

Influenza Vaccine Responses

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Inactivated Vaccine Serology Studies

- **Purpose:** Evaluation of anti-HA antibody titers to recent viruses as compared to those of the recommended vaccine viruses in children, adults and older adults who had received *trivalent* or *quadrivalent* inactivated vaccine (2015-2016 formulation).
- **Serum samples:** Two panels of sera from adults, 2 panels from older adults and 1 panel from pediatric population were analyzed from **trivalent** vaccine trials. Three panels of sera from adults, 3 panels from older adults and 1 panel from pediatric population was analyzed from a **quadrivalent** vaccine trial. Sera were collected prior to and 21-28 days post-vaccination. Most of the panels were pre-screened to avoid sera with low antibody titers.
- **Methods:** Hemagglutination inhibition (HI) assays were used to determine HI titers to recent viruses compared to HI titers of the corresponding vaccine virus. A subset of sera was tested by micro-neutralization assay. The serum panels were distributed to and tested in 6 laboratories from WHOccs and ERLs.

Serum panels used for studies: seasonal **trivalent** vaccine

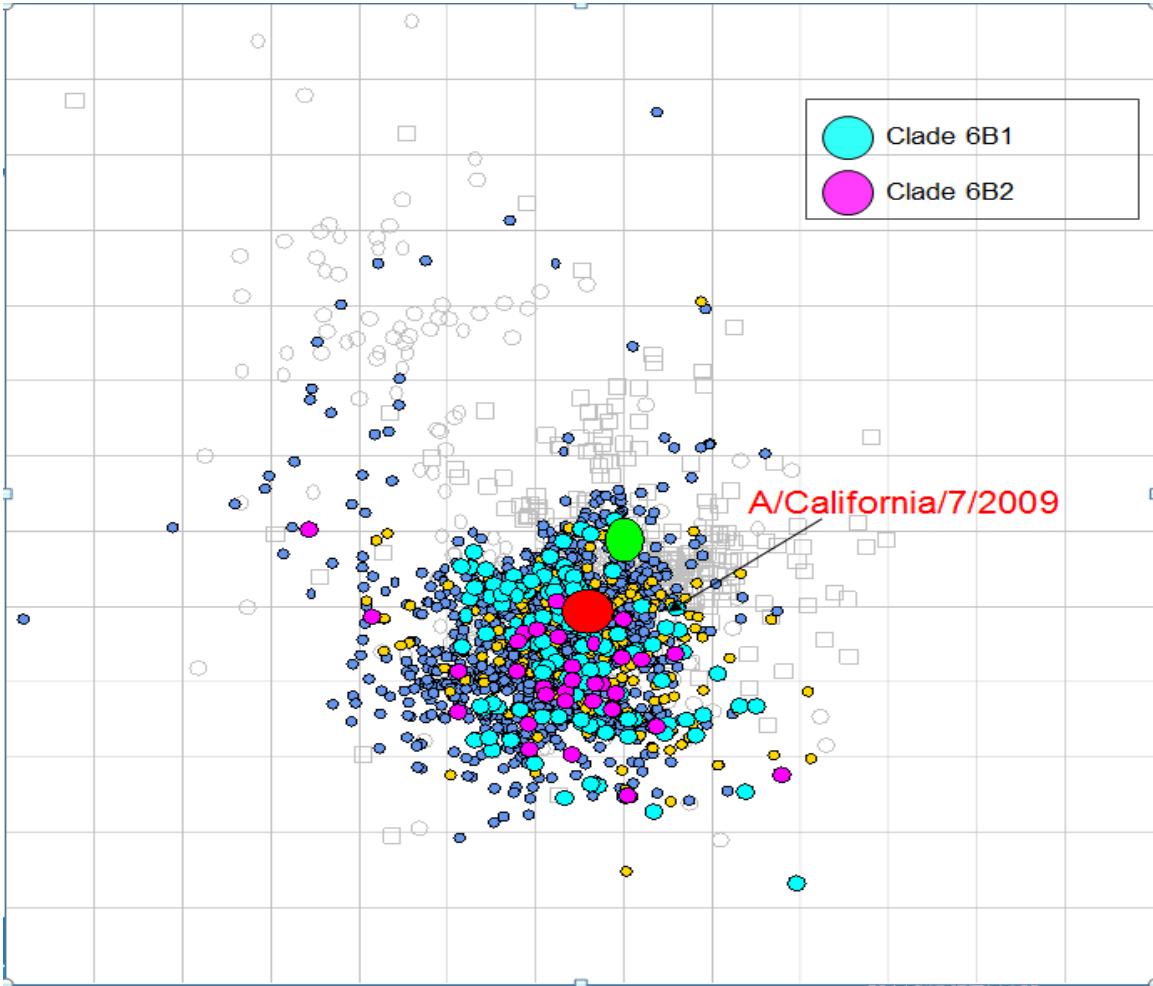
Serum source	Trial	Vaccine strains
AUSTRALIA	ADULTS OLDER ADULTS	A/Christchurch/16/2010 (H1N1pdm09) (NIB-74xp) A/Switzerland/9715293/2013 (H3N2) (NIB-88) B/Phuket/3073/2013
CHINA	CHILDREN (3Yr) ADULTS OLDER ADULTS	A/California/7/2009 (H1N1pdm09) (NYMC X-179A) A/South Australia/55/2014 (H3N2) (IVR-175) B/Phuket/3073/2013

Serum panels used for studies: seasonal **quadrivalent** vaccine

Serum source	Trial	Vaccine strains
USA (Donated by a US mfr.)	ADULTS OLDER ADULTS	A/California/7/2009 (H1N1pdm09) (NYMC X-179A) A/Switzerland/9715293/2013 (H3N2) (NIB-88) B/Phuket/3073/2013 B/Brisbane/60/2008
USA (US CDC)	CHILDREN (16.5 mo) ADULTS OLDER ADULTS	A/California/7/2009 (H1N1pdm09) (NYMC X-179A) A/Switzerland/9715293/2013 (H3N2) (NIB-88) B/Phuket/3073/2013 B/Brisbane/60/2008
JAPAN	ADULTS OLDER ADULTS	A/California/7/2009 (H1N1pdm09) (NYMC X-179A) A/Switzerland/9715293/2013 (H3N2) (NIB-88) B/Phuket/3073/2013 B/Texas/2/2013

