

# The global RSV disease rampant with no vaccine available or in Phase 3 trial to date

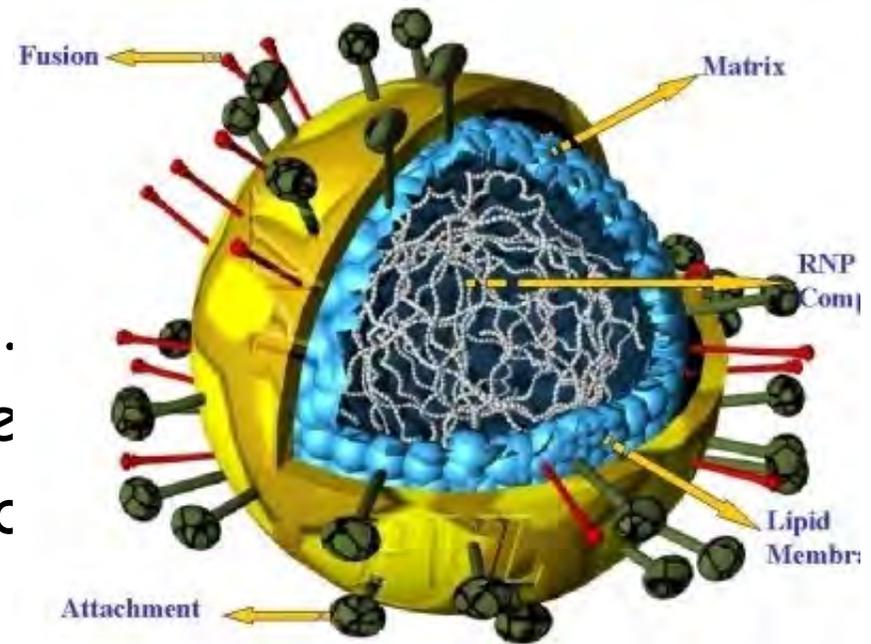
- ❑ Human Respiratory syncytial virus (RSV) was first isolated and in 1957 from children with acute respiratory disease . Infected cells attack neighboring cells to form syncytium.
- ❑ In 1960, infants vaccinated with formalin-inactivated RSV vaccine was not protected but had more severe disease.
- ❑ In 1990 more research done on the fusion or G protein subunits resulted in poor efficacy.
- ❑ Each year, around 3% of all infants 1 year or younger are admitted to hospital with lower respiratory tract viral infection.
- ❑ US estimated 14,000~62,000 hospitalizations with pneumonia associated with RSV infection in over 65 years of age
- ❑ The global RSV disease burden is estimated at 64 million cases and 160,000 deaths every year. In Taiwan, approximately 1,000 cases of infant infected with RSV per year have been reported.

