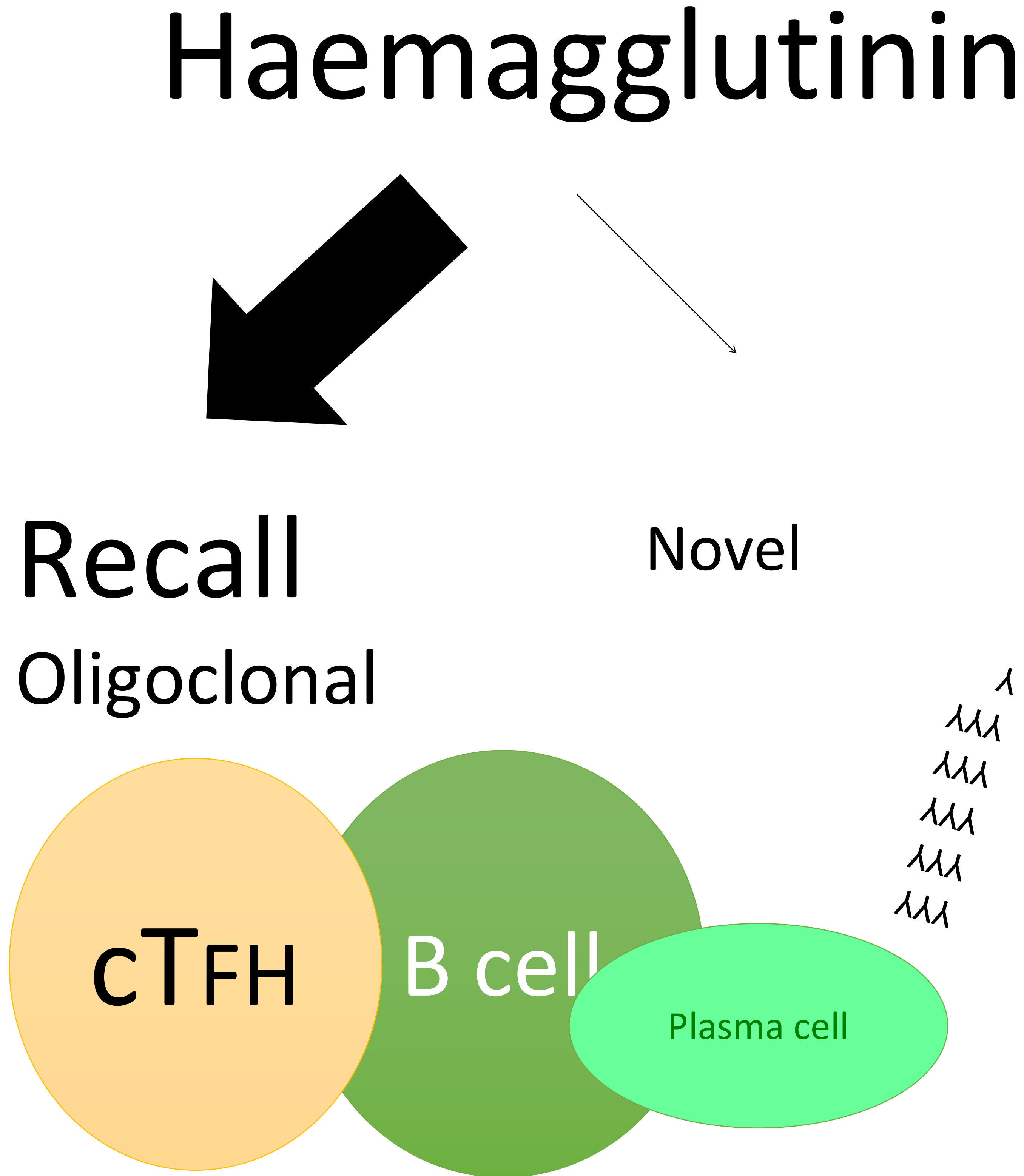


# Equivalent responses to quadrivalent influenza vaccine are detectable in blood and oral fluid in healthcare workers and men living with HIV on ART: findings from the FluAGE study

Megan E. Cole<sup>1</sup>, Zainab Saeed<sup>1</sup>, A. Torm Shaw<sup>1</sup>, Yanping Guo<sup>2</sup>,  
Katja Hoschler<sup>3</sup>, Alan Winston<sup>1,4</sup>, Graham S. Cooke<sup>1</sup>, Sarah  
Fidler<sup>1,4</sup>, Graham P. Taylor<sup>1,2</sup>, and Katrina M. Pollock<sup>1</sup>

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# A suboptimal response to influenza vaccine in PLWH despite ART?



