

Immunization of Pregnant Baboons with  
RSV F Nanoparticle Vaccine  
Protects Infant Baboons Challenged  
with Respiratory Syncytial Virus  
In a Comparable Manner to Palivizumab  
Prophylaxis

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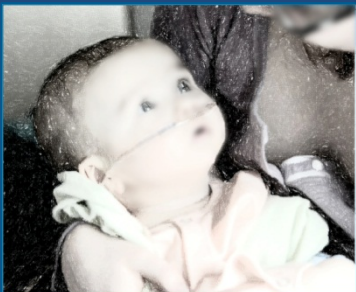
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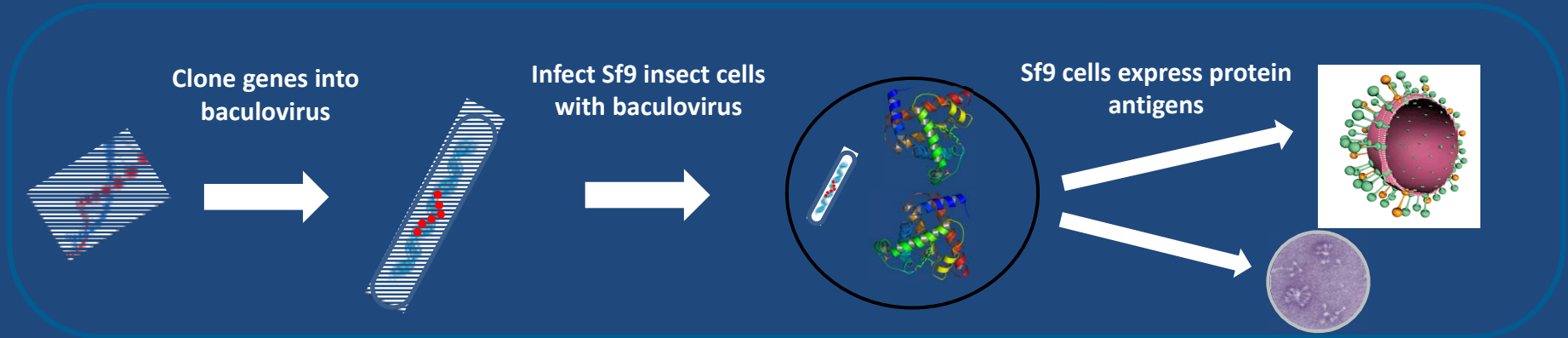
# Respiratory Syncytial Virus (RSV)

- Most frequent cause of infant hospitalization in the US, and causes 200,000 deaths worldwide annually<sup>1,2</sup>
- Severe disease in infancy often leads to recurrent wheezing<sup>3</sup>
- No licensed vaccine or effective antiviral
- Highest rates of hospitalization and severe disease occur < 90 days of age<sup>4</sup>
- Monoclonal antibodies to F protein (palivizumab, motavizumab) reduce hospitalization rates and sequelae in randomized clinical trials<sup>5</sup>
- Palivizumab is expensive, recommended for high-risk infants only

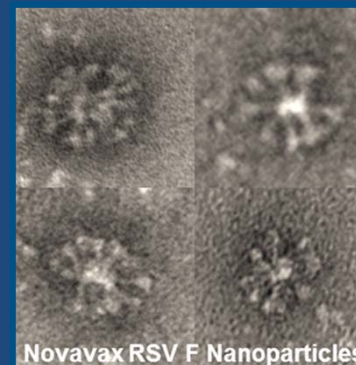
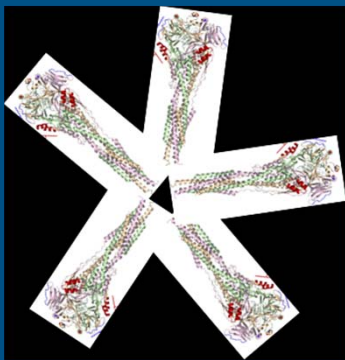


1. Nair, et al. Lancet 2010, 375:1545
2. MMWR , 2013, 263:141
3. Escobar et al. BMC Pediatrics 2013, 13:97;
4. CDC: National Hospital Discharge Survey 2005-2009
5. Yoshihara, Pediatrics 2013; Blanken, NEJM 2013

# Novavax Recombinant F Protein Nanoparticle Vaccine



- RSV F vaccine is composed of recombinant, near-full-length fusion (F) glycoprotein homotrimers
- Purified homotrimers spontaneously assemble into protein micelles of RSV F, may engage TLRs and with potential to drive B-cell antibody affinity maturation



