Universal vaccines against respiratory pathogens

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THE UNIVERSITY of ADELAIDE

gamma vaccines pty limited

International Atomic Energy Agency Scientific Forum

ATOMS IN INDUSTRY

Radiation Technology for Development

15–16 September 2015, Vienna, Austria

Gamma Irradiation at ANSTO

- Co-60 irradiator since 1970
- Very low (1 Gy) to High (> 50 kGy)
- Precision & Accuracy not achievable in industrial irradiation
- Research & Development underpins industrial radiation processing

Dosimetry

- Precise irradiation is enabled by accurate Dosimetry
- Our dosimetry systems are traceable to the Australian Primary Standard for Absorbed Dose

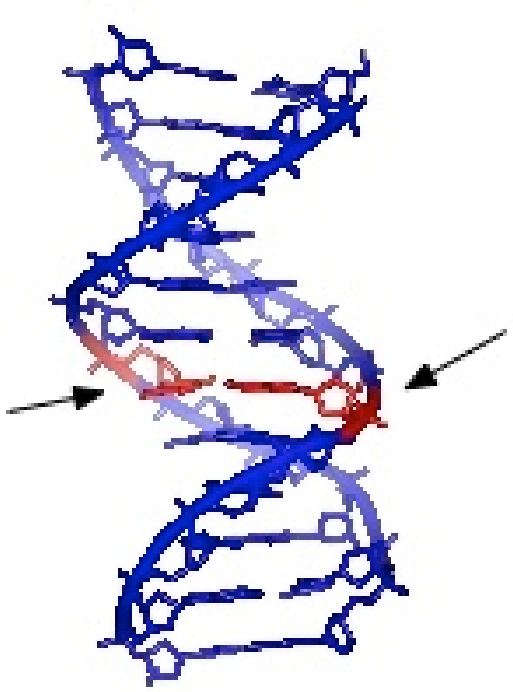
Dosimeter	Dose range	Uncertainty (95% confidence)
Ionisation chambers	1 mGy to 10 Gy	0.7 %
Fricke	50-350 Gy	2.0 %
Low Dose Ceric Cerous	1-12 kGy	3.0 %
High Dose Ceric Cerous	10-50 kGy	3.5 %

Radiation Sterilisation

Two effects on biological systems:

DIRECT EFFECTS:

- Direct interaction with nucleic acids (strand breakage)



INDIRECT EFFECTS

- generation of short-lived free radicals
- causes excess damage to structural components as well as nucleic acid

- HIGH temperature → increases indirect effects
- LOW temperature → reduces indirect effects and direct effects predominate (**PROTECTS PROTEINS**)

Influenza A virus

TYPES: A, B and C

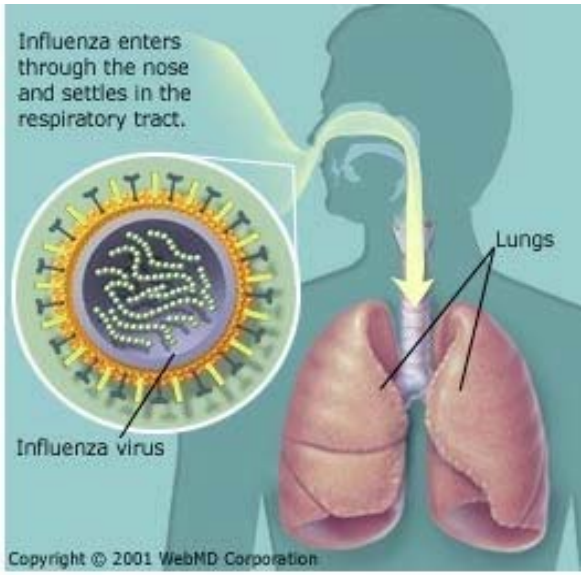
- Type A: (most prevalent) aquatic birds are natural hosts and transmit to humans

TRANSMISSION: airborne droplets

SYMPTOMS: Causes acute inflammation within the upper and lower respiratory tracts