A(H1N1)pdm09 Serology

Antigenic cartography of A(H1N1)pdm09 viruses

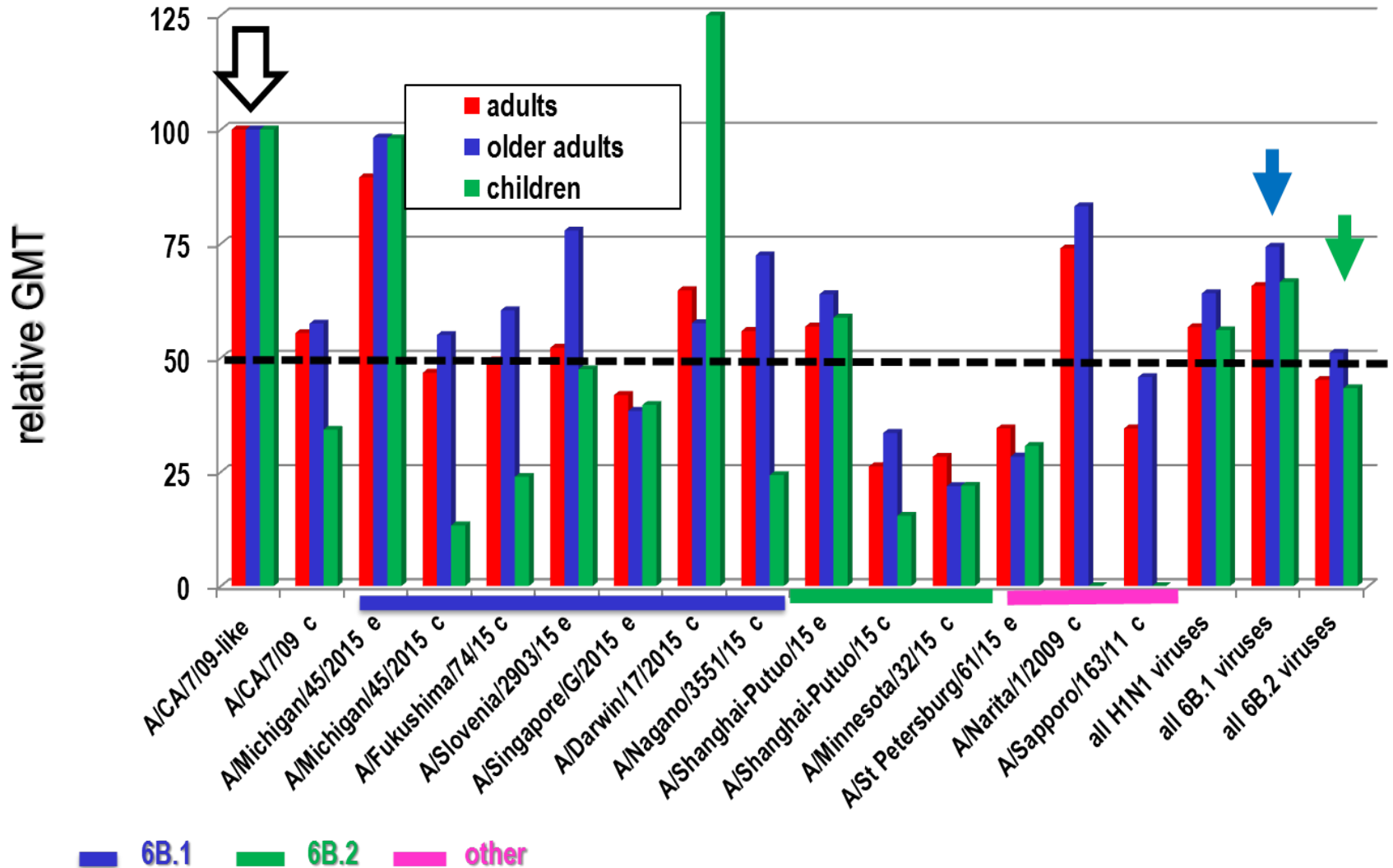


Antigens for serology:

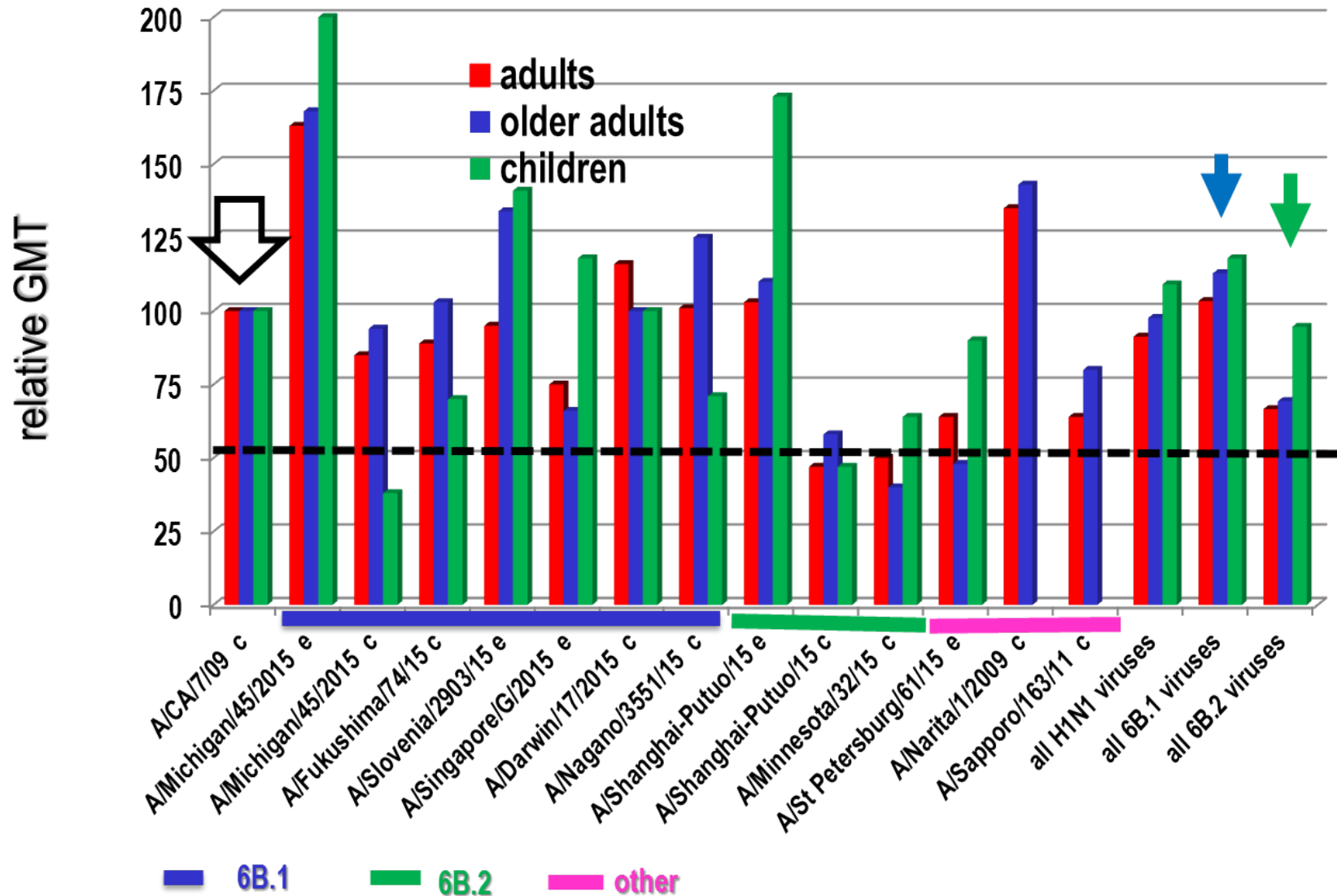
A(H1N1)pdm09

<i>REFERENCE VIRUS</i> A/California/7/2009, A/Christchurch/16/2010 <i>REPRESENTATIVE CURRENT VIRUSES</i>		
A/Michigan/45/2015	(6B.1)	egg
A/Michigan/45/2015	(6B.1)	cell
A/Fukushima/74/2015	(6B.1)	cell
A/Slovenia/2903/2015	(6B.1)	egg
A/Singapore/GP1911/2015	(6B.1)	egg
A/Darwin/17/2015	(6B.1)	cell
A/Nagano/3551/201	(6B.1)	cell
A/Shanghai-Putuo/SWL1680/2014	(6B.2)	egg
A/Shanghai-Putuo/SWL1680/2014	(6B.2)	cell
A/Minnesota/32/2015	(6B.2)	cell
A/St Petersburg/61/2015	(6B)	egg
A/Narita/1/2009 V106I		cell
A/Sapporo/163/2011 (7) K154E, S185I, S190R		cell

COMPARISON OF HI ANTIBODY TITERS TO THE A(H1N1)pdm09 COMPONENT (%GMT) (Using egg-propagated A/California/7/2009 as reference)



COMPARISON OF HI ANTIBODY TITERS TO THE A(H1N1)pdm09 COMPONENT (%GMT) (Using cell-propagated A/California/7/2009 as reference)