# RSV Therapy and Market

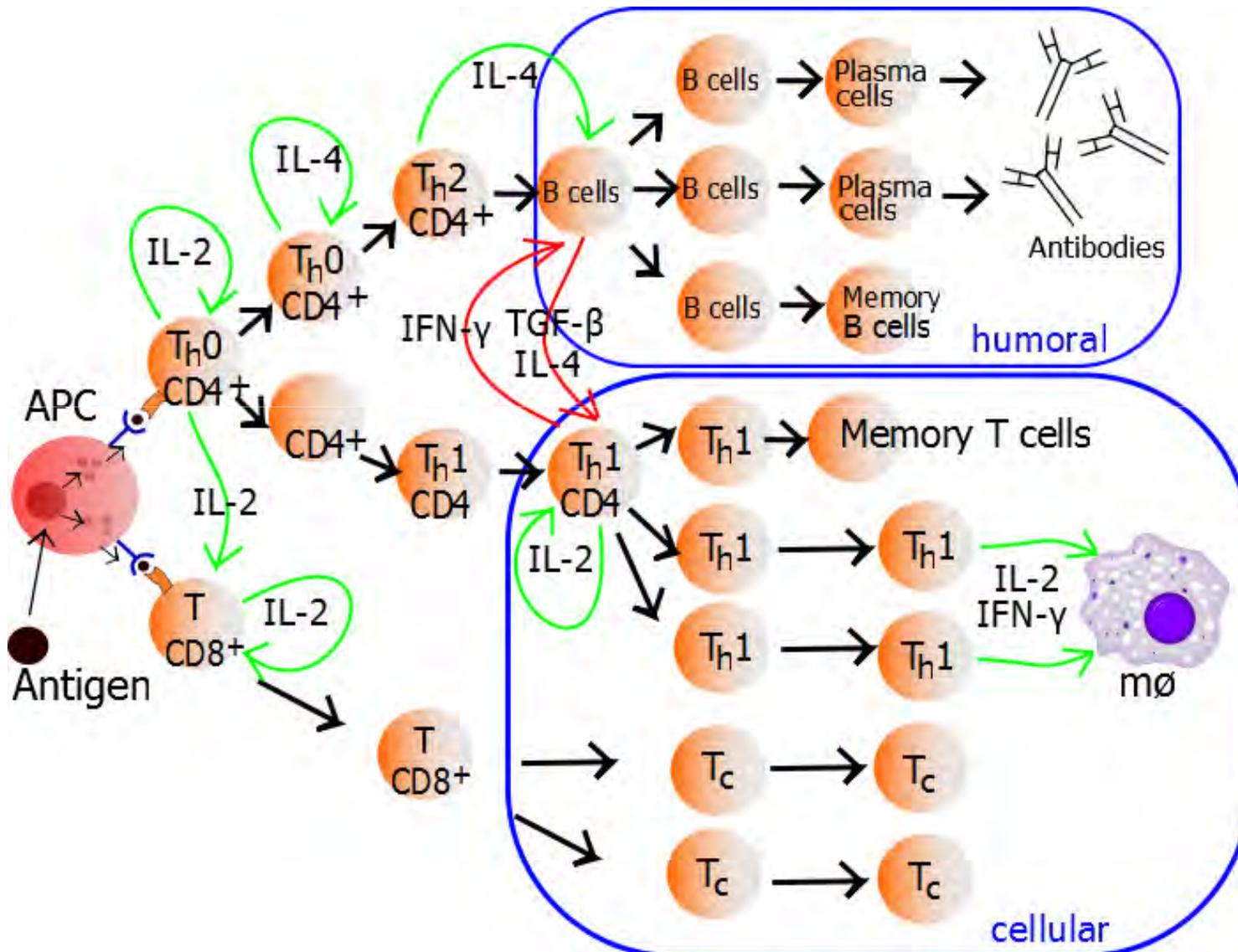
- ❑ Currently, the most successful product for RSV treatment is the prophylactic monoclonal antibody Synagis<sup>®</sup> (FDA approved in 1998), which is directed against the fusion (F) glycoprotein of the RSV virus in high-risk pediatric patients with stable sales of \$1.2 billion over 2009 ~ 2010.
- ❑ It has been estimated that an RSV vaccine could have peak sales of USD 700-750 million at least (Datamonitor, 2010)

# What is RSV? Why vaccine so difficult?

- ❑ An enveloped single-stranded RNA Pneumovirus of the Paramyxoviruidae family
- ❑ Two subgroups A and B, it was found that the G protein is only 43% homology in sequence whereas F protein is over 90% so most research focus on F protein.
- ❑ The disease aggravation Seen with FRSV may be due to inhibited cellular immune Th1 CTL response by activated humoral Th2.
- ❑ Currently strategy includes life attenuated and RNAi nucleocapsid and a Sendai virus vector.