- headache, fever, runny nose, sore throat, coughing

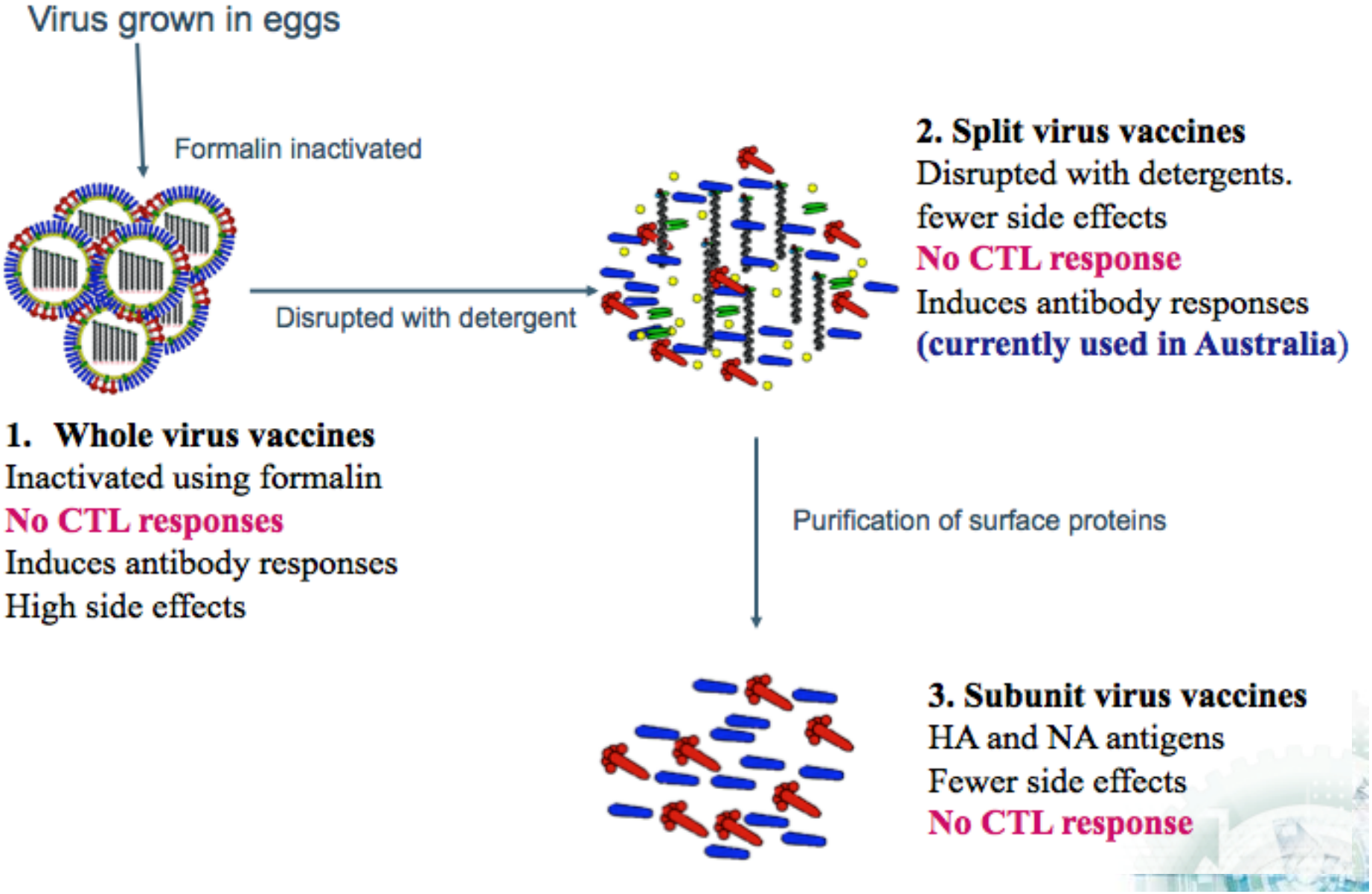
OUTCOME: Causes more than 250,000 deaths annually (elderly and young children more susceptible to disease)



Epidemiology

Year	Flu	Deaths worldwide
1918/1919	Spanish influenza (H1N1)	50 million
1957	Asian influenza (H2N2)	4 million
1968/1969	Hong Kong influenza (H3N2)	4 million
2009	Swine Flu (H1N1)	200,000