## HIV infection Worsens Age-Associated Defects in Antibody Responses to Influenza Vaccine FREE

Varghese K. George ✉, Suresh Pallikkuth, Anita Parmigiani, Maria Alcaide, Margaret Fischl, Kristopher L. Arheart, Savita Pahwa [Author Notes](#)

*The Journal of Infectious Diseases*, Volume 211, Issue 12, 15 June 2015, Pages 1959–1968,

## Impact of aging and HIV infection on serologic response to seasonal influenza vaccination

Pallikkuth, Suresh<sup>a</sup>; De Armas, Lesley, R.<sup>a</sup>; Pahwa, Rajendra<sup>a</sup>; Rinaldi, Stefano<sup>a</sup>; George, Varghese, K.<sup>a</sup>; Sanchez, Celeste, M.<sup>a</sup>; Pan, Li<sup>a</sup>; Dickinson, Gordon<sup>b,d</sup>; Rodriguez, Allan<sup>b</sup>; Fischl, Margaret<sup>c</sup>; Alcaide, Maria<sup>b</sup>; Pahwa, Savita<sup>a</sup>

*AIDS*: June 1, 2018 - Volume 32 - Issue 9 - p 1085–1094

# Quadrivalent influenza vaccine is preferred for PLWH

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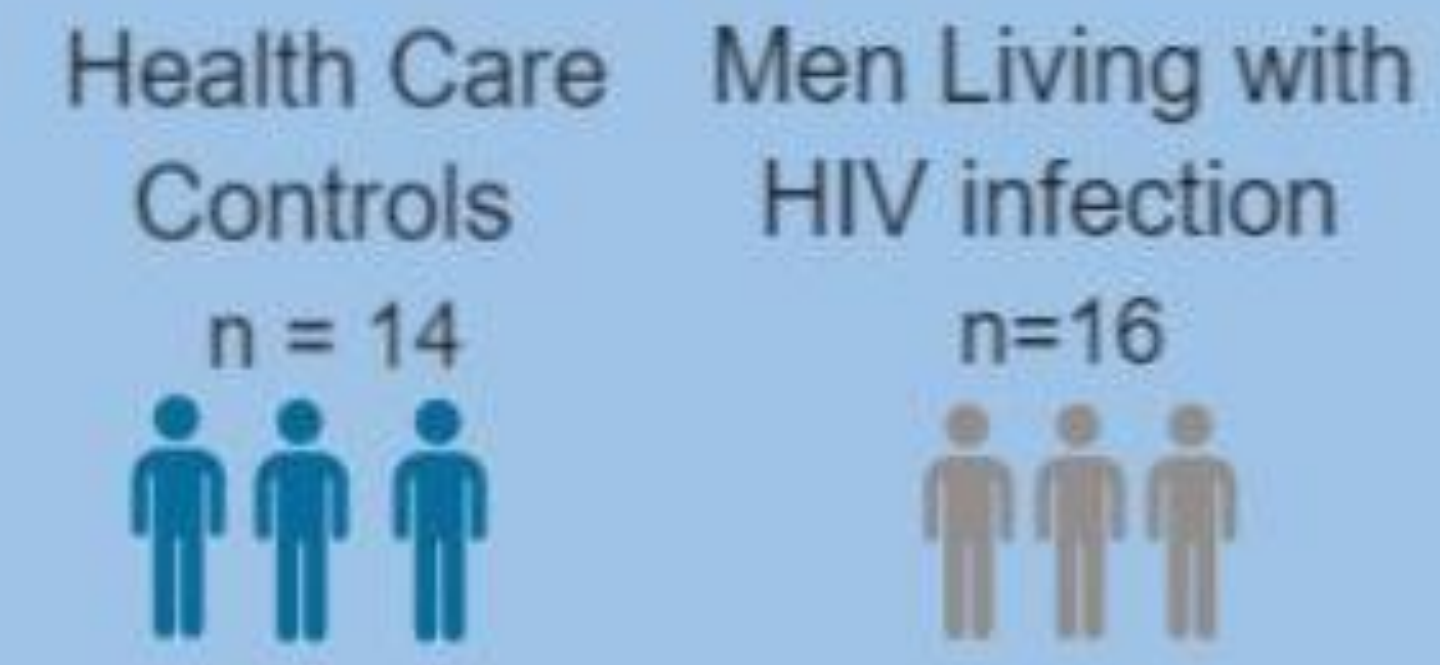
## British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015

Season	A/H1N1	A/H3N2	B	Additional B strain for QIV
2014/2015	A/California/7/2009	A/Texas/50/2012	B/Massachusetts/2/2/2012	N/A
2015/2016	A/California/7/2009	A/Switzerland/9715293/2013	B/Phuket/3073/2013	N/A
2016/2017	A/California/7/2009	A/HongKong/4801/2014	B/Brisbane/60/2008	N/A
2017/2018	A/Michigan/45/2015	A/HongKong/4801/2014	B/Brisbane/60/2008	B/Phuket/3073/2013