# Proliferating helper T cells differentiate into two major CD4+ cells known as Th1 and Th2 and CD8+ Cytotoxic T cells



# 生策會生醫創新商機媒合 產學合作開發模式

- Reviewed 生策會2010國家新創獎說明書
- TWi遴選 several 具市場競爭力與商品價值之投資標的 in 2010.
- 生策會 arranged meetings to review these projects and TWi visited several sites.
- 生策會 helped to chart the pathway for the collaboration with several follow up meetings
- Established 產學合作 co-development 3 year plan in February 2012.
- US IND and tFDA submission is planned 6 months post production of GMP materials in NHRI.

# NHRI RSV Vaccine Program

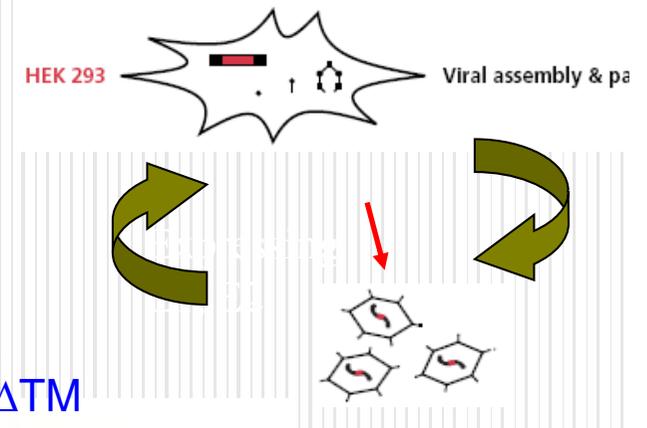
- Must inducing a balanced Cellular and Humoral response
  - Infect the cell with non-replicating Adenovirus vector to induce cellular responses.

- RSV vaccine is capable of preventing infection by different strains of RSV

- target RSV B1 strand F-protein with 90% homology to A2 and etc

- Bioengineered recombinant Human Embryo Kidney 293A cell with truncated  $\Delta E1/\Delta E3$  (replication-incompetent) Ad5 vector encoding gene and

1. RSV-B1 fusion (F) glycoprotein gene, F0,
2. Or F0 $\Delta$ TM (Transmembrane truncated version)



# Study Protocol

## Immunization followed by RSV challenge

### Day 0 (Prime; i.n.)

$1 \times 10^7$  pfu/50 $\mu$ L

- 1.rAd-F0
- 2.rAd-F0 $\Delta$ TM
- 3.rAd-LacZ
- 4.HIRSV-B1

### Day 20 (Boost; i.n. s.c. i.p.)

$1 \times 10^7$  pfu/50 $\mu$ L

- 1.rAd-F0
- 2.rAd-F0 $\Delta$ TM
- 3.rAd-LacZ
- 4.HIRSV-B1

### Day 50 (Challenge; i.n)

$1 \times 10^6$  pfu

- 1.Live RSV-B1



### Day 14 (Collect Serum)

- 1.Ab titer against HIRSV-B1
- 2.Ab titer against Ad5
- 3.Virus Specific neutralizing activity