Current Inactivated Vaccines



1. Whole virus vaccines
Inactivated using formalin
No CTL responses
Induces antibody responses
High side effects

2. Split virus vaccines
Disrupted with detergents.
fewer side effects
No CTL response
Induces antibody responses
(currently used in Australia)

3. Subunit virus vaccines
HA and NA antigens
Fewer side effects
No CTL response

The composition of influenza A virus vaccines for use in Southern Hemisphere influenza seasons recommended by the WHO were:

2006 Season

- an A/New Caledonia/20/99 (H1N1)-like virus
- an A/California/7/200 4(H3N2)-like virus

2007 Season

- an A/New Caledonia/20/99 (H1N1)-like virus
- an A/Wisconsin/67/2005 (H3N2)-like virus

2008 Season

- an A/Solomon Islands/3/2006 (H1N1)-like virus
- an A/Brisbane/10/2007 (H3N2)-like virus

2009 Season

- an A/Brisbane/59/2007 (H1N1)-like virus
- an A/Brisbane/10/2007 (H3N2)-like virus

Pandemic H1N1 virus was not part of Flu vaccine composition for 2009 season

2010 Season

- **an A/California/7/2009 (H1N1)-like virus**
- **an A/Perth/16/2009 (H3N2)-like virus**

www.nature.com

www.jhsph.edu

Thus: we are playing a catch up game with influenza virus!

Current Flu vaccines: Strain specific vaccines

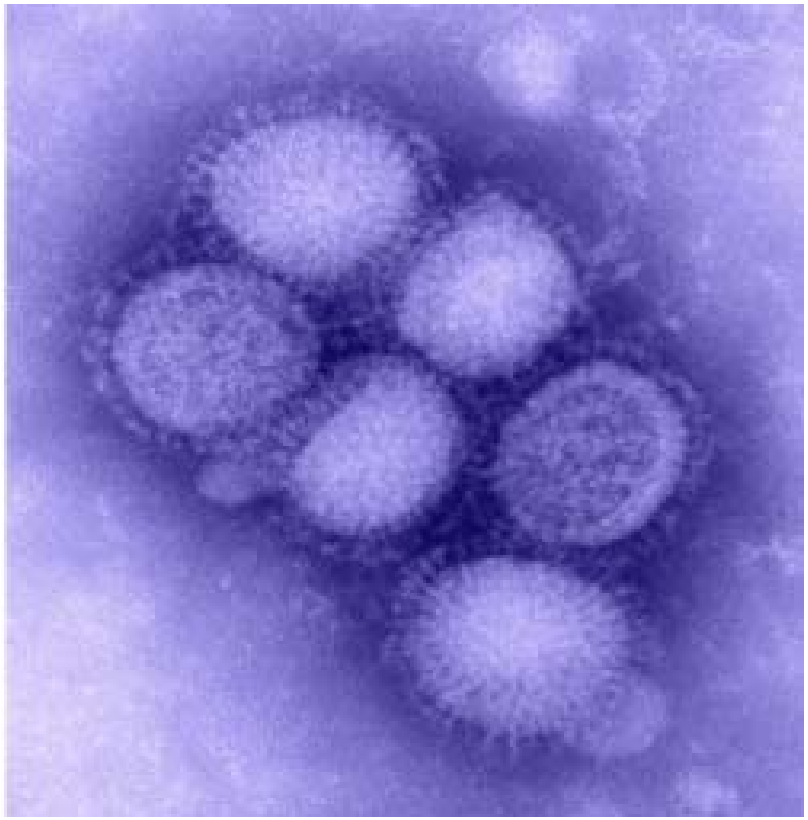
What is the alternative:
Cross-reactive T-cell based vaccine

- Irradiation to inactivate influenza viruses to create more effective vaccines
- Adelaide University with Gamma Vaccines research to validate commercial product