# FluAGE Study

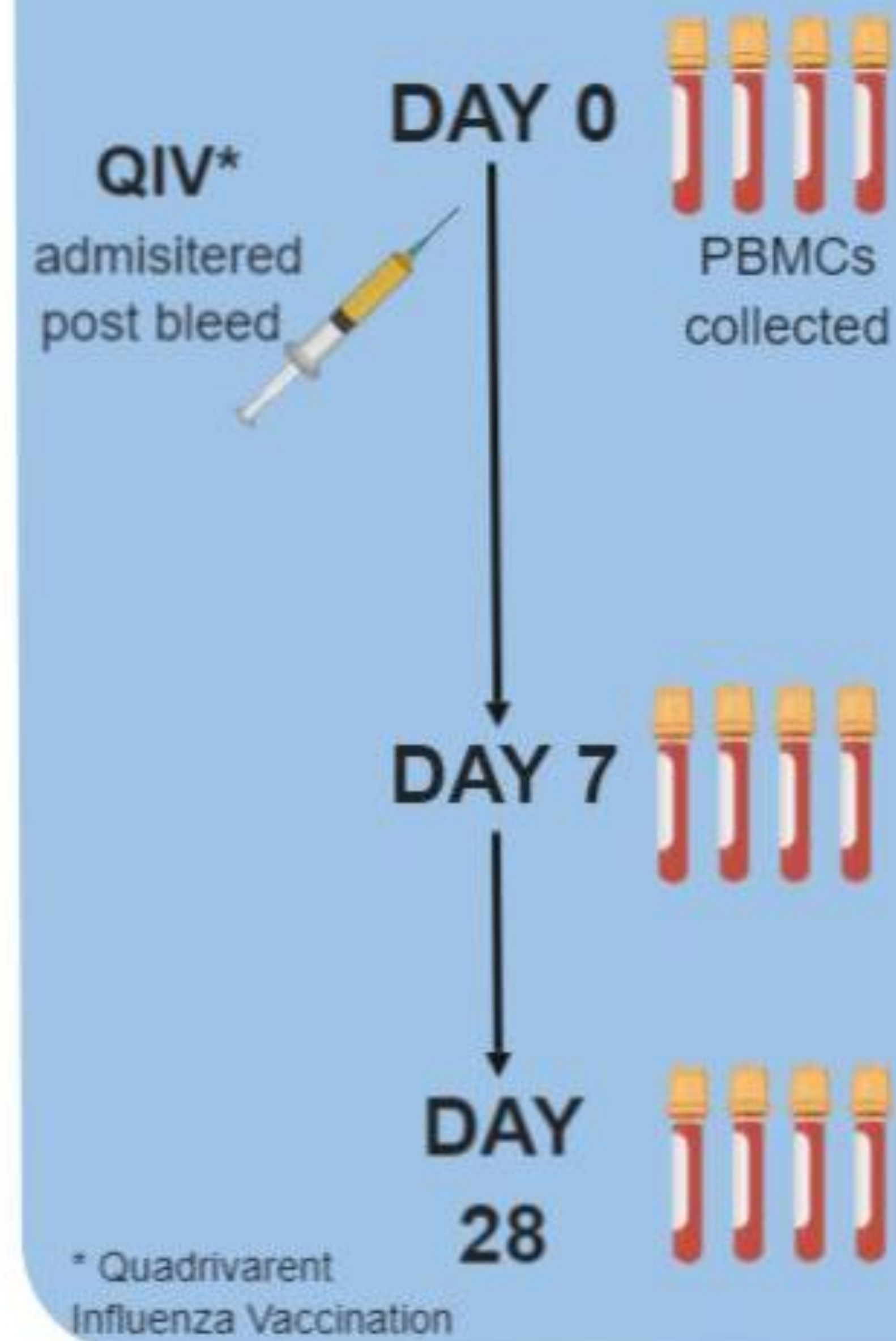
Despite viral suppression with ART, is the cellular and antibody response to quadrivalent influenza vaccine compromised in men living with HIV infection?