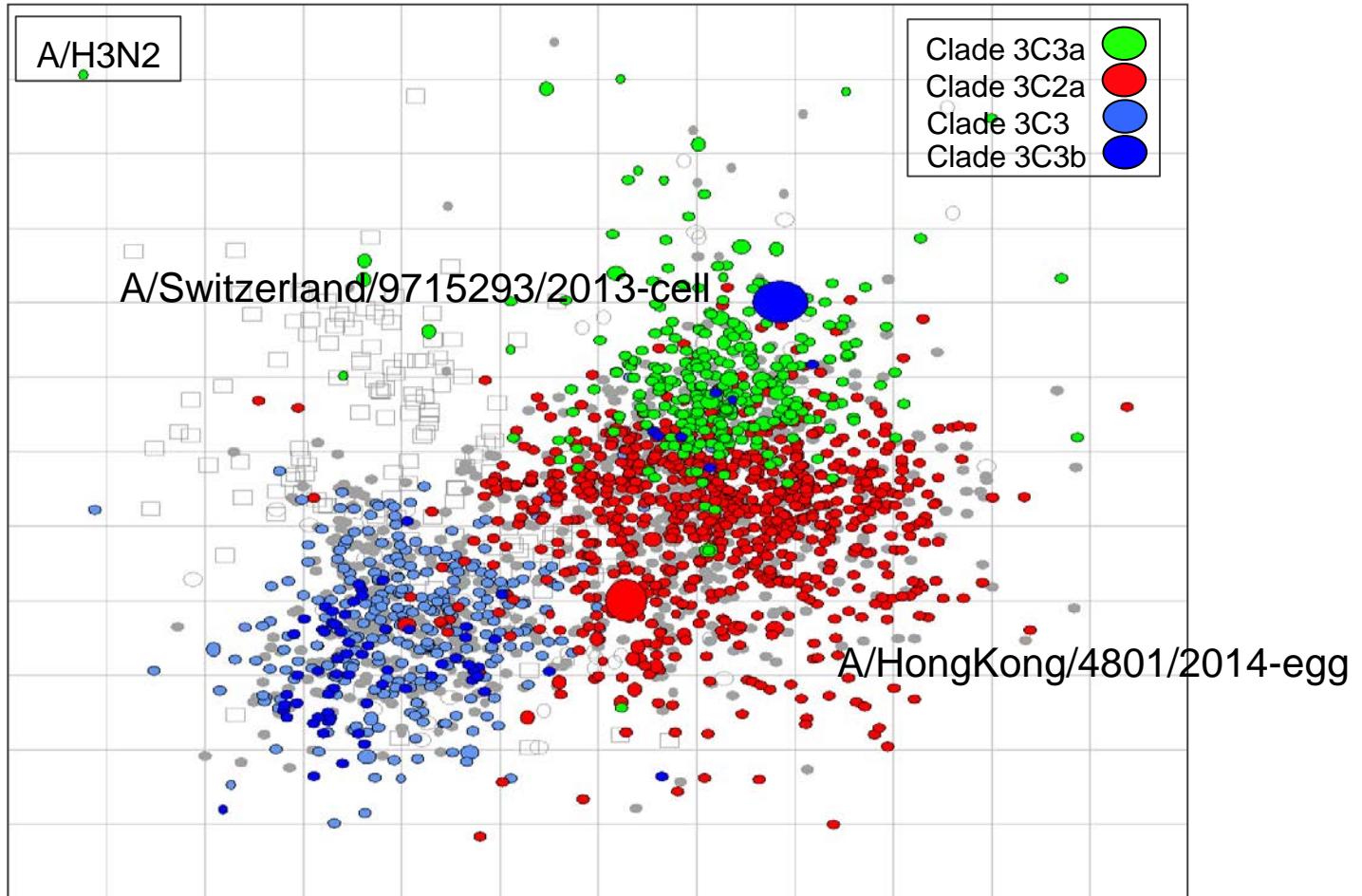


A(H1N1)pdm09-summary

- The majority of representative A(H1N1)pdm09 viruses tested reacted well with human sera collected from individuals who received vaccines containing A/California/7/2009 antigens
- Some recent viruses within 6B.1 and 6B.2 subclades reacted poorly with some serum panels.

A(H3N2) Serology

Antigenic cartography of A(H3N2) viruses

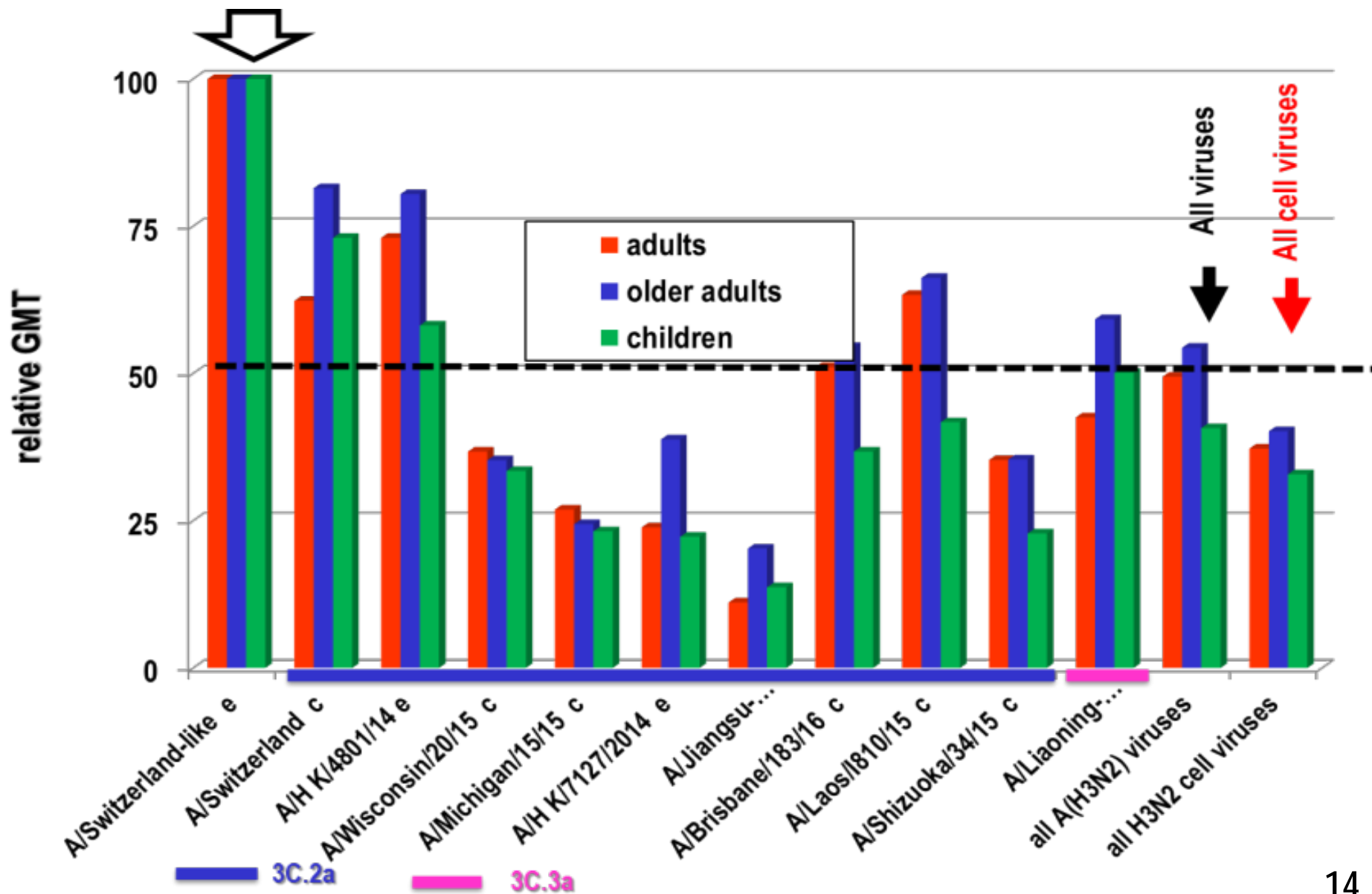


Antigens for serology:

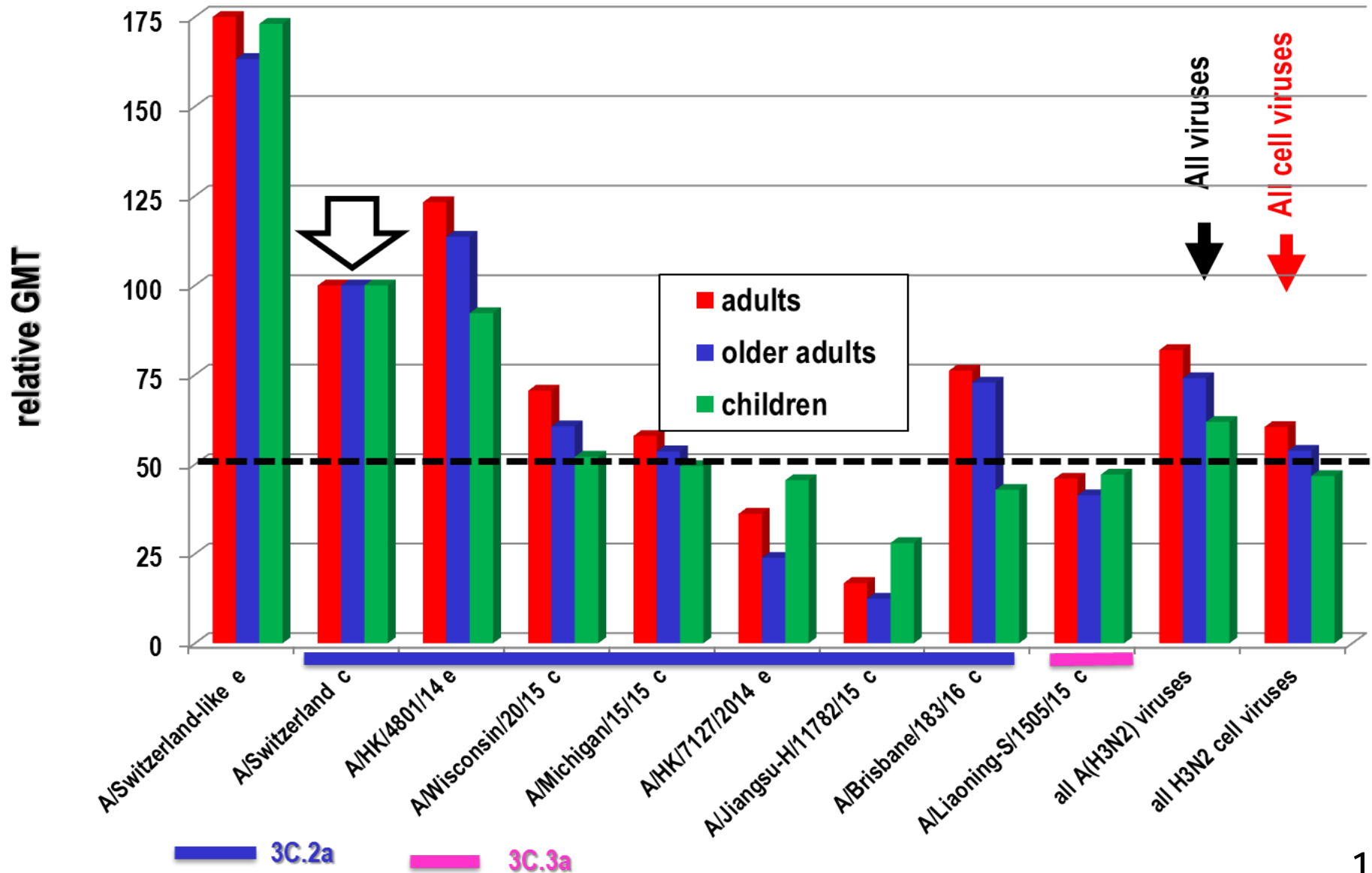
A(H3N2)

REFERENCE VIRUS <i>A/Switzerland/9715923/2013-like</i> <i>South Australia/55/2014</i> REPRESENTATIVE CURRENT VIRUSES		
<i>A/Hong Kong/4801/2014</i>	(3C.2a)	egg
<i>A/Wisconsin/20/2015</i>	(3C.2a)	cell
<i>A/Michigan/15/2015</i>	(3C.2a)	cell
<i>A/Hong Kong/7127/2014</i>	(3C.2a)	egg
<i>A/Jiangsu-Hailing/11782/2015</i>	(3C.2a)	cell
<i>A/Brisbane/183/2015</i>	(3C.2a)	cell
<i>A/Laos/l810/2015</i>	(3C.2a)	cell
<i>A/Shizuoka/34/2015</i>	(3C.2a)	cell
<i>A/Montana/28/2015</i>	(3C.2a)	cell
<i>A/Alaska/232/2015</i>	(3C.2a)	cell
<i>A/Nebraska/4/2014</i>	(3C.2a)	cell
<i>A/Liaoning-Shuangta/1505/2015</i>	(3C.3a)	cell
<i>A/Pennsylvania/09/2015</i>	(3C.3b)	cell