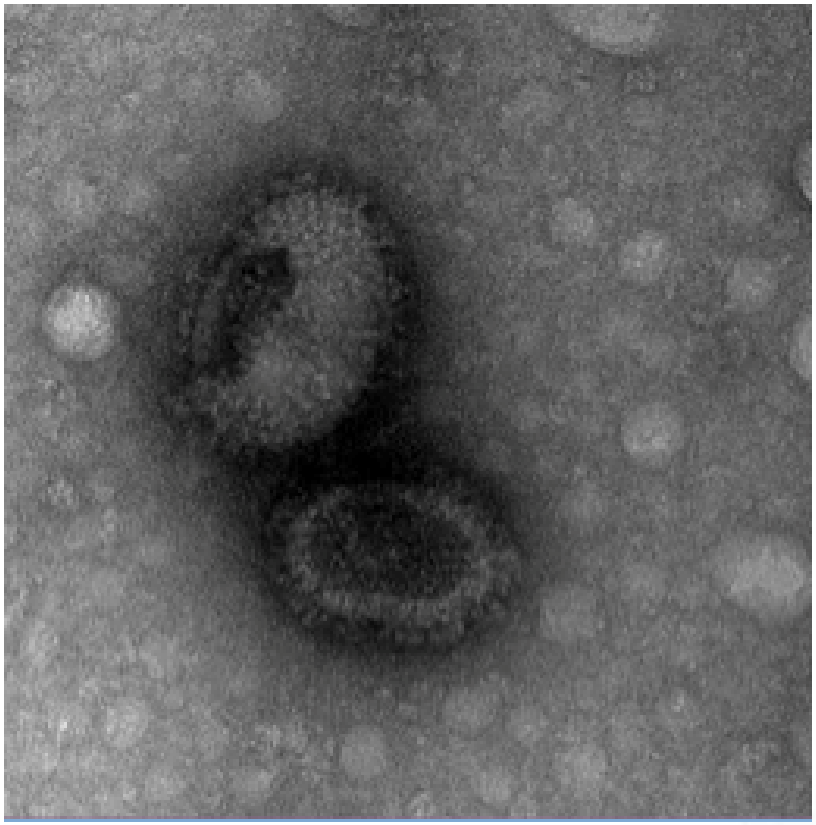
Gamma-irradiated influenza A virus vaccine

Transmission electron microscopy

A/California/07/2009 H1N1



Gamma-irradiated H1N1



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Effect of inactivation method on the cross-protective immunity induced by whole 'killed' influenza A viruses and commercial vaccine preparations

Yoichi Furuya,[1] Matthias Regner,[1] Mario Lobigs,[2] Aulikki Koskinen,[1] Arno Müllbacher[1] and Mohammed Alsharifi[1]

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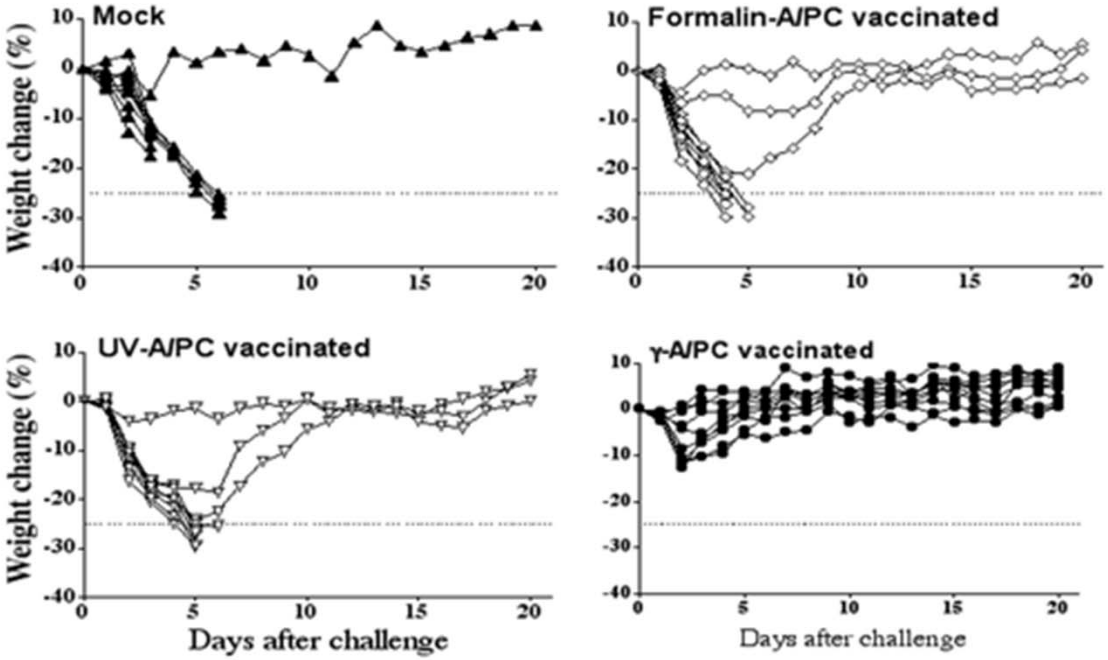
A: Homologous challenge with A/PC