## Infant Baboon Model of RSV Infection: Rationale

- Infant (28 day) baboons develop tachypnea and labored breathing following RSV challenge, like humans but unlike other NHP models
- Infant baboons develop bronchiolar obstruction with exfoliated epithelial and inflammatory cells, like humans, unlike rodent models

Hypothesis: Maternal Vaccination May Protect Infants Against RSV Challenge in a Manner Similar to Palivizumab

# Palivizumab Passive Transfer Protocol

## Protocol

### Study Day -1 (infant age 27 days)

IM 15mg/Kg Palivizumab or placebo

### Day 0

Infant sedated

Blood, BAL collection, clinical measures  
2X10<sup>8</sup> pfu RSV A2 challenge IT

### Day 5

Infant sedated

Blood, BAL collection, clinical measures

### Day 7

Infant sedated

Blood, BAL collection, clinical measures

### Day 10

Infant sedated

Blood, BAL collection, clinical measures

## End Point Assays

### Blinded Observations

Respiratory rate (sedated and awake)  
BAL Total Leukocyte count, viral load  
Histopathology

### Serology on serum and BAL fluid

1. Palivizumab competition ELISA (PCA)
2. Micro neutralization (MN)
3. Anti-F IgG ELISA

Challenge of infants done in pairs (1 palivizumab and 1 placebo), n=4 per group

# Maternal Immunization-Infant Challenge Protocol

## Protocol

Mother immunized 3<sup>rd</sup> trimester:  
60µg RSV F adsorbed to AlPO<sub>4</sub> x 3 at 4 week intervals

### Day 0 (infant age 28 days)

Infant sedated  
Blood, BAL collection, clinical, PFT  
2X10<sup>8</sup> pfu RSV A2 challenge

### Day 5

Infant sedated  
Blood, BAL collection, clinical, PFT

### Day 7

Infant sedated  
Blood, BAL collection, clinical, PFT

### Day 10

Infant sedated  
Blood, BAL collection, clinical, PFT

## End Point Assays

### Blinded Observations

Respiratory rate  
BAL Total Leukocyte count, viral load  
WOB, PEFR  
Histopathology

### Serology on serum and BAL:

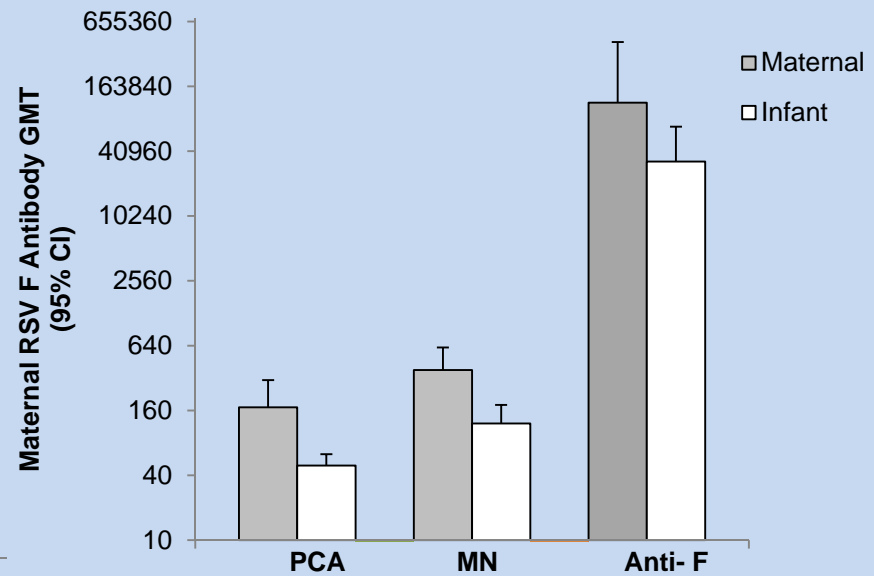
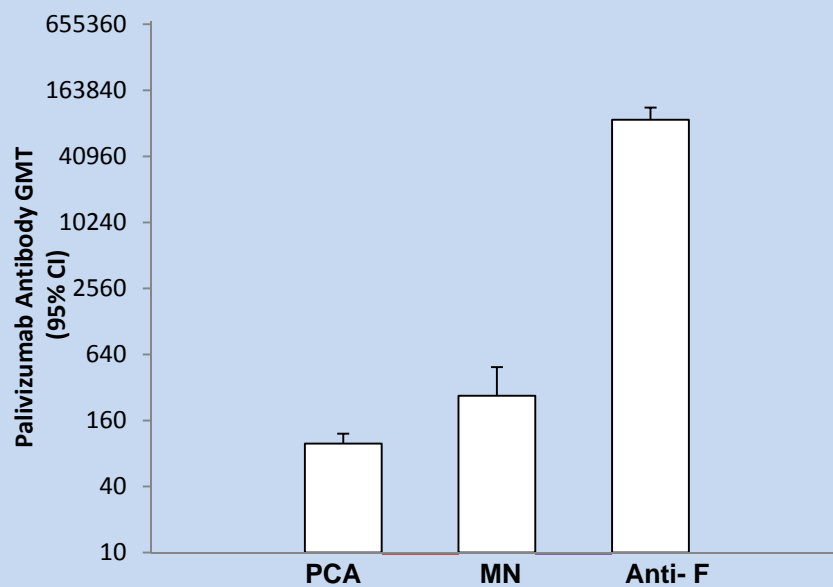
1. Palivizumab competition (PCA)
2. Micro neutralization (MN)
3. Anti-F IgG ELISA

