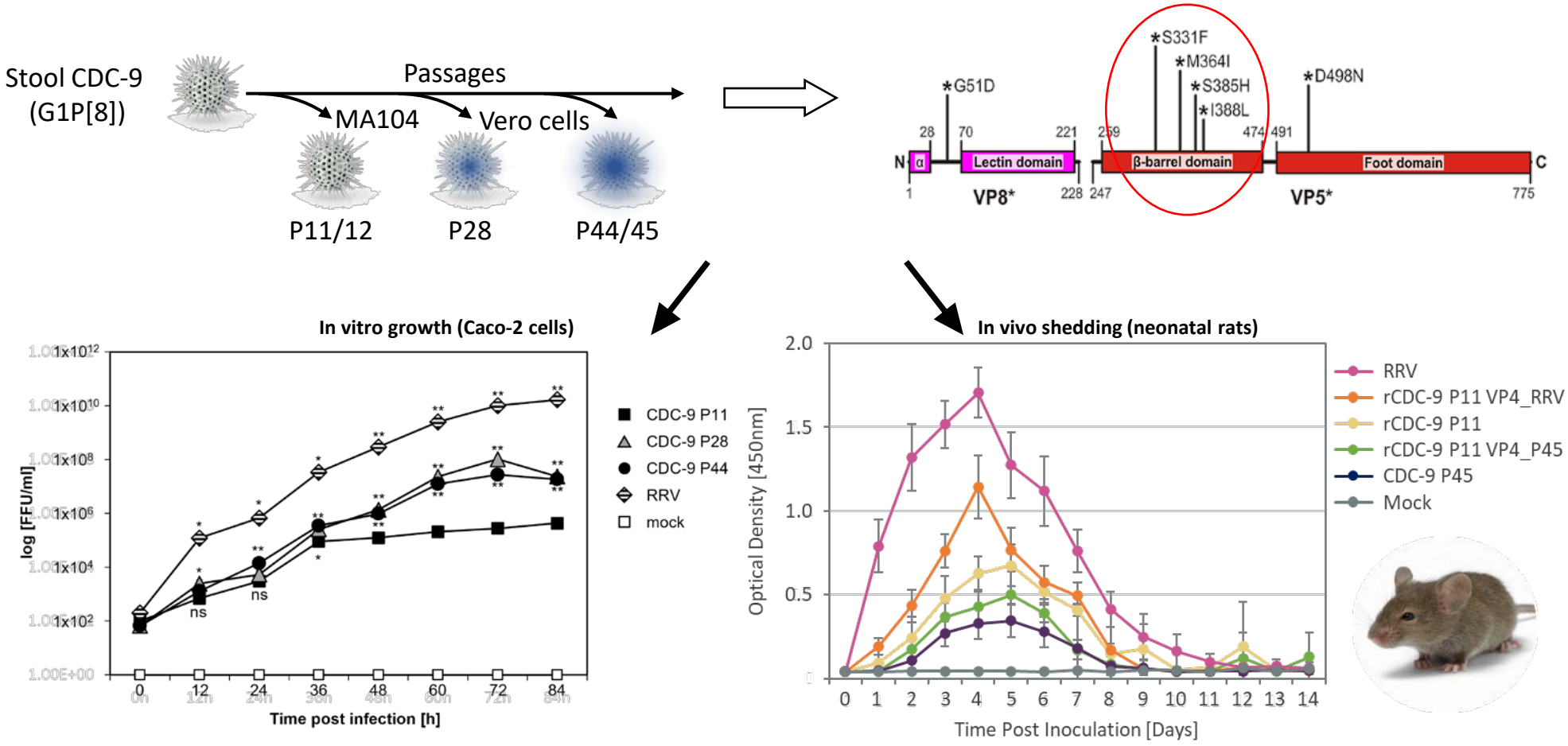
Parenteral rotavirus vaccine design

Which antigen should be included:

VP8, VP5, Whole Virion ?

CDC
Centers for Disease Control and Prevention

VP5 not VP8 is involved in rotavirus adaptation and attenuation

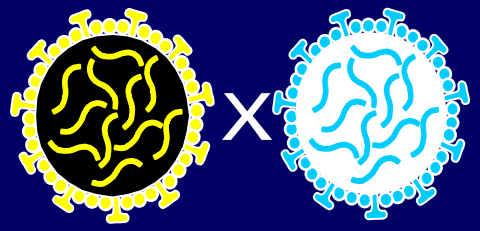


- **Sequence changes in VP4 during serial passages lead to adaptation in vitro and attenuation in vivo**
- **VP5, not VP8, is involved in virus virulence/attenuation and should be included in vaccine design**
- **Three of the four mutations in VP5 are conserved in Rotarix as well**

Poster #1003

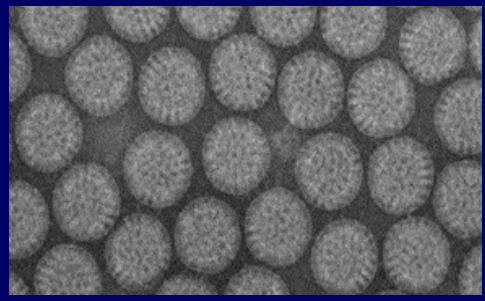
Resch et al. 2020 J Virol; Jenni et al. 2022 J Virol

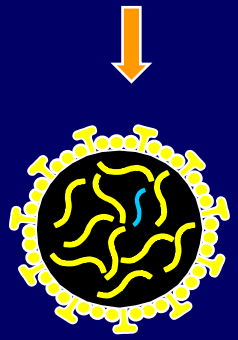
IRV: Human Strain CDC-9 with High Growth & Stability