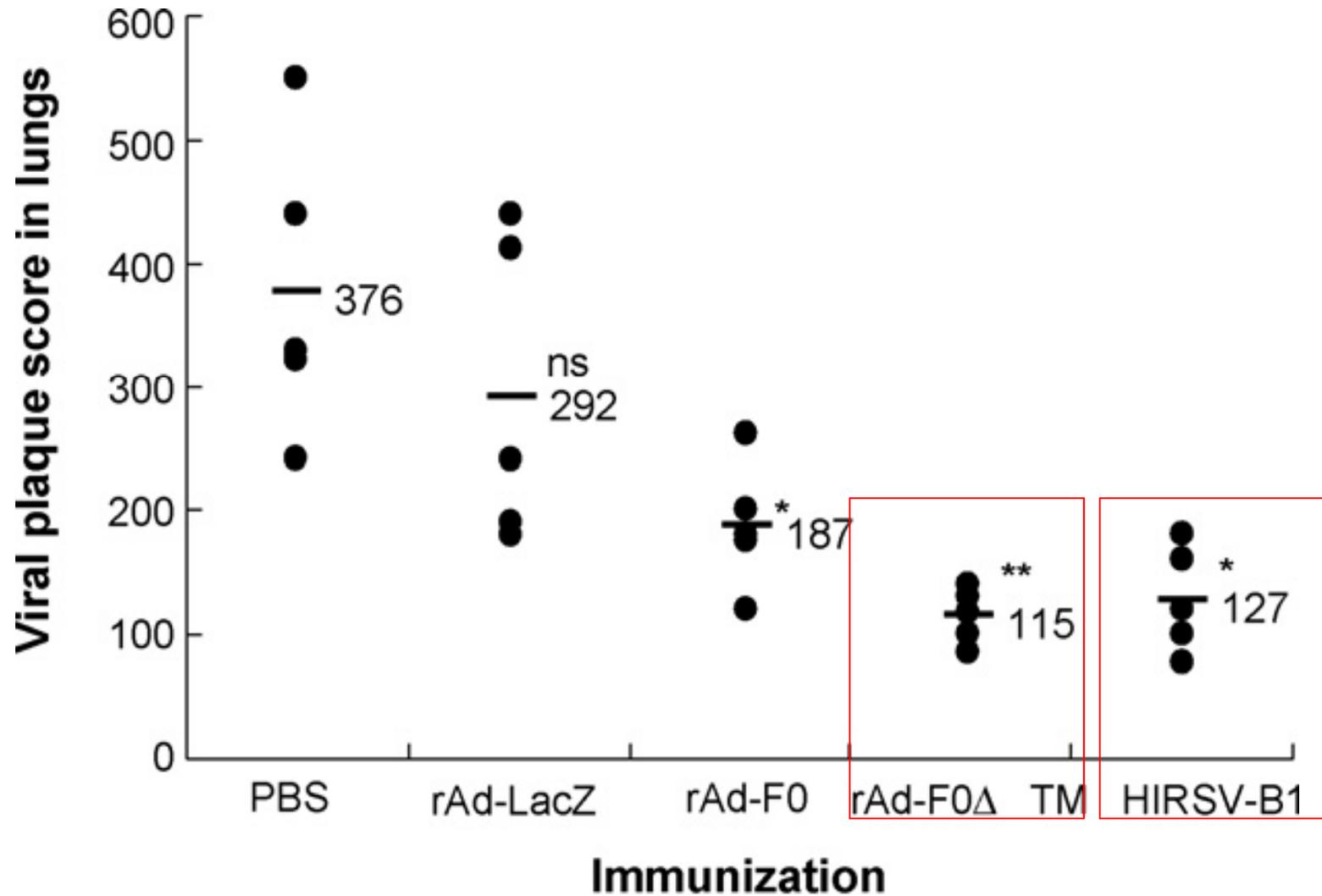
### Day 30 (Collect Serum)