Challenge of infants done in pairs (1 maternal vaccination and 1 unvaccinated), n=5 per group

# Antibody Titers Present in Infants at Time of RSV Challenge

Palivizumab given Challenge Day -1  
Infant titers measured Day 0

Maternal and Infant titers measured on  
Challenge Day 0 and 26 respectively



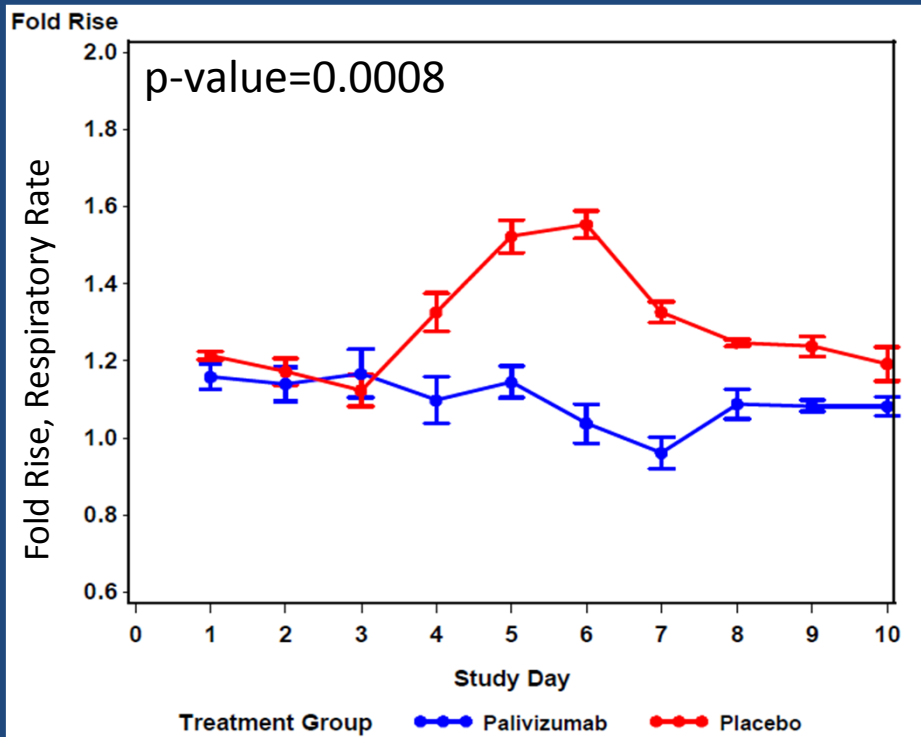
PCA: Palivizumab competing antibodies, PCA reported as EU ( 2X=  $\mu\text{g/ml}$ ) MN: Micro neutralization