Homotypic challenge with H3N2 (A/PC)

I.N Vaccination	Protection
Formalin-H3N2	NO
UV-H3N2	NO
γ-H3N2	**Yes**

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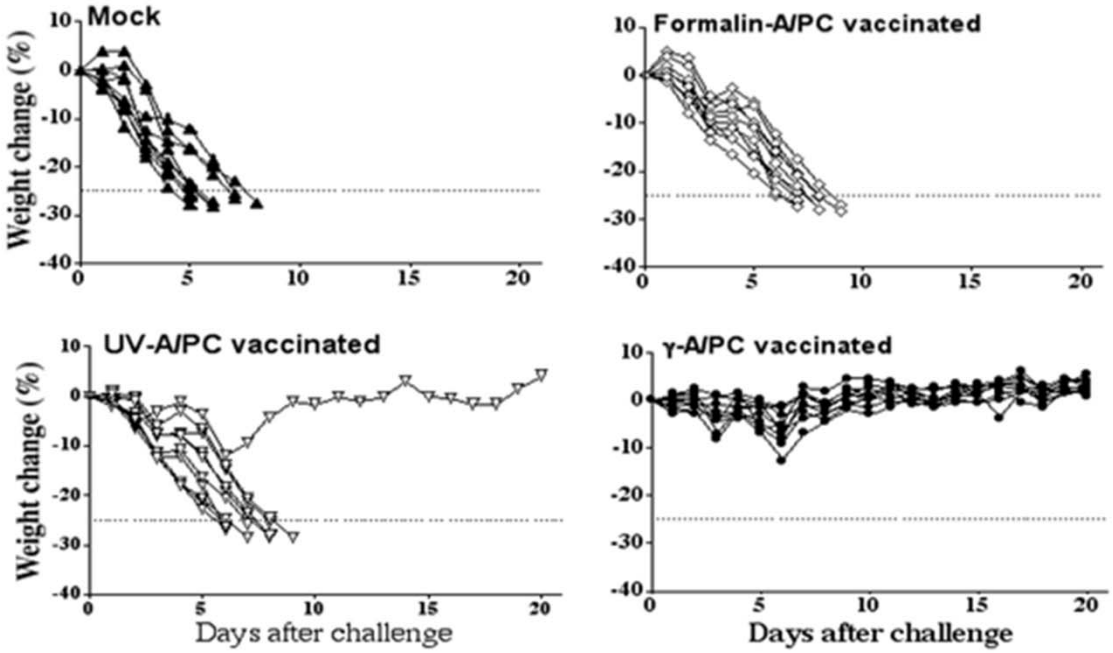
B: Heterosubtypic challenge with A/PR8



Heterosubtypic challenge with H1N1 (A/PR8)

I.N Vaccination	Protection
Formalin-H3N2	NO
UV-H3N2	NO
γ-H3N2	**Yes**

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0022-538X/10/$12.00 doi:10.1128/JVI.02508-09