# 1. Recruitment

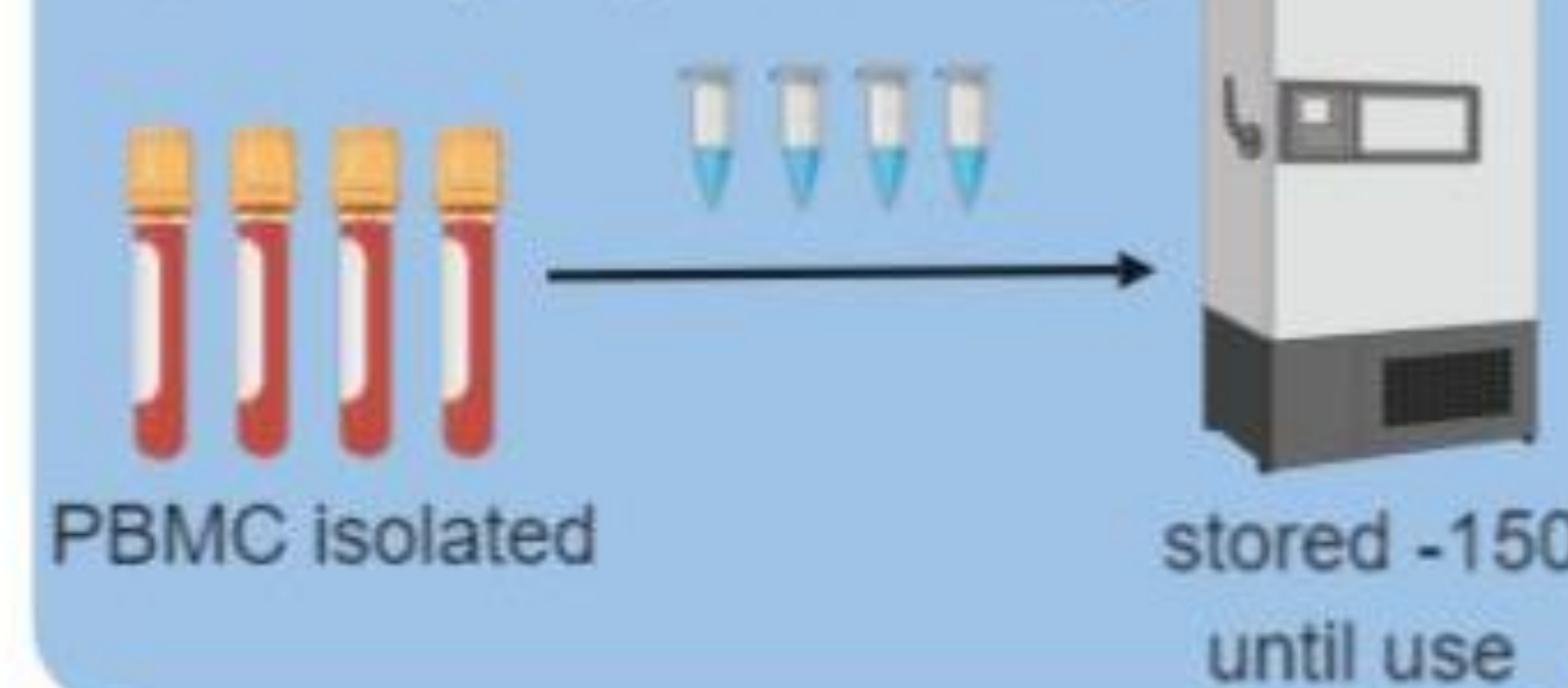


# 2. Study Design

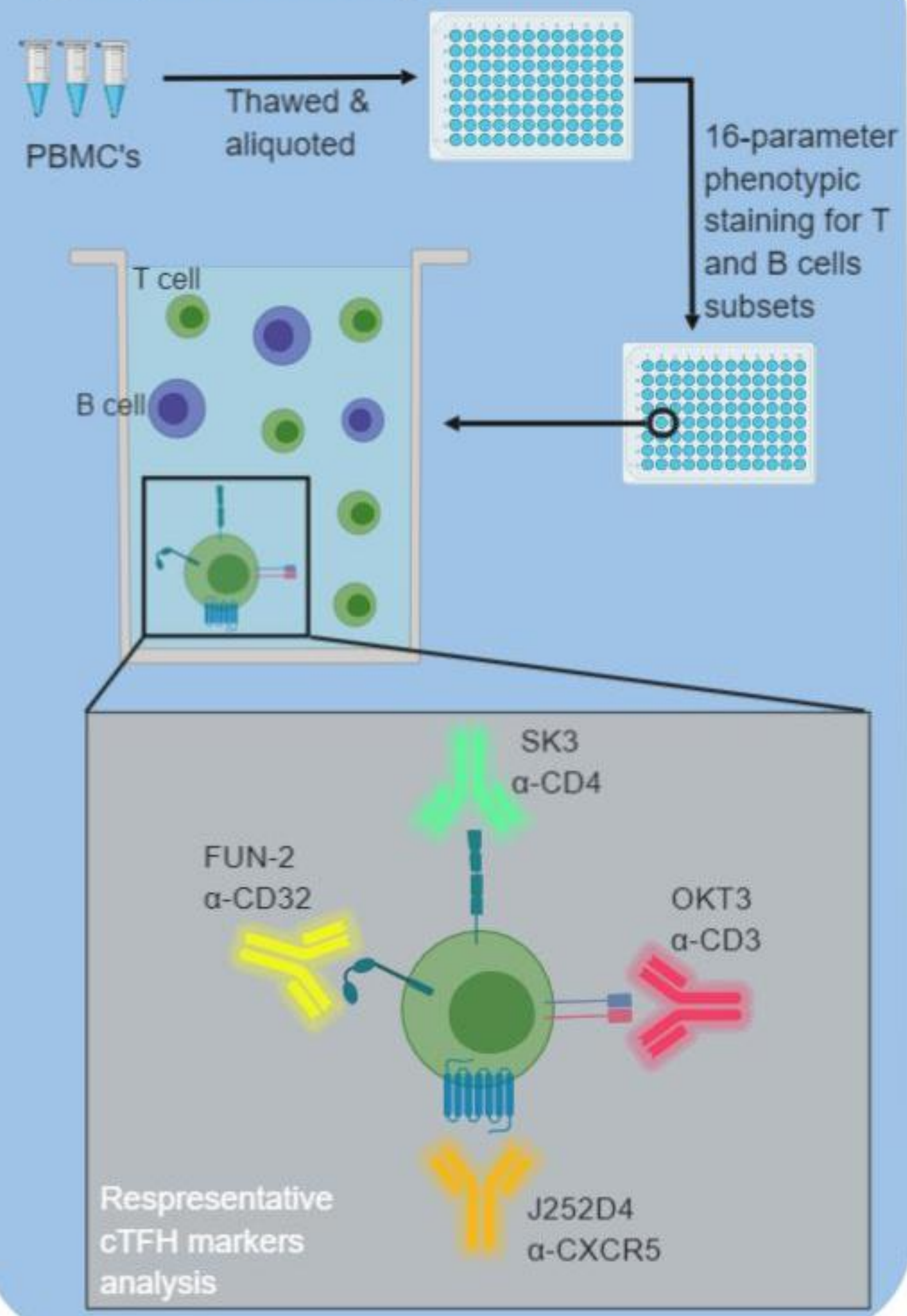
2017/18 Northern Hemisphere Influenza season