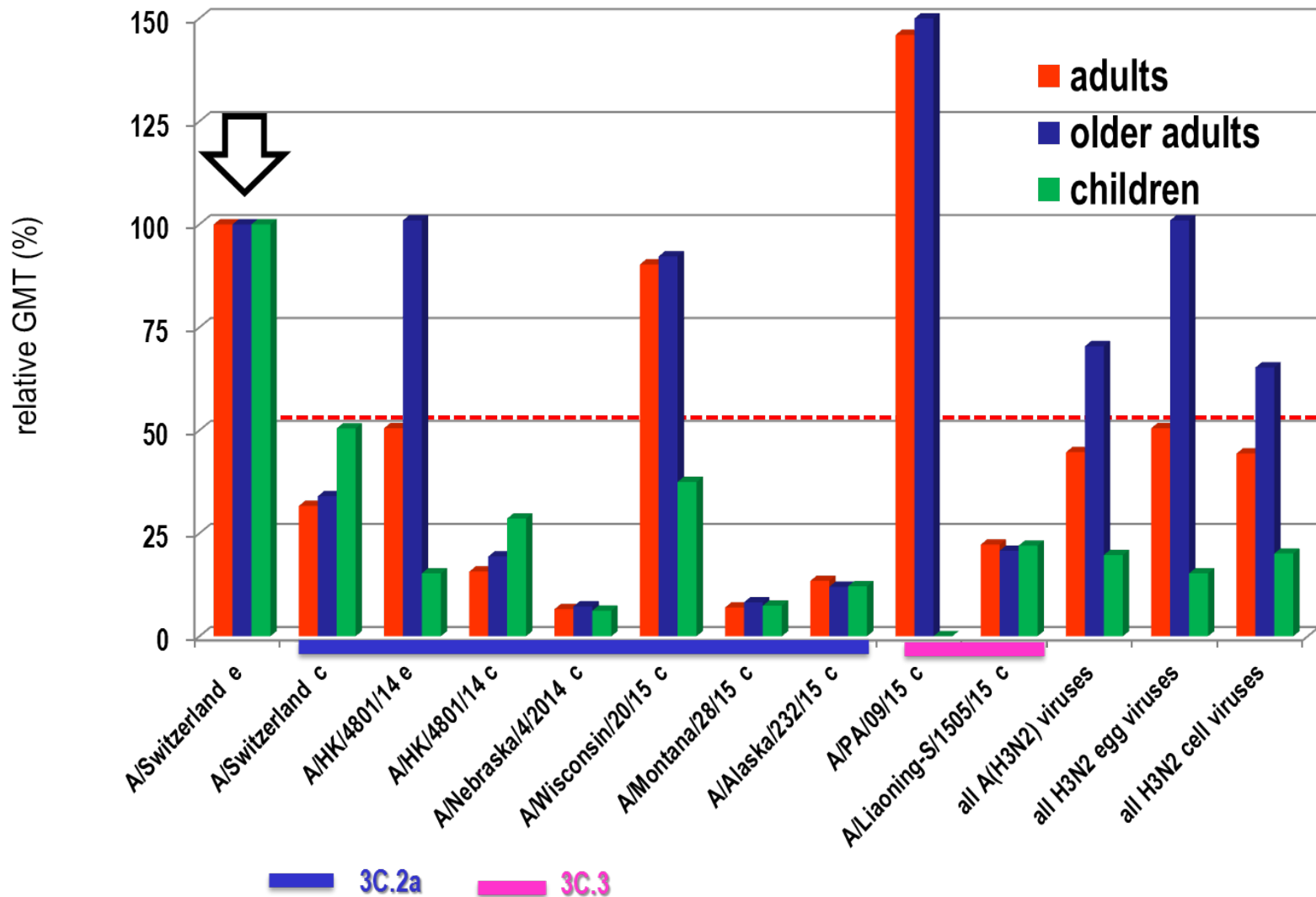
COMPARISON OF HI ANTIBODY TITERS TO THE A(H3N2) COMPONENT:
 (Using A/Switzerland/9715293/2013 egg-grown virus as reference)



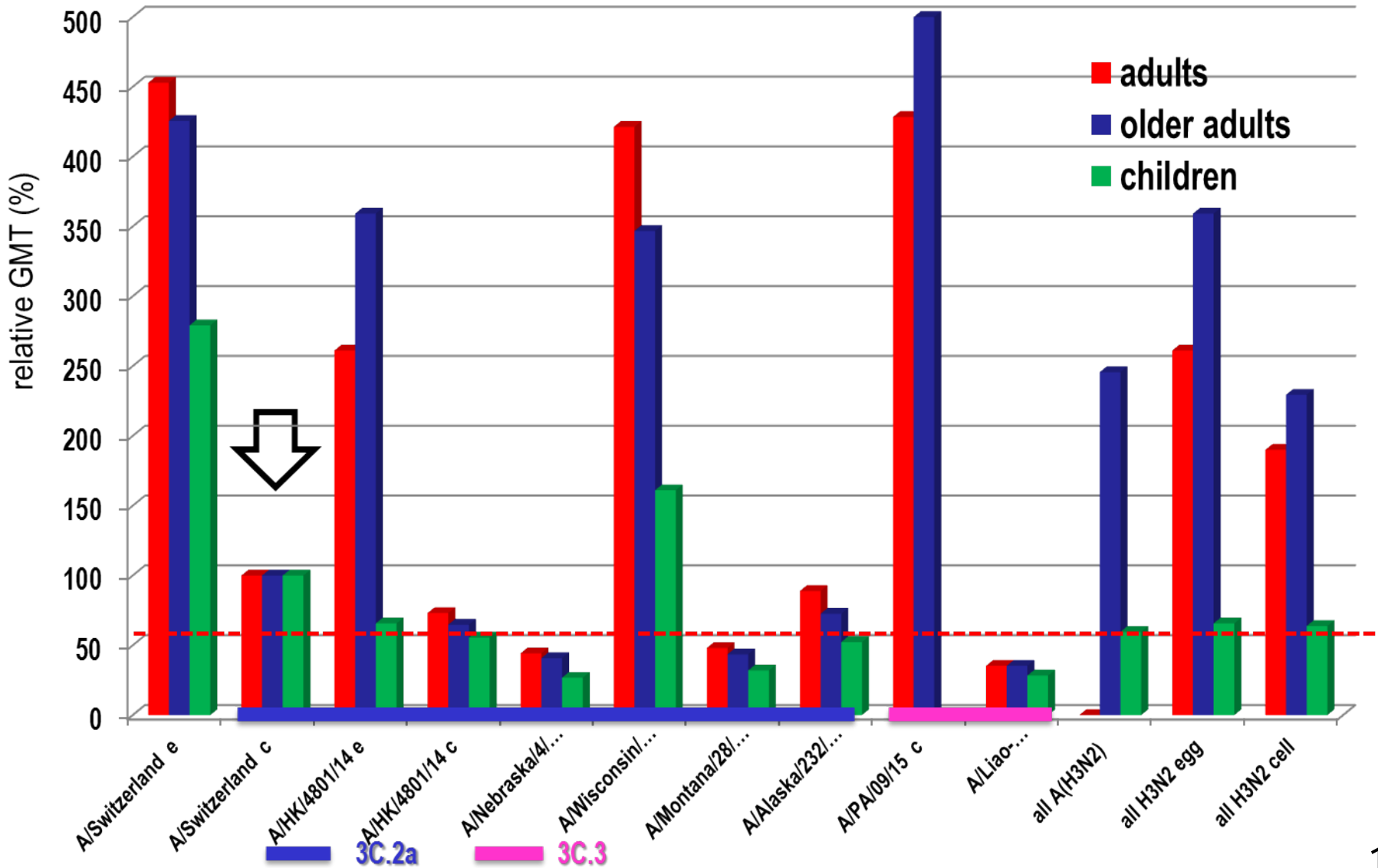
COMPARISON OF HI ANTIBODY TITERS TO THE A(H3N2) COMPONENT:
 (Using A/Switzerland/9715293/2013 **ell-grown** virus as reference)