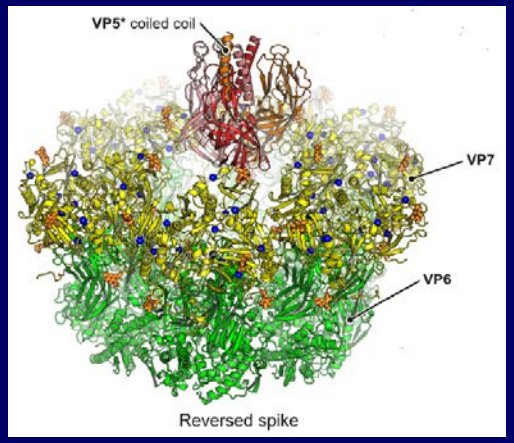


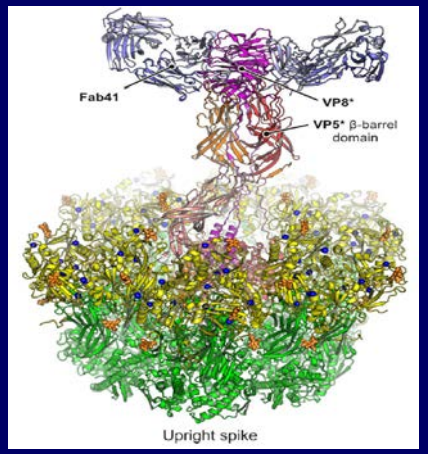
MA104 Cells →

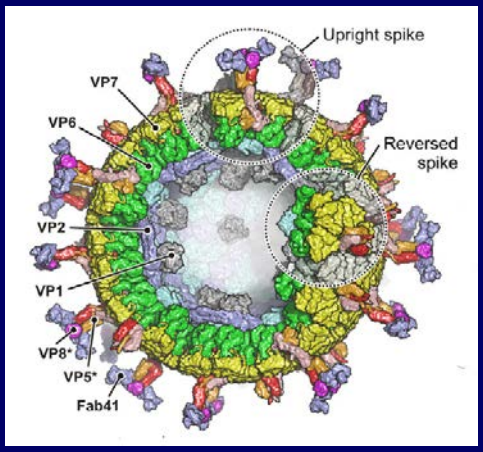
Vero Cells →











Stool virus

No sequence change
~ 10^5 ffu/ml
Unstable, virulent

Several aa changes
~ 10^{7-8} ffu/ml
Stable, attenuated

Esona et al, Human Vac, 2010; Resch et al, J Virol, 2020; Jenni et al, J Virol, 2022

CDC
Centers for Disease Control and Prevention

OBJECTIVES: Develop an IRV to improve rotavirus vaccine efficacy and safety

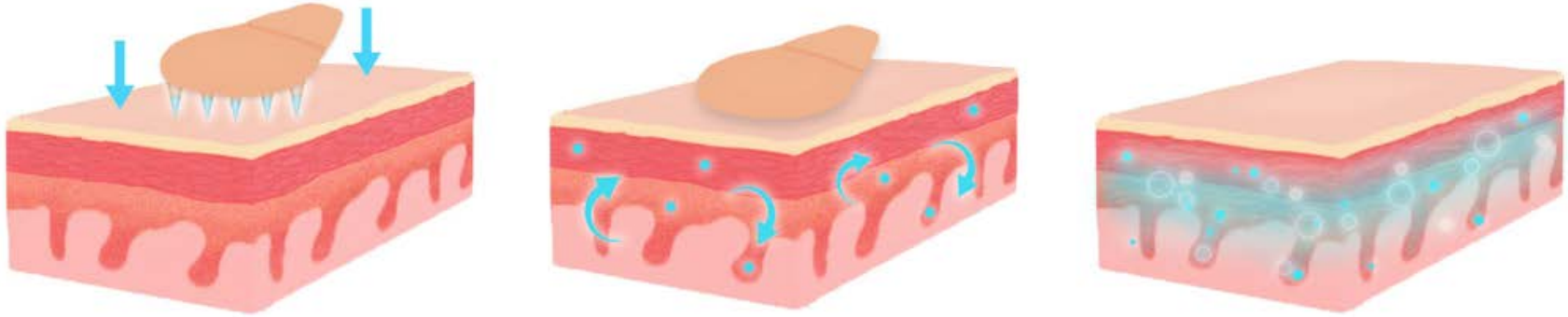
- -- by intramuscular (IM) administration
- -- via skin vaccination using a microneedle patch (MNP)

Long-term goals: Add IRV to licensed combination vaccines

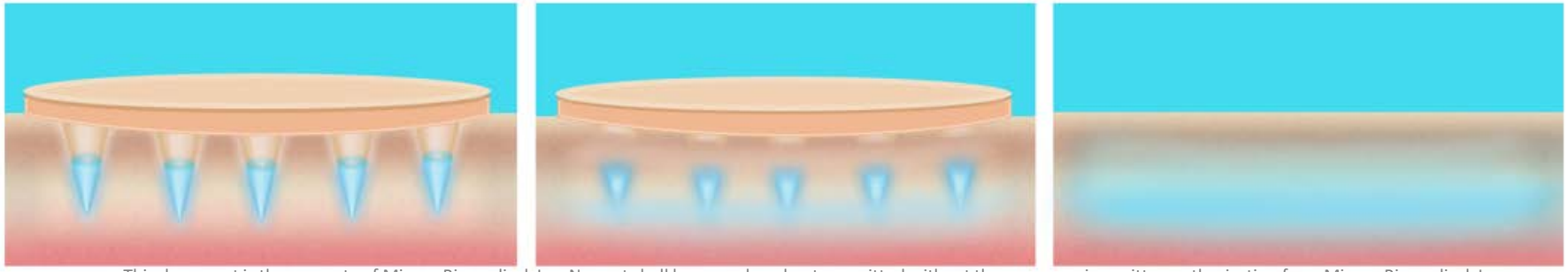
- -- Heptavalent (DTP,Hib,HBV,IPV,IRV) for primary immunization (IM)
- -- IRV-IPV as a booster dose (MNP)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Microneedles dissolve in the skin to deliver actives with no sharps waste