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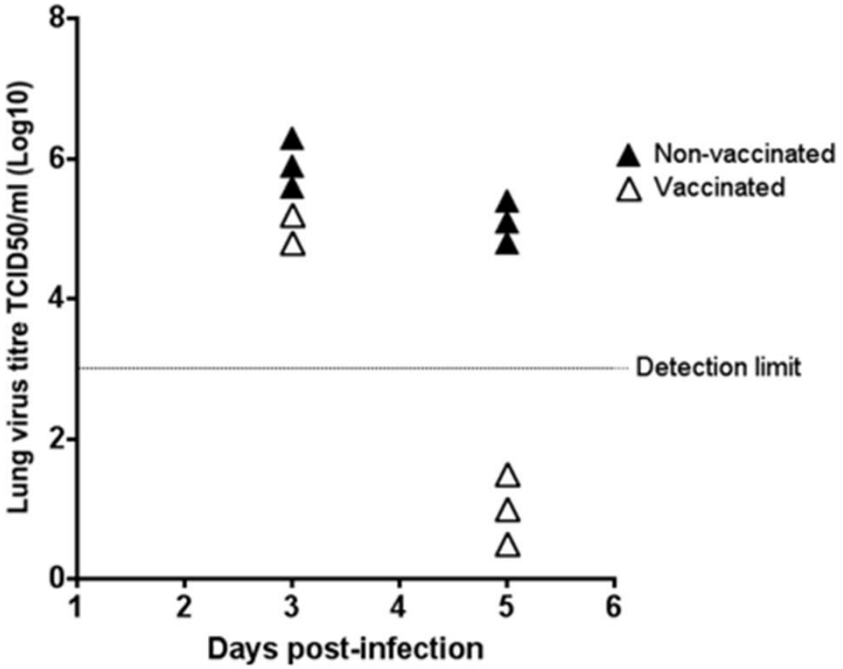
Vaccination with **γ-H3N2**
Challenged with **H1N1**



Early clearance of influenza virus from the lung of vaccinated animals

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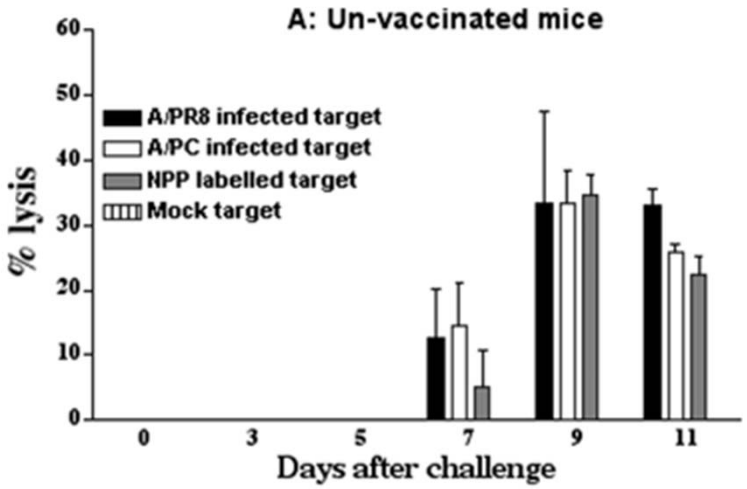

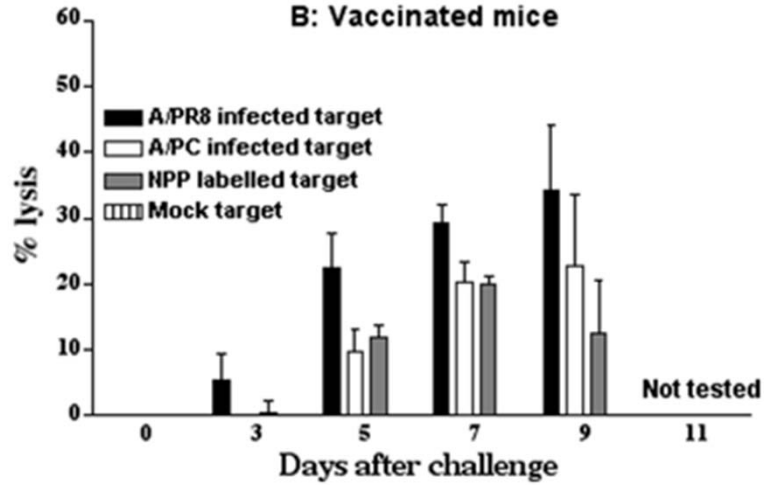

Early T-cell responses in the lung of vaccinated animals

Thank you!