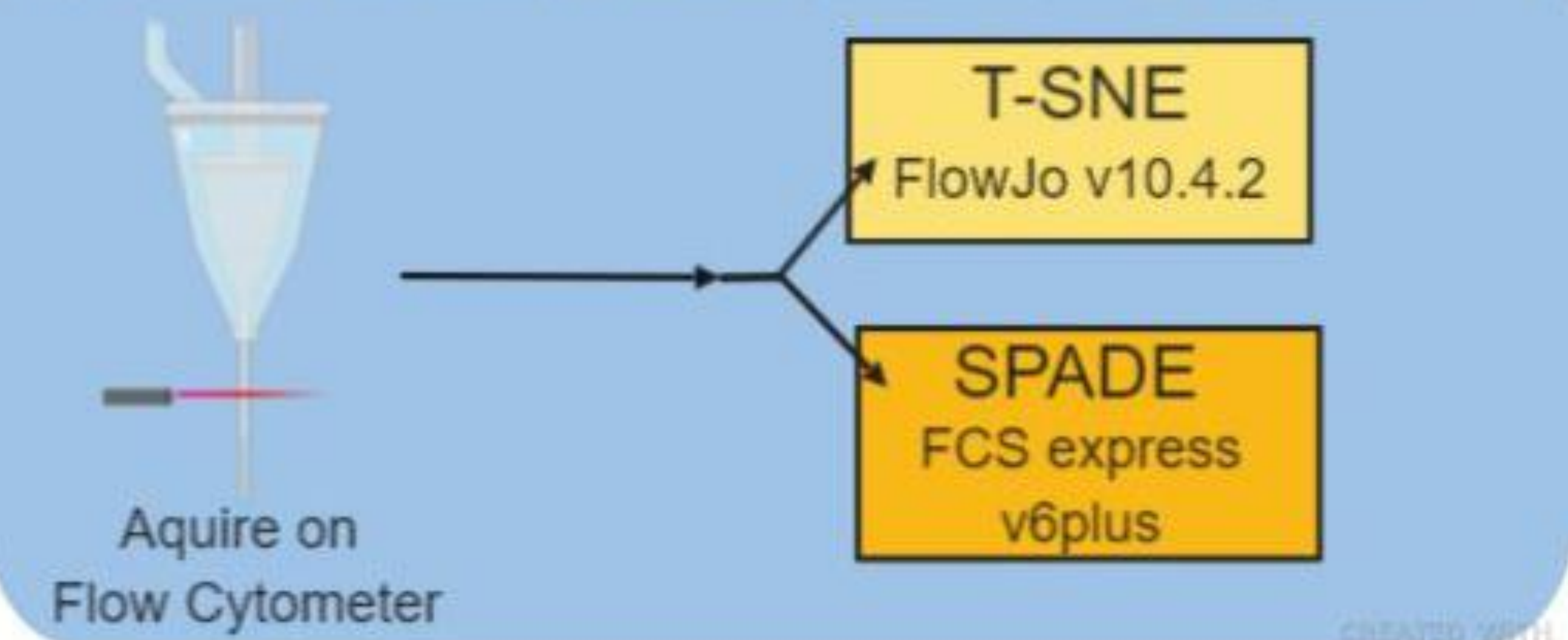
# 3. Sample processing



# 4. Experiment design



# 5. Analysis using unsupervised algorithms



# Participant characteristics

			Control subjects		Early treated HIV		Chronic treated HIV	
<b>Sex</b>	<b>Male</b>	<b>(%)</b>	14	(100)	8	(100)	8	(100)
<b>Ethnicity</b>	<b>White British</b>	<b>(%)</b>	8	(57.1)	3	(37.5)	2	(25)
	<b>White Other</b>	<b>(%)</b>	5	(35.7)	5	(62.5)	5	(62.5)
	<b>Black British</b>	<b>(%)</b>	1	(7.2)	0	(0)	1	(12.5)
<b>Age</b>		<b>Median (IQR)</b>	37	(29-49)	48	(42-58)	50	(38-55)
<b>CD4 count at vaccination, cells/<math>\mu</math>l</b>		<b>Median (IQR)</b>			789	(665-1033)	609	(454-931)
<b>CD8 count at vaccination, cells/<math>\mu</math>l</b>		<b>Median (IQR)</b>	-	-	720	(558-1034)	686	(477-1350)
<b>CD4:CD8 ratio</b>		<b>Median (IQR)</b>	-	-	1	(0.91-1.41)	0.85	(0.61-1.21)
<b>Nadir CD4 count</b>		<b>Median (IQR)</b>	-	-	522	(466-734)	170	(80-410)
<b>HIV viral load at vaccination &lt;20 RNA copies/ml</b>		<b>(%)</b>	-	-	8	(100)	8	(100))
<b>Duration HIV viral load suppressed (months)</b>		<b>Median (IQR)</b>	-	-	19	(6.8-26.5)	90	(53.0-159.0)