- 1.Ab titer against HIRSV-B1
- 2.Virus Specific neutralizing activity

### Day 55 (Sacrifice)

- 1.Viral load determination in lungs by plaque forming assay

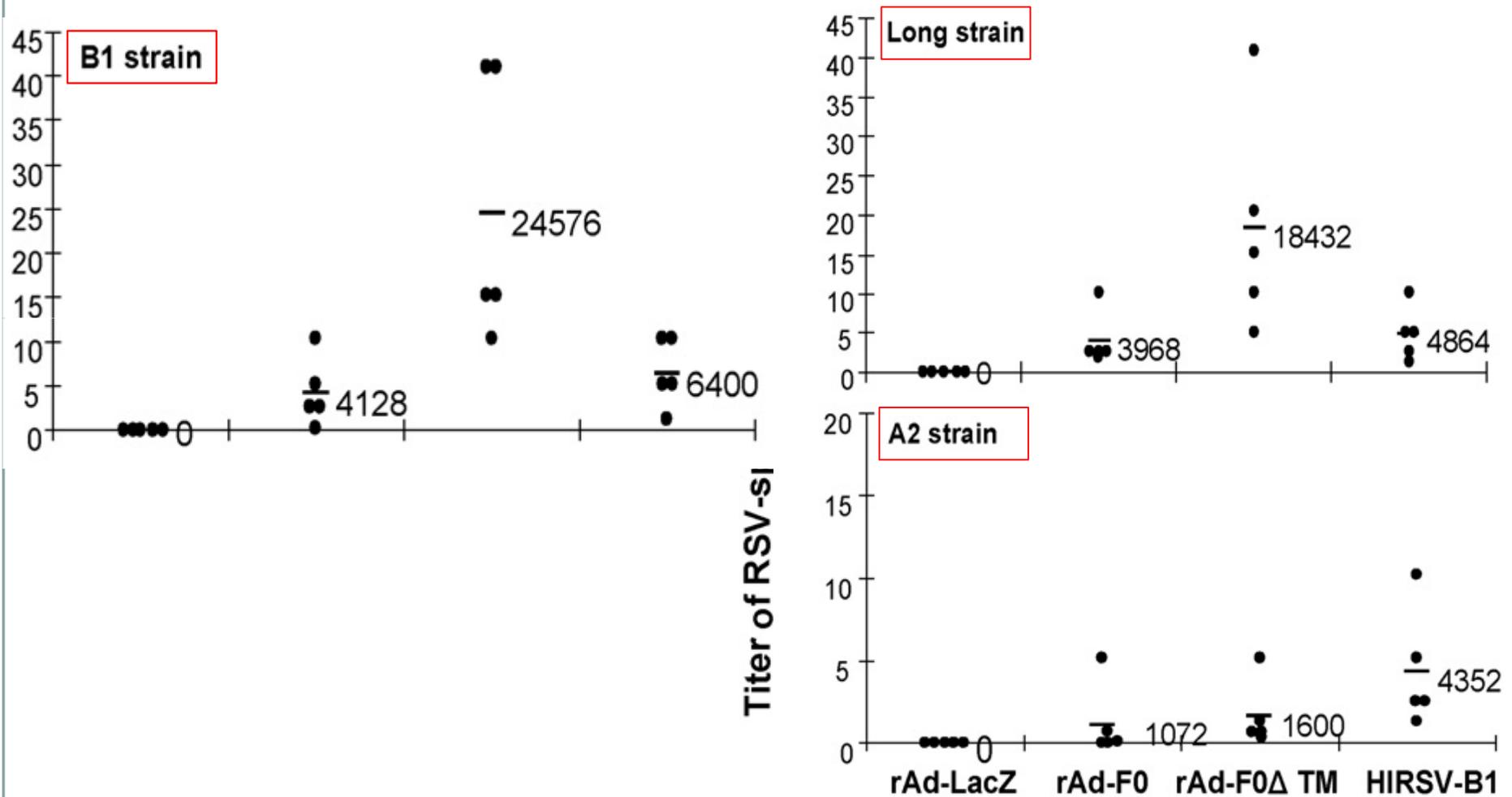
# RSV Vaccine immunized mice showed protection against RSV