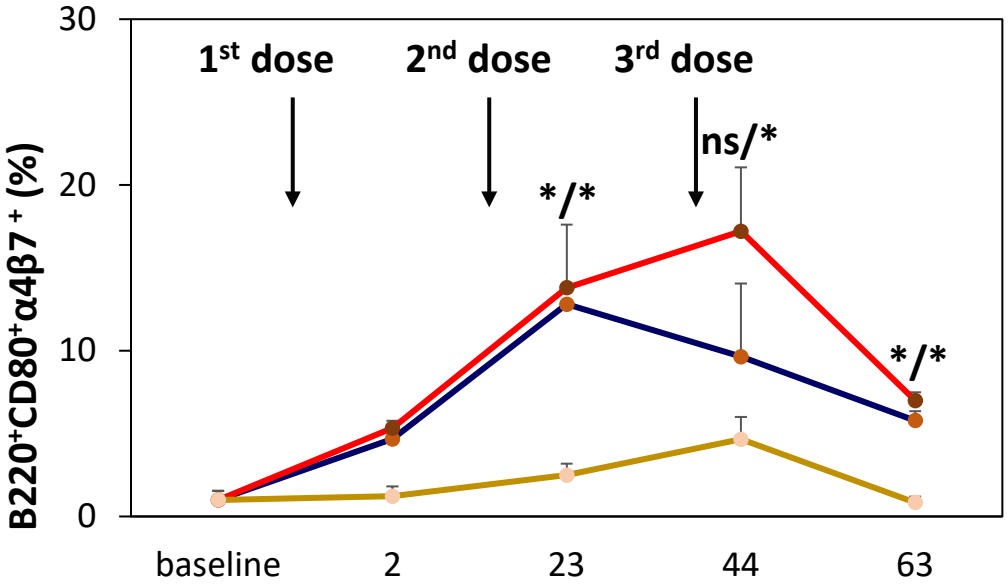


MNs are applied to skin, penetrate epidermis and upper dermis → **MNs dissolve or biodegrade and separate from backing** → **MNs release their cargo, backing is discarded as non-sharps waste**

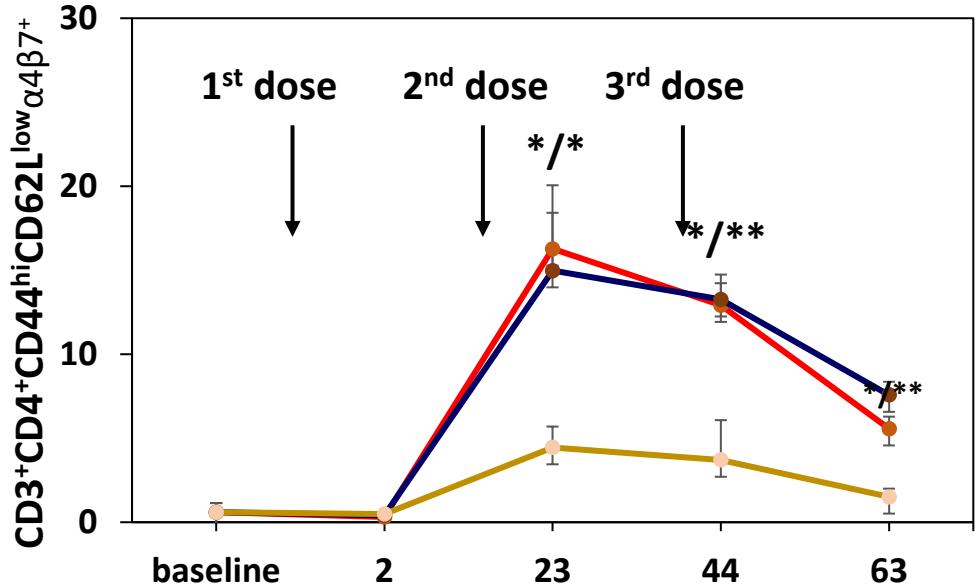


IRV vaccination activates gut homing B & T cells in immune systems

B Cell (MLN)



CD4 T Cell (Spleen)