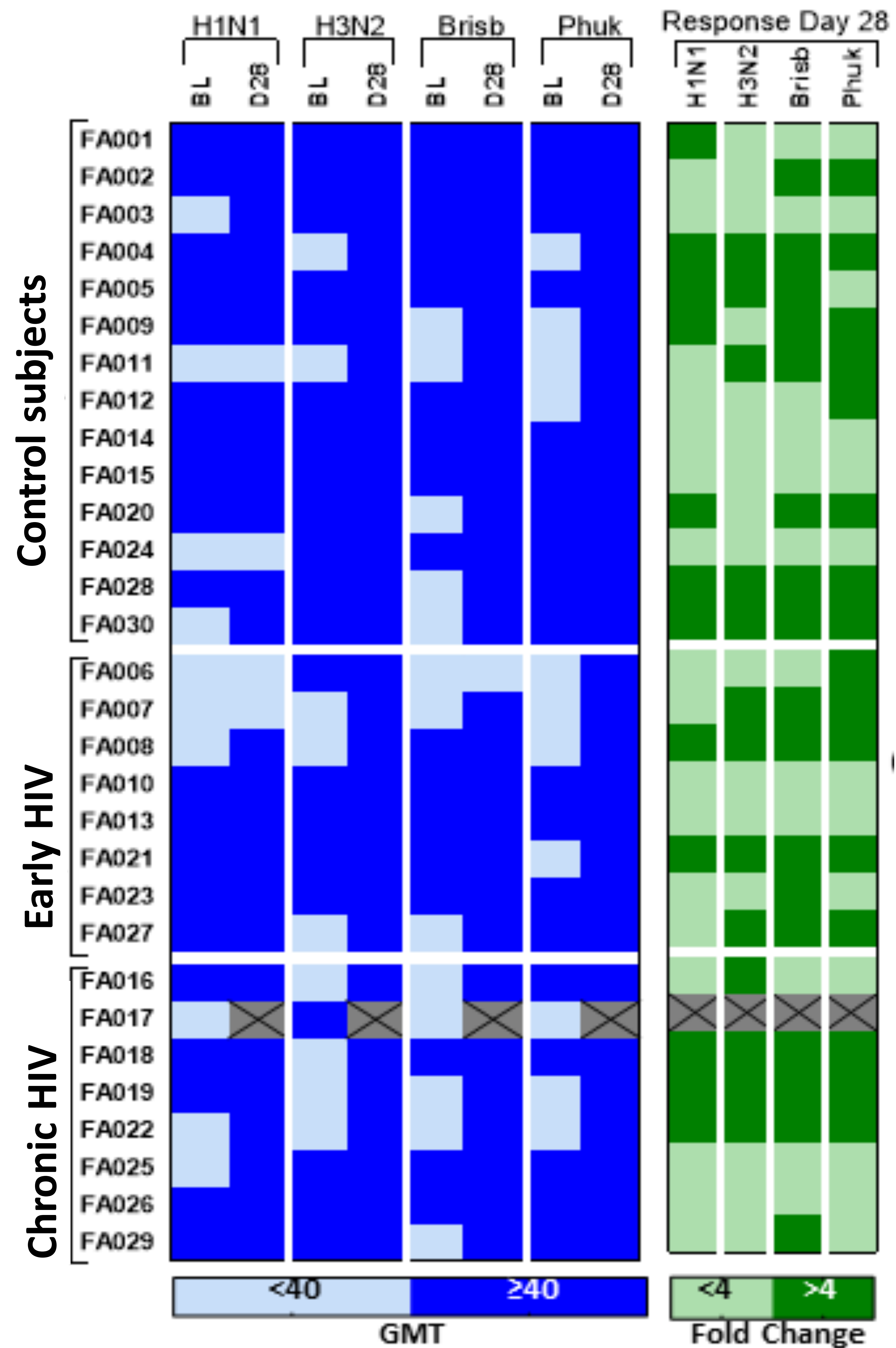
Early treated HIV infection = individuals diagnosed with primary HIV infection and started on ART within three months (HEATHER)

Chronic treated HIV infection = individuals diagnosed and treated as part of routine clinical care