RSV titers in infants of vaccinated mothers are similar to palivizumab titers

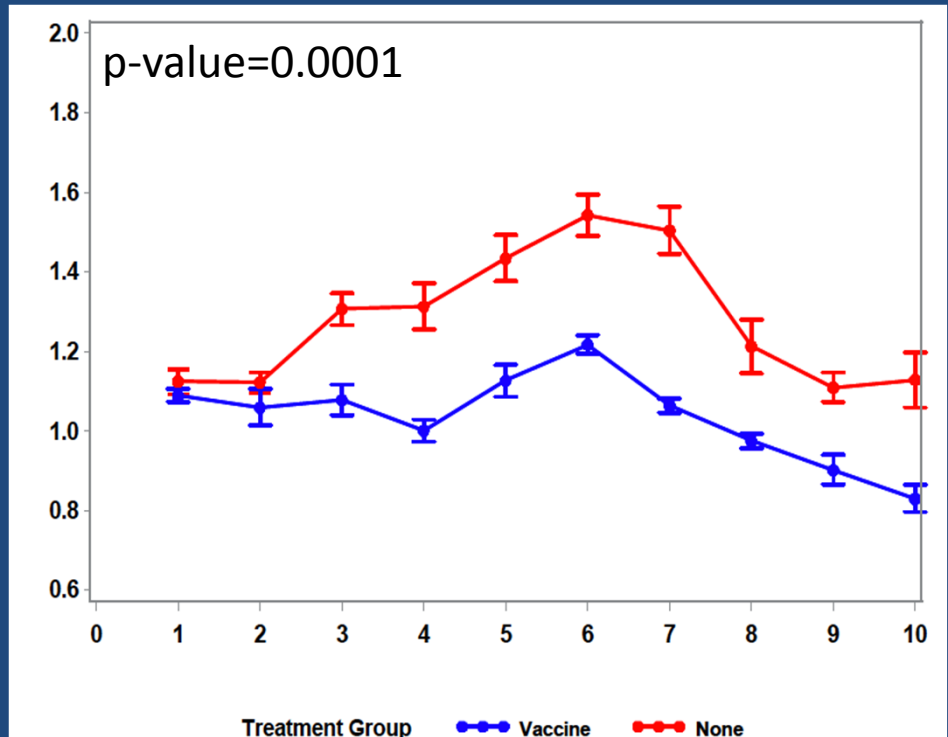
# Palivizumab and Maternal Immunization Prevent Tachypnea in Infant Baboons Challenged with RSV

Fold Rise in Respiratory Rate Above Baseline

Palivizumab study



Maternal immunization study



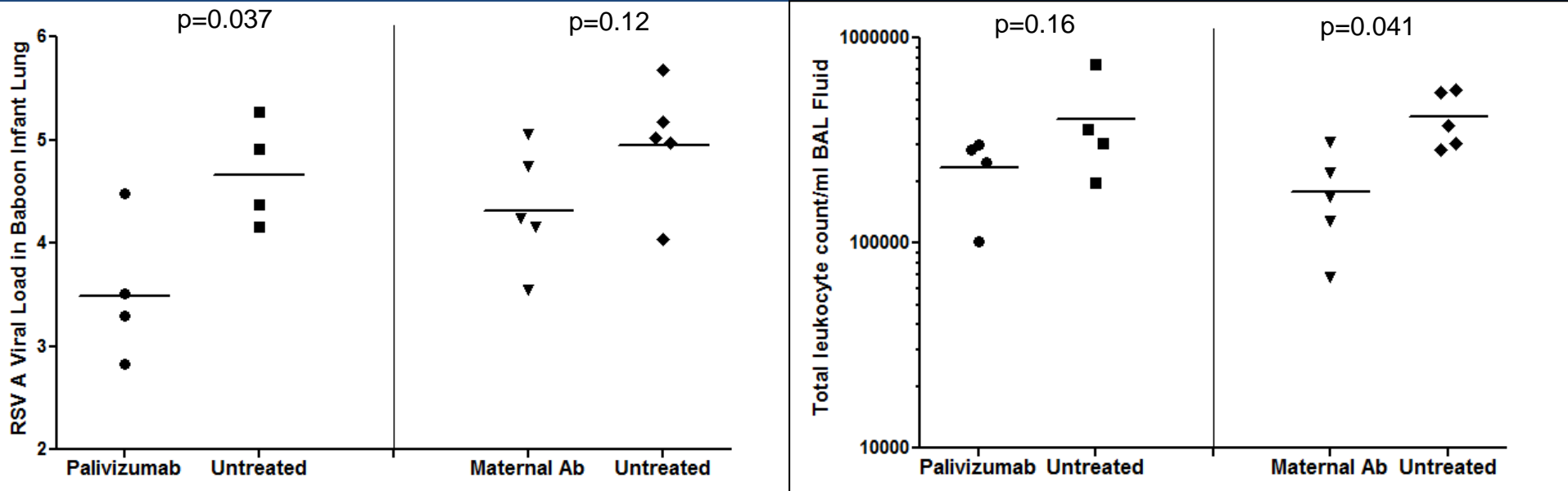
P- values were calculated using t-test from Anova. Error bars represent standard errors of the mean (SEM)