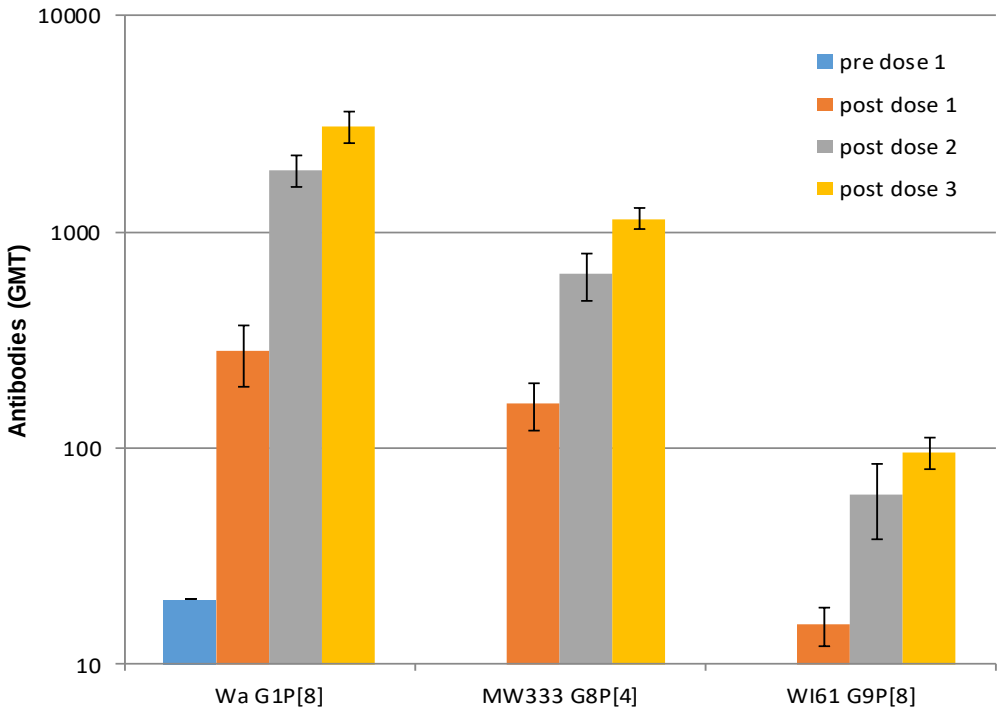


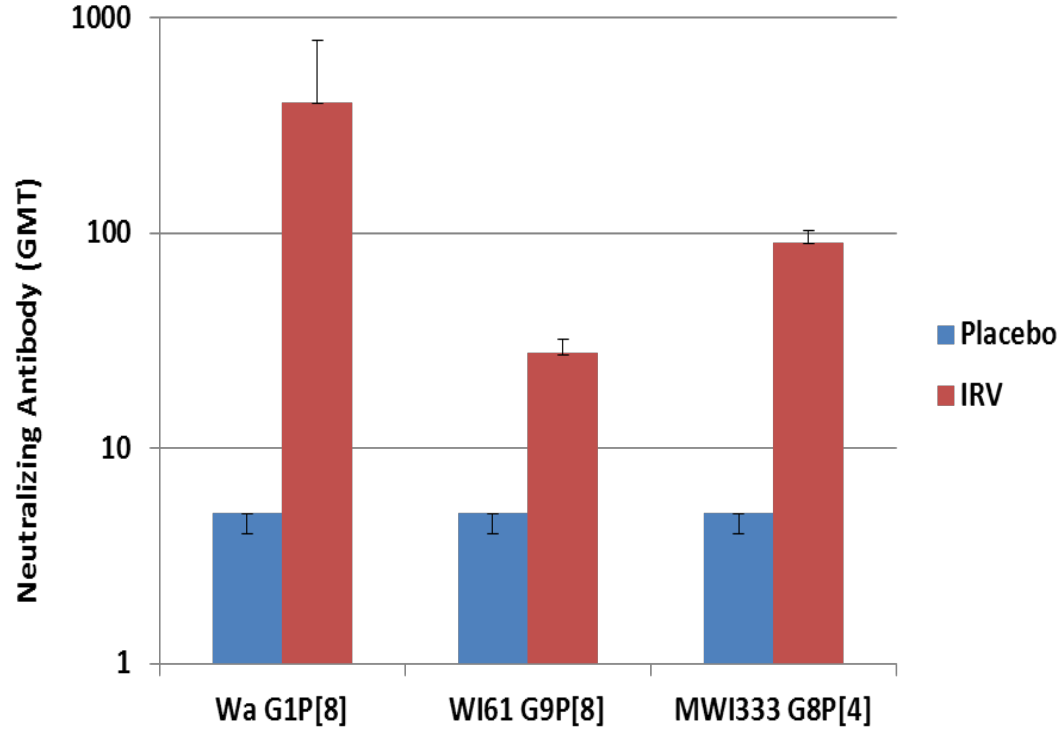
Time post first vaccination (days)

Placebo 1µg IRV 5µg IRV

T Resch et al Scientific Reports, 2018; * < 0.05, ** < 0.01

CDC-9 IRV induces cross neutralizing antibody to homotypic and heterotypic strains