MN ANTIBODY TO THE A(H3N2) COMPONENT:
 (using egg-propagated A/Switzerland/9715293/2013 as reference)



MN ANTIBODY TO THE A(H3N2) COMPONENT:
 (using cell-propagated A/Switzerland/9715293/2013 as reference)



A(H3N2)-summary

- Compared to HI titers against the egg-propagated A/Switzerland/9715293/2013 vaccine virus, geometric mean HI titers (GMT) of antibodies to some representative recent viruses were significantly reduced.
- When measured against cell culture-propagated virus, GMT of antibodies against recent viruses were relatively higher.
- Neutralization tests performed on a subset of serum panels confirmed these findings.

Influenza B Serology

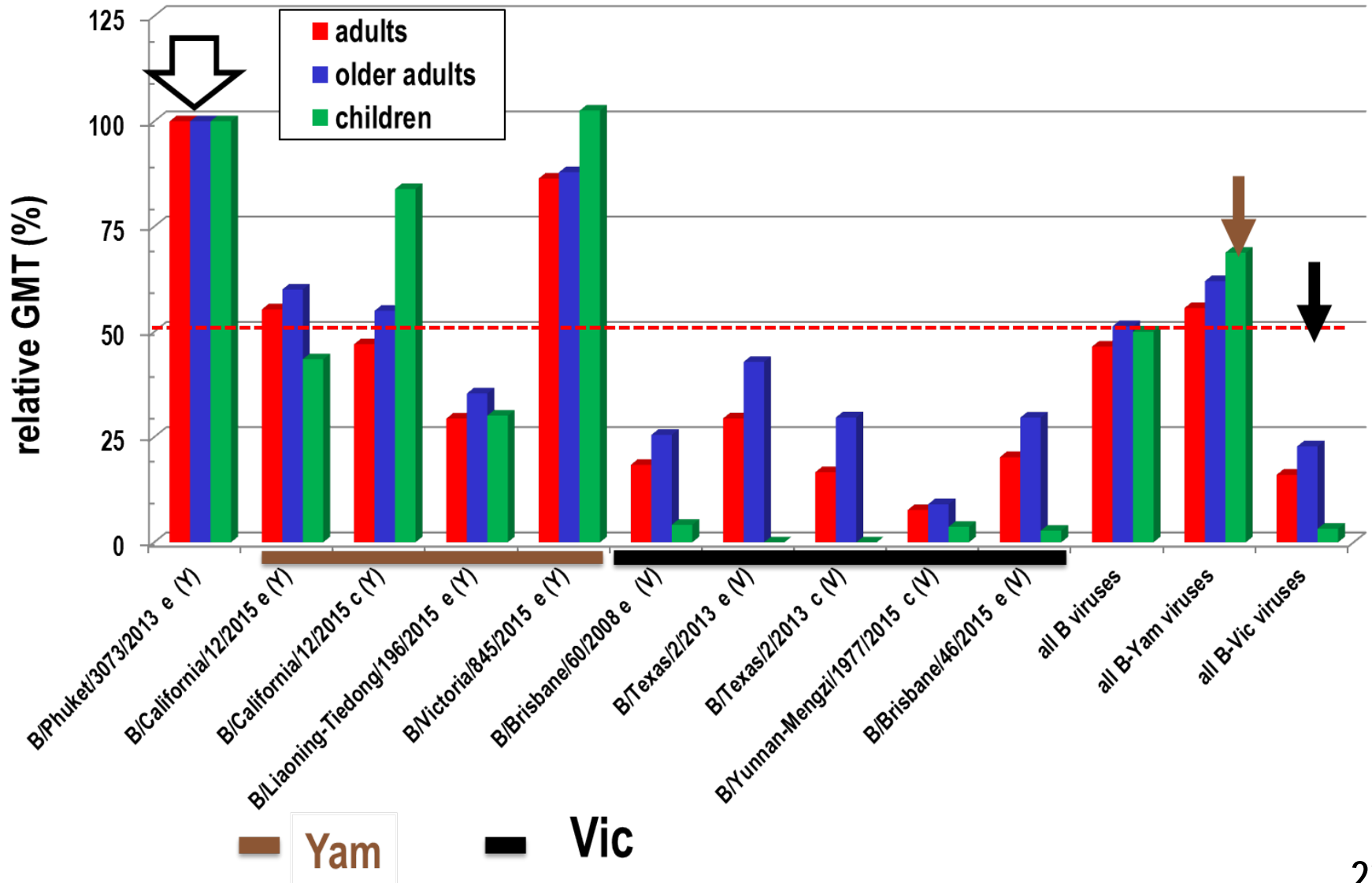
Antigens for serology: influenza B

REFERENCE VIRUSES B/Phuket/3073/2013 egg and cell (Yam) B/Brisbane/60/2008 egg (Vic, quadrivalent vaccine only)	
REPRESENTATIVE CURRENT VIRUSES	
Yamagata lineage	
B/California/12/2015	egg
B/California/12/2015	cell
B/Laos/99/2015	cell
B/Liaoning-Tiedong/196/2015	egg
B/Victoria/845/2015	egg
B/Okinawa/8/2015	cell
Victoria lineage	
B/Texas/2/2013	egg
B/Texas/2/2013	cell
B/Sapporo/23/2015	cell
B/Yunnan-Mengzi/1977/2015	egg
B/Brisbane/46/2015	egg
B/Victoria/502/2015	egg