# Effect of Palivizumab and Maternal Vaccination on Viral Recovery and Total Leukocyte cells in BAL Fluid In Infants

Lung Viral Load Day 5

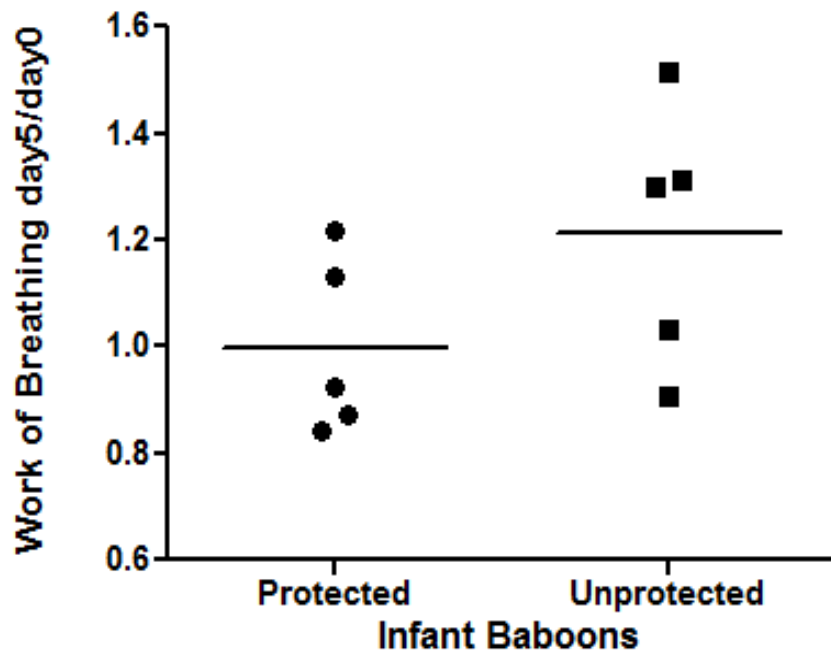
BAL Total Leukocyte Day 5



P values were calculated using a Student's t Test

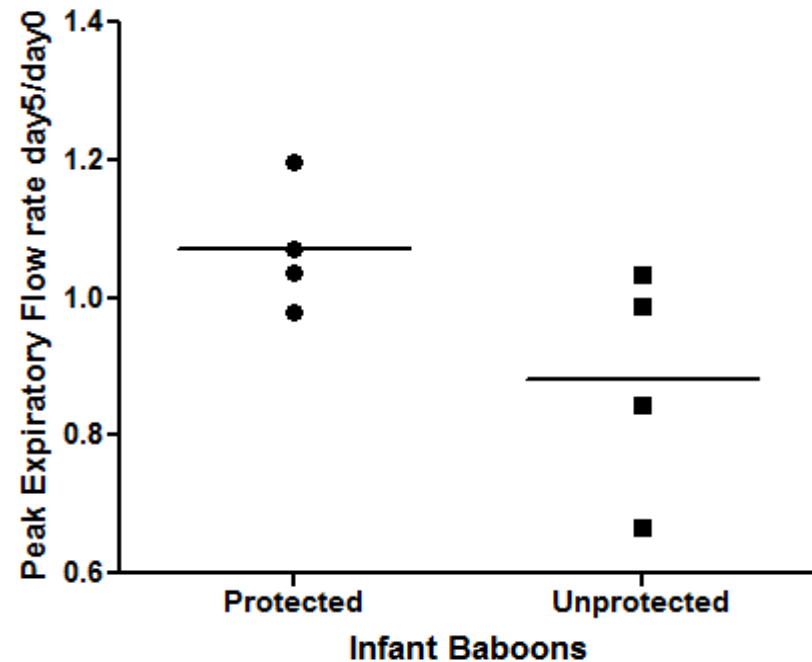
# Pulmonary Function Tests in Infants of Vaccinated Mothers and Untreated Controls

Work of Breathing Day 5



Work of breathing reduced in protected infants

Peak Expiratory Flow Day 5



Peak expiratory flow rate greater in protected infants

## Conclusions: Non-Human Primate Safety and Efficacy Study

- Maternal immunization provided infant baboons with antibody titers similar to those following palivizumab administration.
- Maternal immunization was associated with reduced tachypnea and dyspnea in infants following RSV challenge; this reduction was similar in degree to that produced by palivizumab prophylaxis.
- Maternal immunization provided positive changes in viral replication, BAL leukocyte response, work of breathing and PEFr
- Effects of maternal immunization were similar to those following palivizumab administration
- Maternal immunization with RSV F may be a reasonable strategy to prevent severe RSV illness in normal human newborns