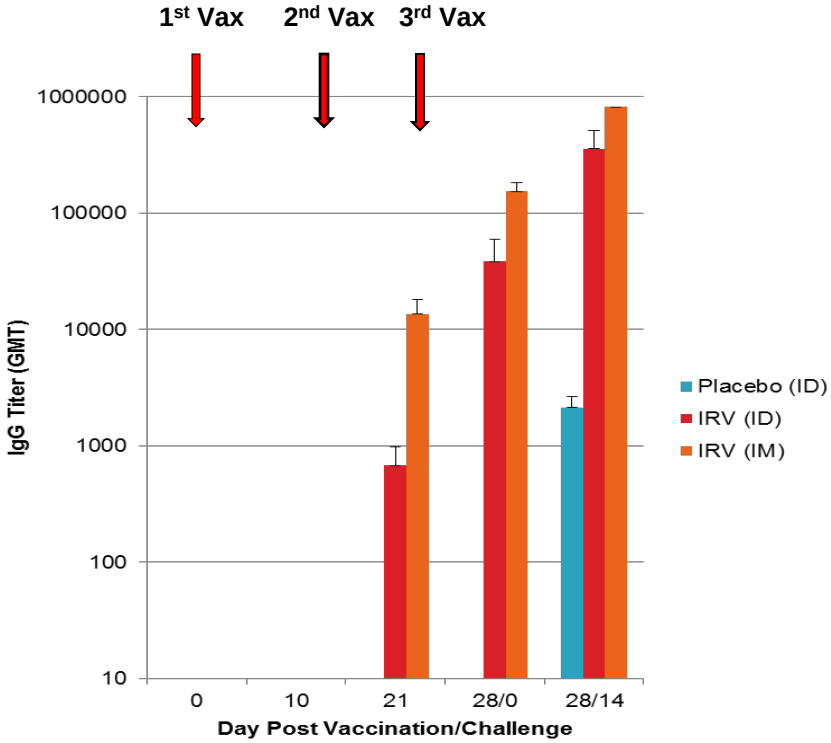


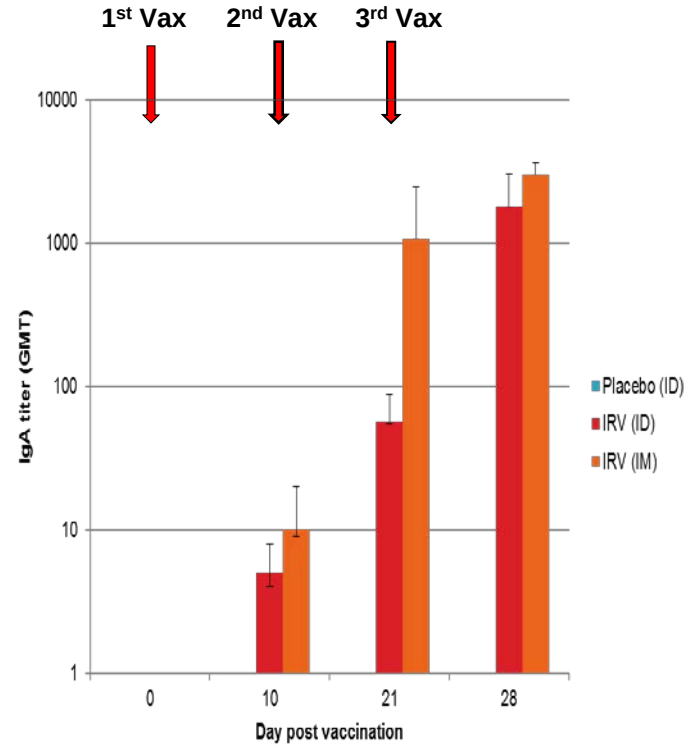


Jiang et al, Human Vaccines & Immunotherapeutics 2013

Wang et al Vaccine 2010

ID & IM immunization induces comparable IgG & IgA titers in gnotobiotic piglets



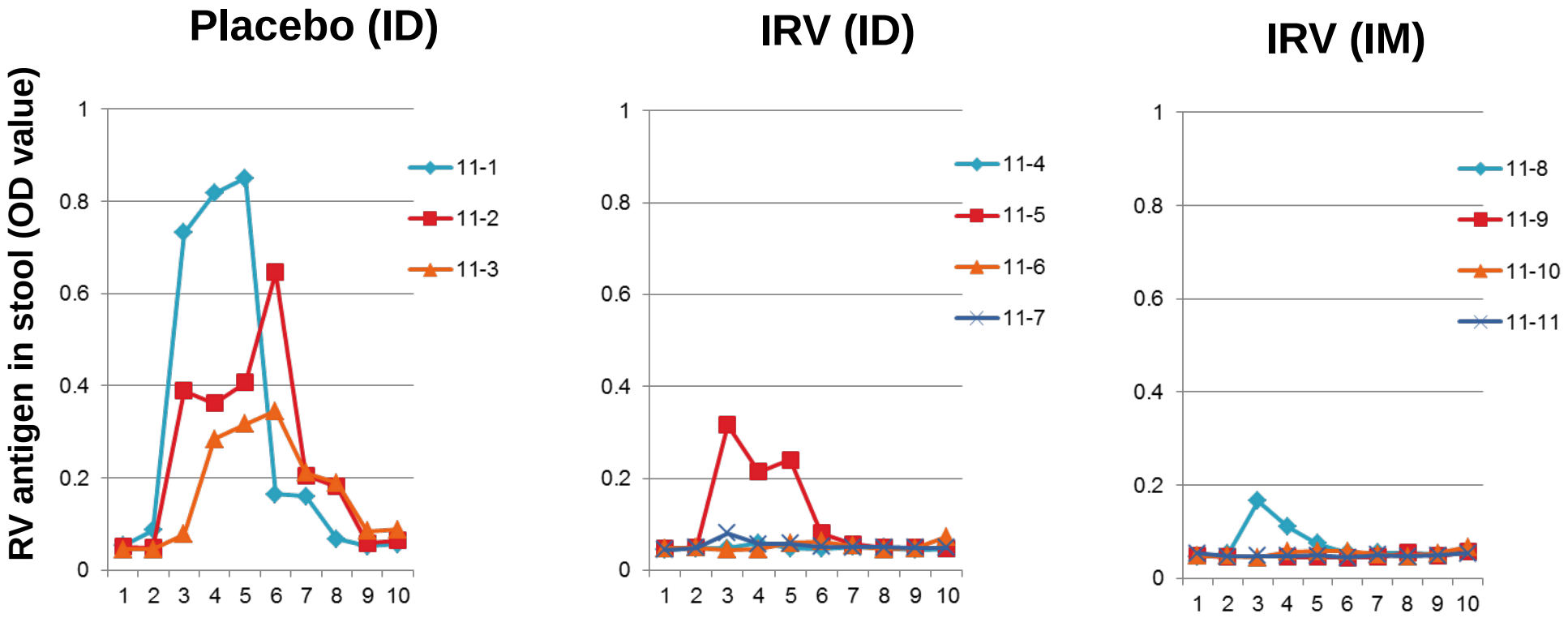


ID: 5 µg Ag; IM: 5 µg Ag + 600 µg Al(OH)3; Placebo: diluent

Wang et al Vaccine (2010)
Wang et al PLOS One (2016)

CDC
Centers for Disease Control and Prevention

IRV induces protection against oral challenge in piglets



Days after oral challenge

RV shedding in stool was measured by EIA

Wang et al Vaccine (2010)
Wang et al PLOS One (2016)