# Antibody responses despite baseline seroprotection

Dark blue = seroprotection

Dark green = antibody response

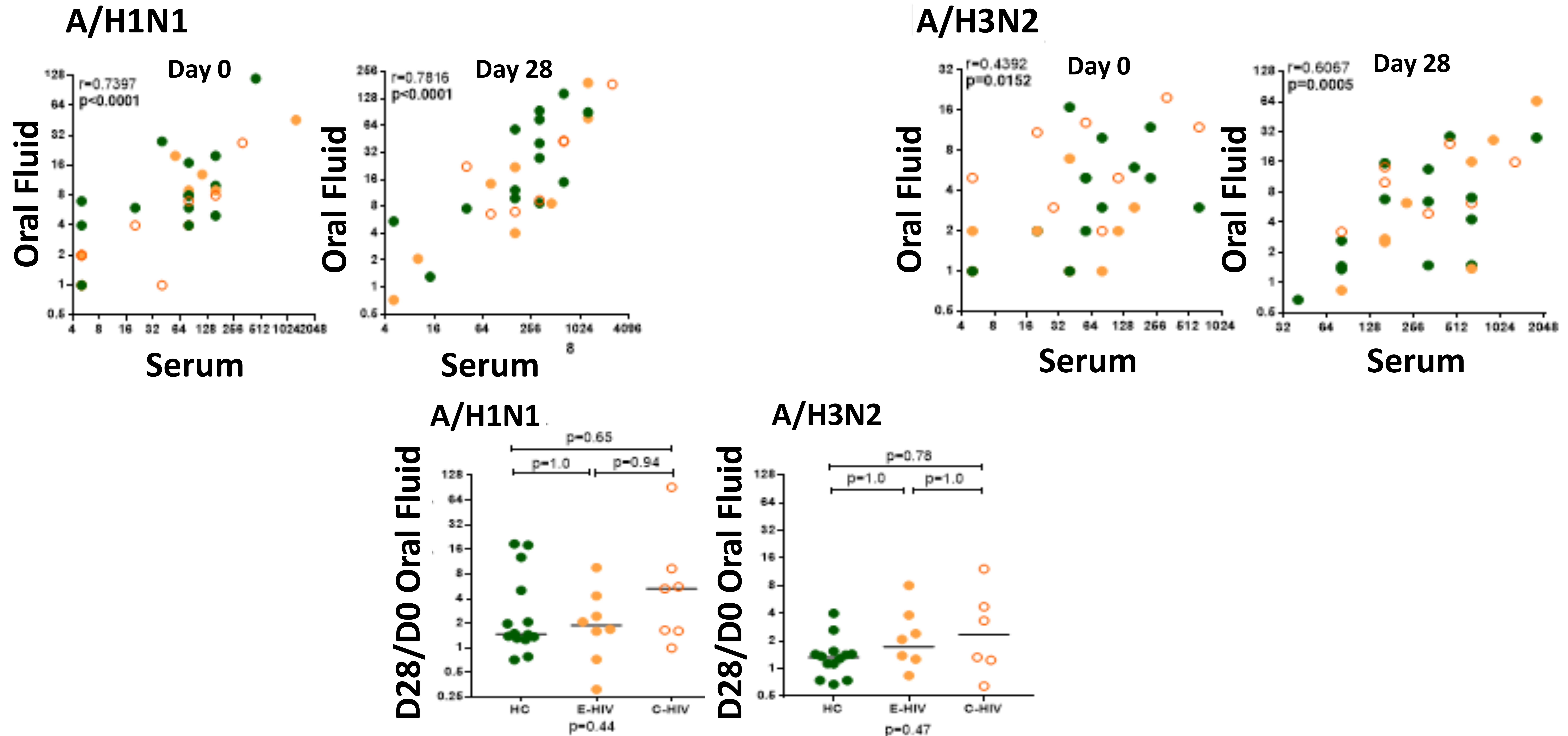


# Equivalent antibody protection in healthcare workers and PLWH

Haemagglutination inhibition titre $\geq 40$	Control subjects		Early treated HIV		Chronic treated HIV	
	n	(%)	n	(%)	n	(%)
A/H1N1	12	(85.7)	6	(75)	7	(100)
A/H3N2	14	(100)	8	(100)	7	(100)
B/Brisbane	14	(100)	7	(87.5)	7	(100)
B/Phuket	14	(100)	8	(100)	7	(100)