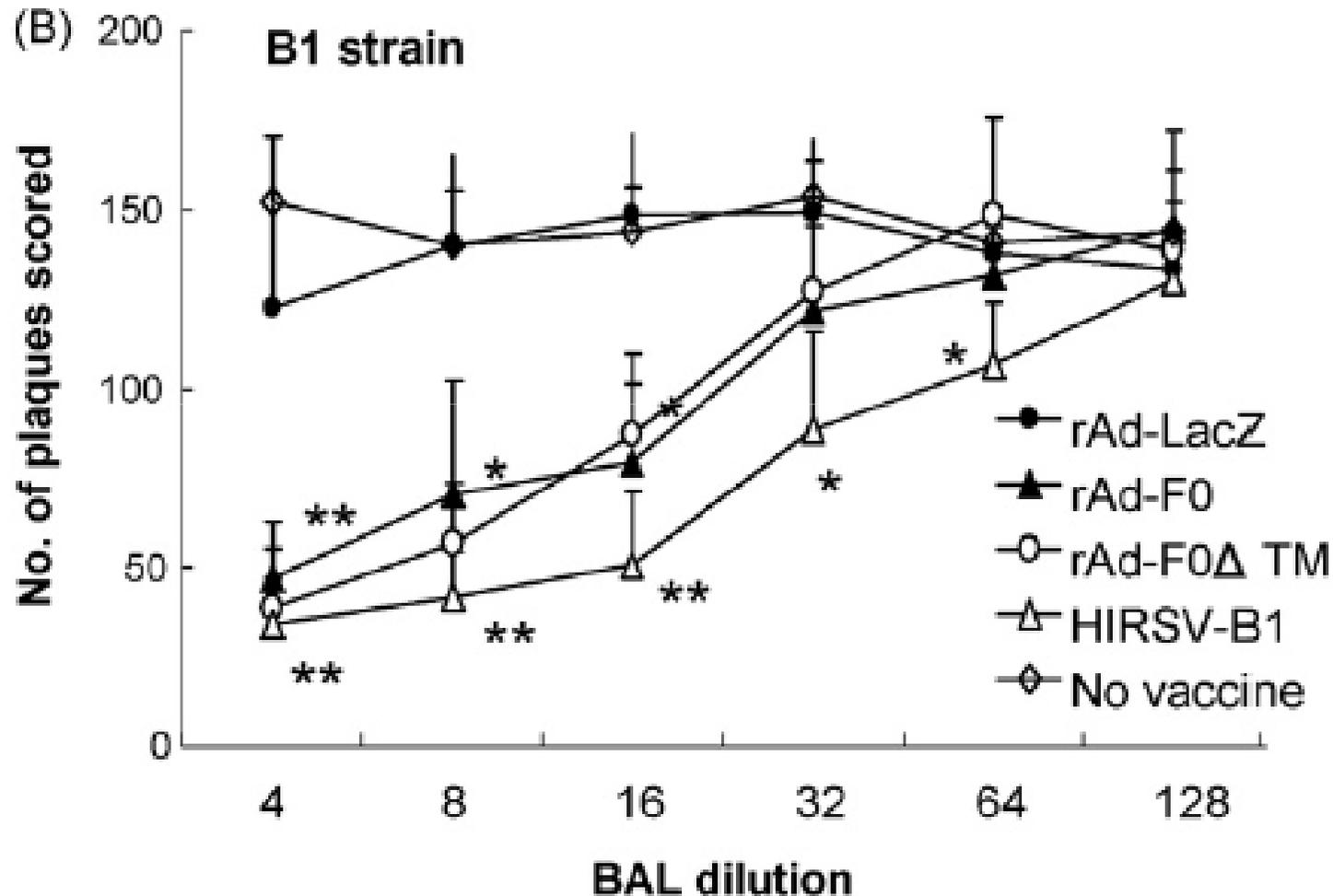
# Cross reactivity of Immune sera IgG antibodies titer against 3 strains of RSV