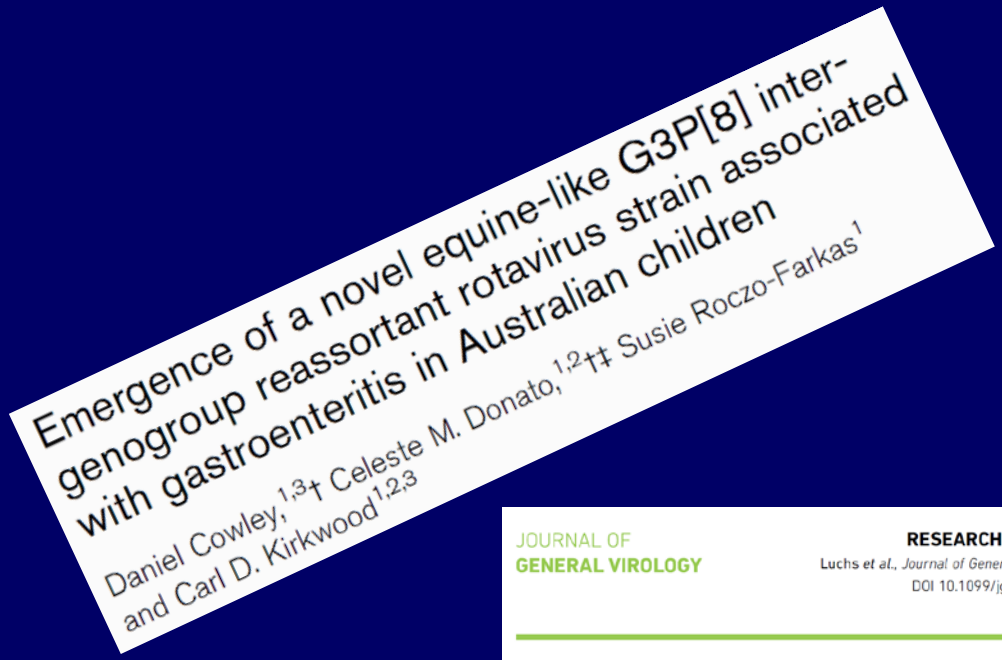
CDC
Centers for Disease Control and Prevention

IRV Development - Summary

- **Parenterally administered IRV is highly effective in pre-clinical studies**
  - **Cross-neutralizing antibody (homotypic & heterotypic strains), Intestinal immunity**
  - **Protective efficacy against oral challenge in piglets**
- **Established GMP manufacturing process & analytics**
  - **Validated processes and release assays**
  - **GMP vaccine bulk has been prepared, stability study is in progress**
- **Toxicology**
  - **IM IRV study is completed: no adverse local or systemic effects in Wistar rats/guinea pigs**
  - **MNP IRV study is in progress**
- **Received written responses to Pre IND package (IM & MNP) – Green light to proceed. IND package preparation is in progress**
- **Phase 1 clinical trials of IM & MNP IRV are scheduled in Q3/Q4 2023**

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Emergence of Equine-like, DS-1-like G3P[8] Strains



Emergence of a novel equine-like G3P[8] inter-genogroup reassortant rotavirus strain associated with gastroenteritis in Australian children

Daniel Cowley,[1,3]† Celeste M. Donato,[1,2]†‡ Susie Roczo-Farkas[1] and Carl D. Kirkwood[1,2,3]

ELSEVIER

Contents lists available at ScienceDirect

Infection, Genetics and Evolution

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

Short communication

Equine-like G3 rotavirus strains as predominant strains among children in Indonesia in 2015–2016

JOURNAL OF GENERAL VIROLOGY

RESEARCH ARTICLE

Luchs *et al.*, *Journal of General Virology* 2019;100:7–25

DOI 10.1099/jgv.0.001171

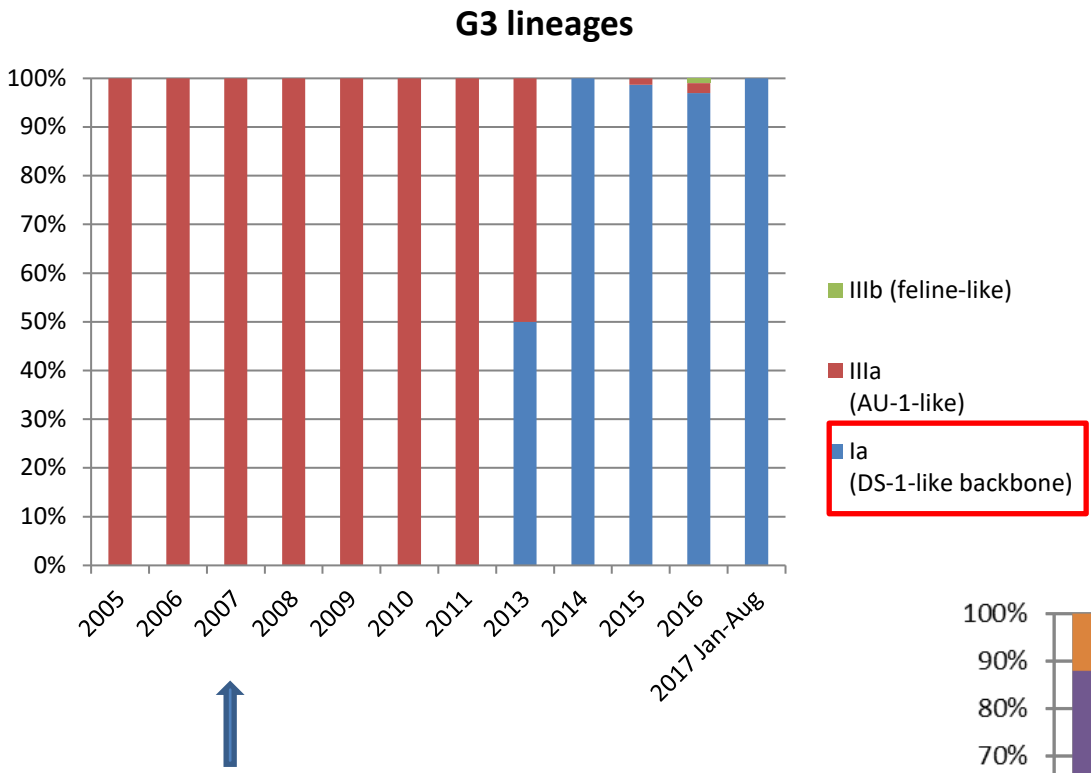
MICROBIOLOGY SOCIETY

Spread of the emerging equine-like G3P[8] DS-1-like genetic backbone rotavirus strain in Brazil and identification of potential genetic variants