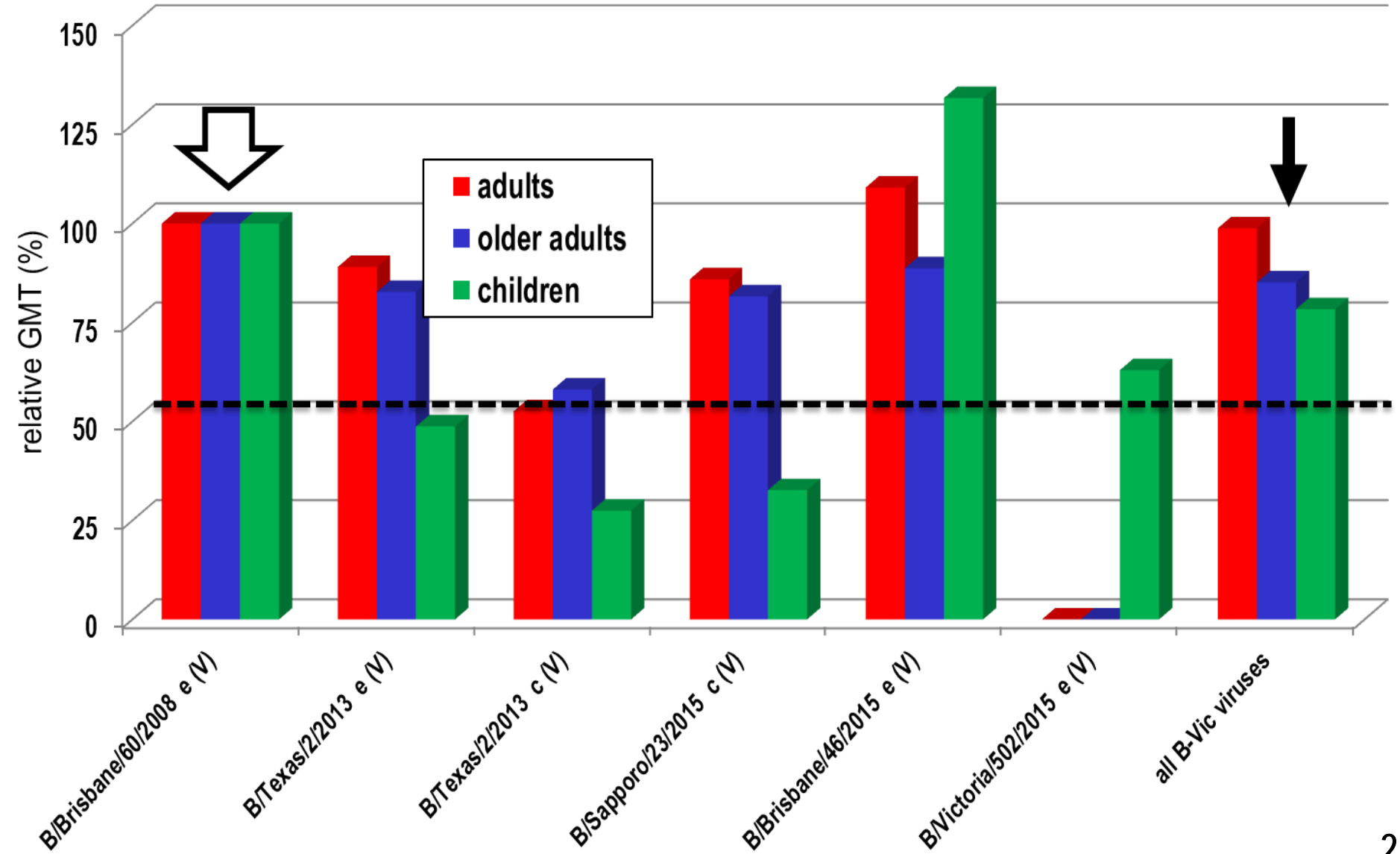
COMPARISON OF HI ANTIBODY TITERS TO THE B COMPONENT

Serum panels from recipients of **trivalent** vaccines

(Using **B/Phuket/3073/2013 (Yam)** egg-propagated virus as reference)



COMPARISON OF HI ANTIBODY TITERS TO B-VICTORIA LINEAGE COMPONENT
Serum panels from recipients of **quadrivalent** vaccines



B-summary

- GMTs of antibodies against the majority of recent B/Yamagata/16/88 lineage viruses were similar to HI titers against Phuket/3073/2013 vaccine virus.
- As expected, GMTs to B/Victoria/2/87 lineage viruses were reduced in panels from trials of trivalent vaccines not containing a B/Victoria/2/87 lineage antigen, whereas serum panels from trials of quadrivalent vaccines showed good reactivity with recent B/Victoria/2/87 lineage viruses.

Summary

H1N1pdm09

The majority of representative viruses reacted well with human sera collected from individuals who received vaccines containing **A/California/7/2009**-like antigens.

H3N2

Geometric mean titres against some A(H3N2) viruses were significantly reduced compared to HI titres against egg-grown vaccine virus **A/Switzerland/9715293/2013**, but less so when compared to cell-propagated vaccine virus.

B

B/YAMAGATA/16/88-lineage

Vaccines containing **B/Phuket/3073/2013** antigen elicited anti-HA antibodies of similar geometric mean titres to the vaccine virus and representative recent Yamagata lineage viruses

B/VICTORIA/2/87-lineage

B Victoria lineage viruses reacted poorly with human sera from trivalent vaccines not containing **B/Brisbane/60/2008** antigens. As expected, vaccines containing this antigen induced antibodies that reacted well with recent B/Victoria lineage viruses.