Subgroup B

Subgroup A

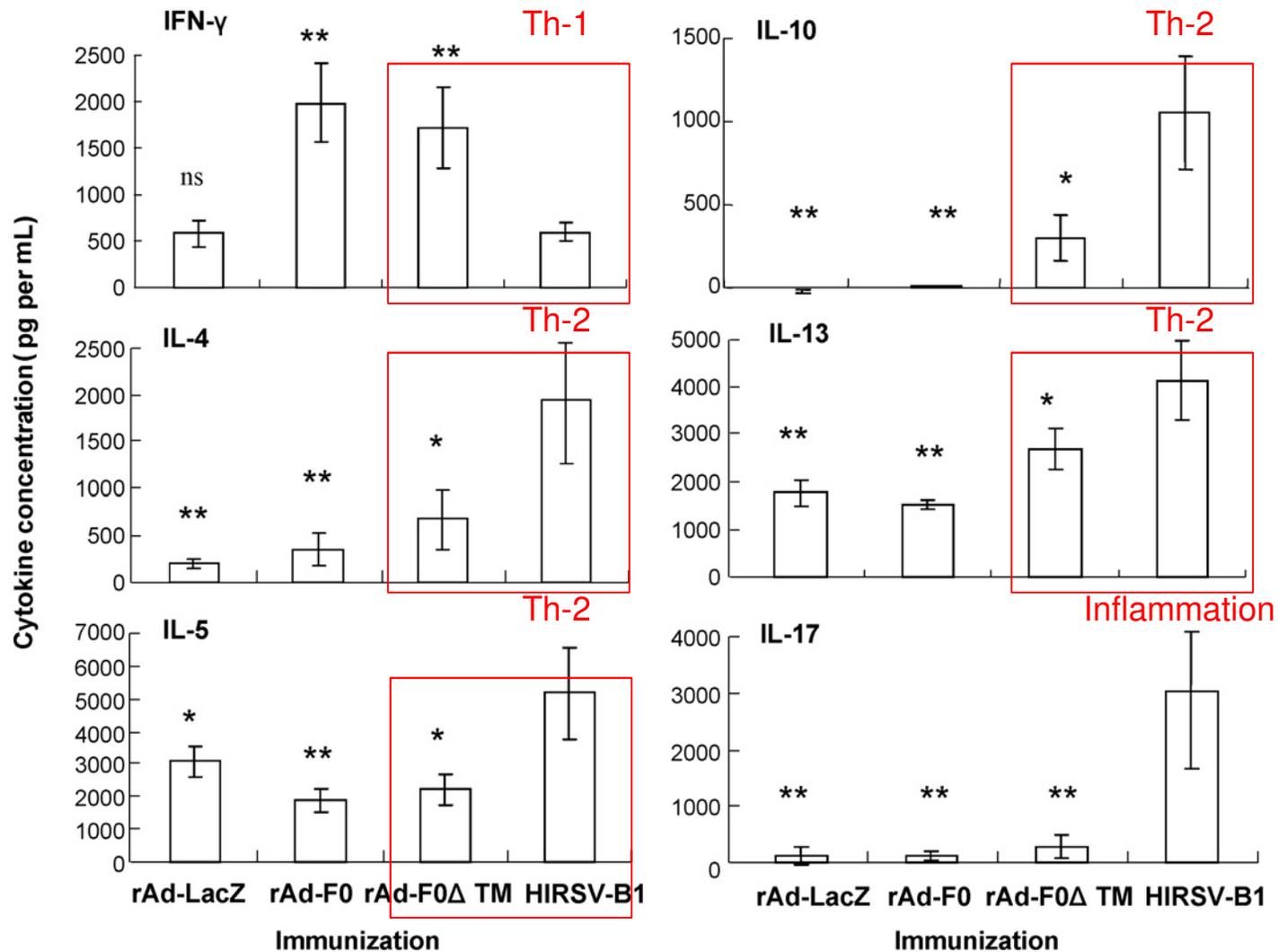


# Virus-neutralizing activity of Bronchioaveola Lavage from immunized mice via the intranasal route.



Infected HEP2 cell Plaques counts after incubation with sera and B1 strain RSV virus

# Induction of Th1 Th2 and Inflammatory IL-17 from immunized mice splenocytes cultured in the presence of HIRSVB1 for 48 h



# Acknowledgement

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- 黃嫻倫、雷佑甯

Q & A