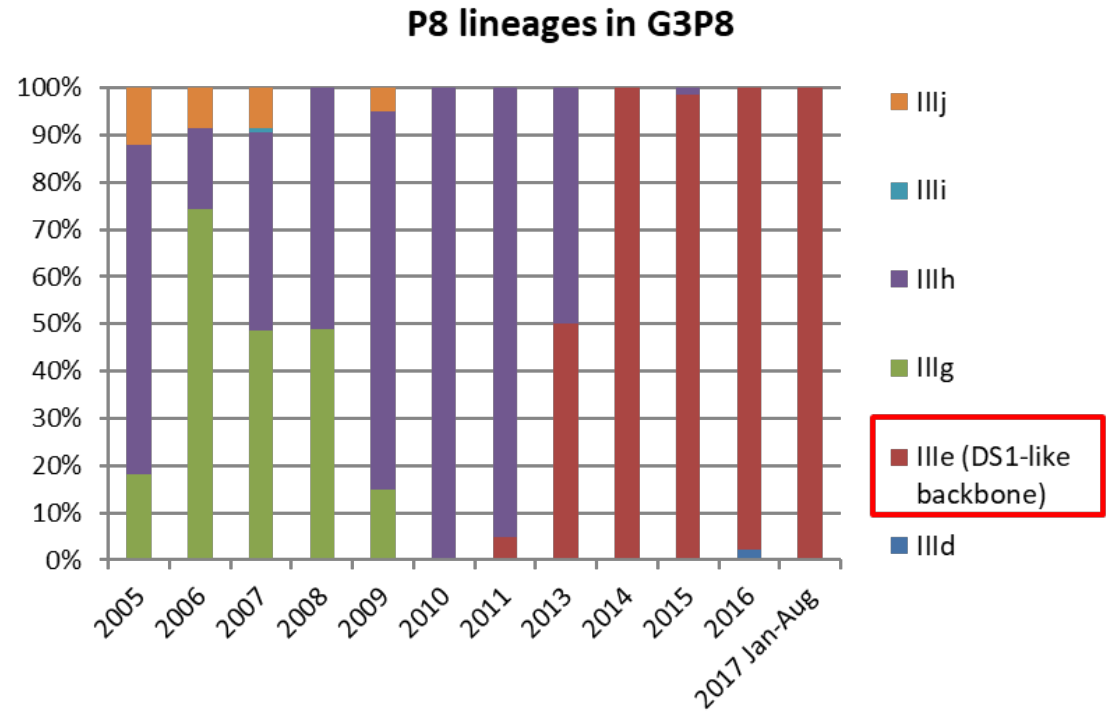
CDC

Centers for Disease Control and Prevention

Equine-like, DS-1-like G3P8 strains predominate in recent years, Taiwan

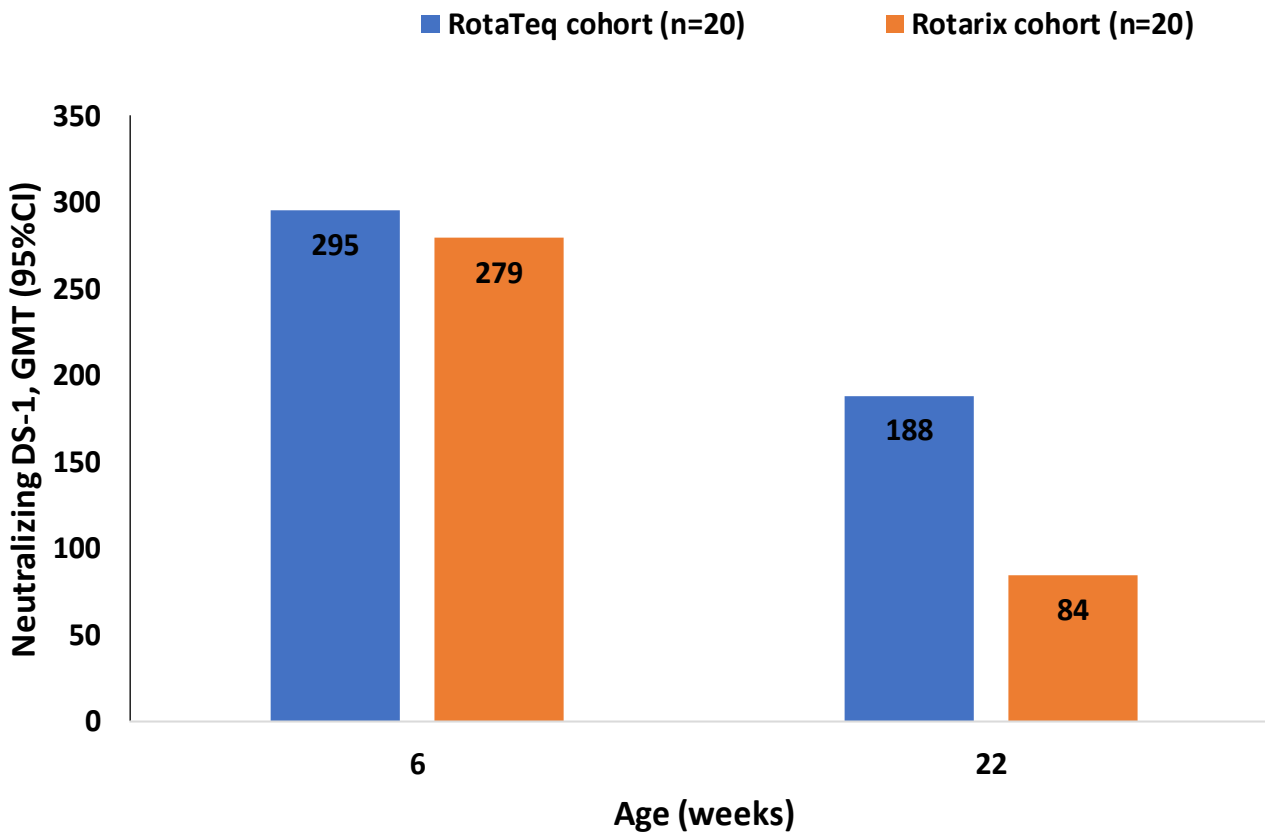


Vaccine introduced



Wu, FZ, unpublished data

Children vaccinated with Rotarix appear to have lower neutralizing antibody titers against DS-1 (G2P[4]) strain than those with RotaTeq vaccination, Bangladesh



Poster #1040

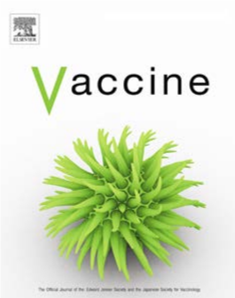
D Velasquez, J Hull, et al, unpublished data

Emergence of Equine-like, DS-1 like Strains
Observations & Implications

- Were not detected in pre-vaccine era
- Appears to be predominate in countries/territories that use Rotarix
- Children who receive Rotarix vaccine appear to have lower cross neutralizing antibody response to DS-1 strains
- There appears to be evidence for vaccine-induced selective pressure and lower population immunity, leading to selection emergence of novel DS-1 like zoonotic strains in countries that use Rotarix
- Need to monitor Rotavac and Rotasiil

Do we need to add a DS-1 like vaccine ?

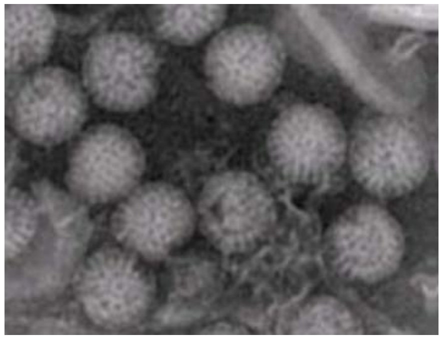
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION



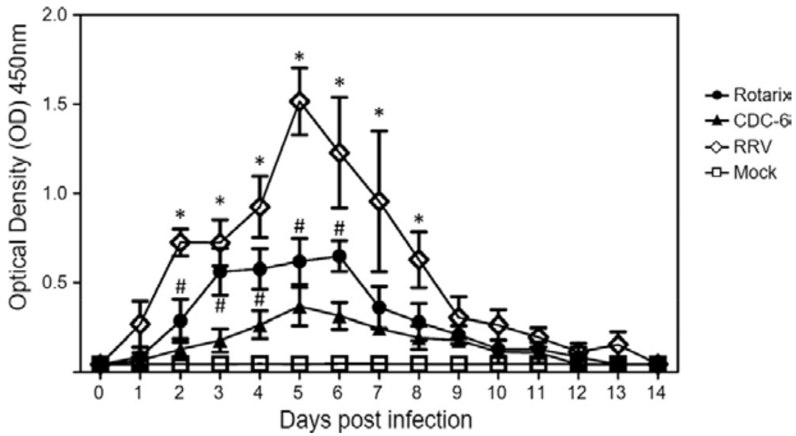
A DS-1 like G9P[6] human strain CDC-6 as a new rotavirus vaccine candidate

Yuhuan Wang, Theresa Resch, Mathew D. Esona, Sung-Sil Moon, Baoming Jiang *

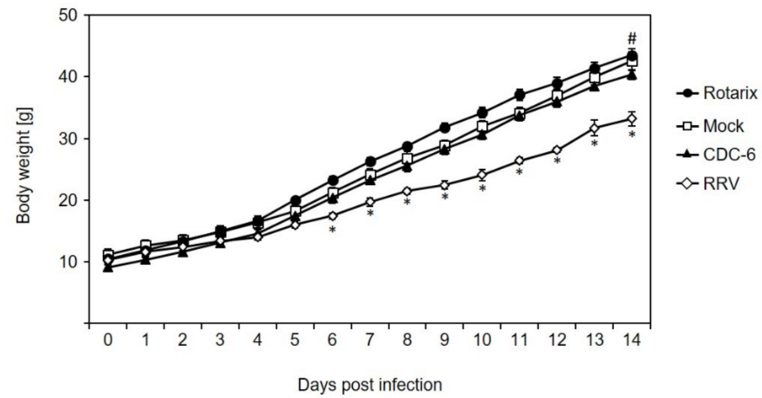
Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30329, USA



G9P[6]



Reduced RV shedding (similar to Rotarix)



Normal body weight gain

- **10^8 ~ 10^9 titer in Vero cells**
- **Structurally stable (>90% TLP)**
- **Safe & attenuated in neonatal rats**
- **Broad susceptibility in children**

Y Wang et al, Vaccine, 2018

CENTERS FOR DISEASE CONTROL AND PREVENTION

Acknowledgments

The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

Bill & Melinda Gates foundation

NIH NIAID

Stanford University

Harry Greenberg

HARVARD UNIVERSITY

Stephen Harrison

EMORY UNIVERSITY

Evan Anderson

Cristina Rostad

Georgia Tech

Mark Prausnitz

OHIO STATE

Linda Saif

Anastasia Vlasova

POONAWALLA GROUP SERUM INSTITUTE OF INDIA LTD.

ZFSW The Biologics Company

WRAIR Walter Reed Army Institute of Research Soldier Health • World Health

Micron Biomedical

Meridian Life Science, Inc.

CDC FOUNDATION Helping CDC Do More, Faster

CDC Centers for Disease Control and Prevention