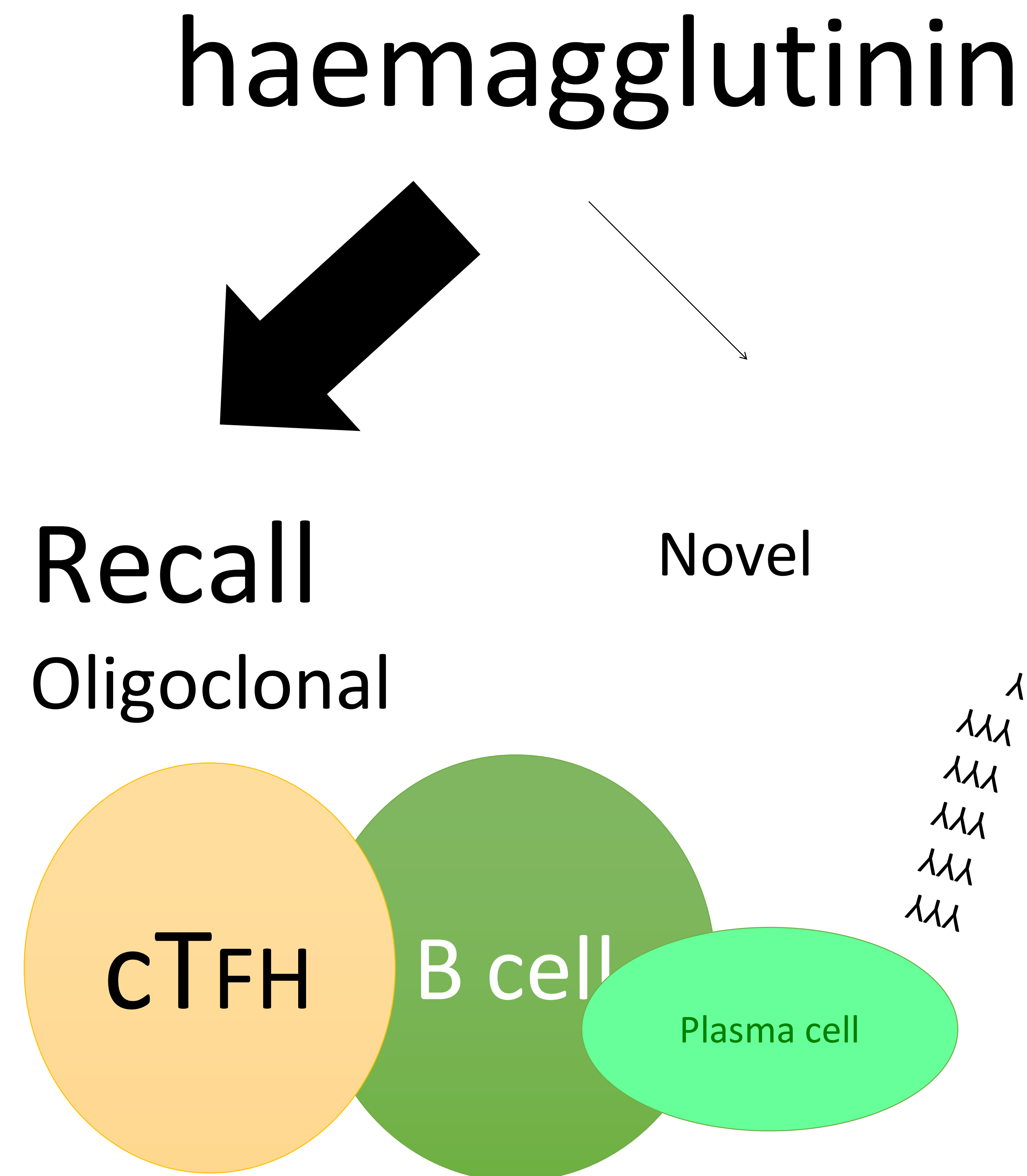


# Influenza/A-specific antibody in blood and oral fluid

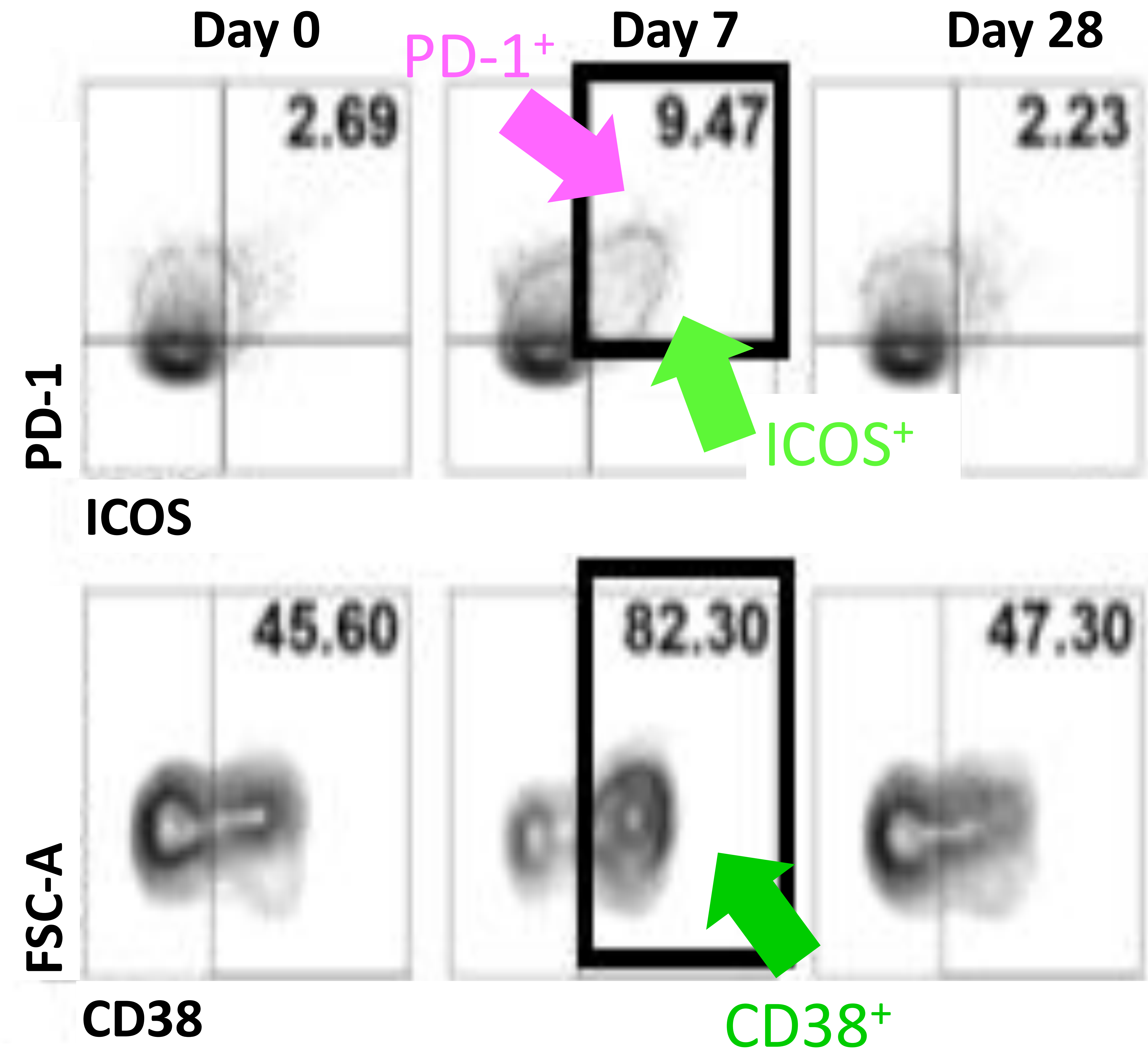
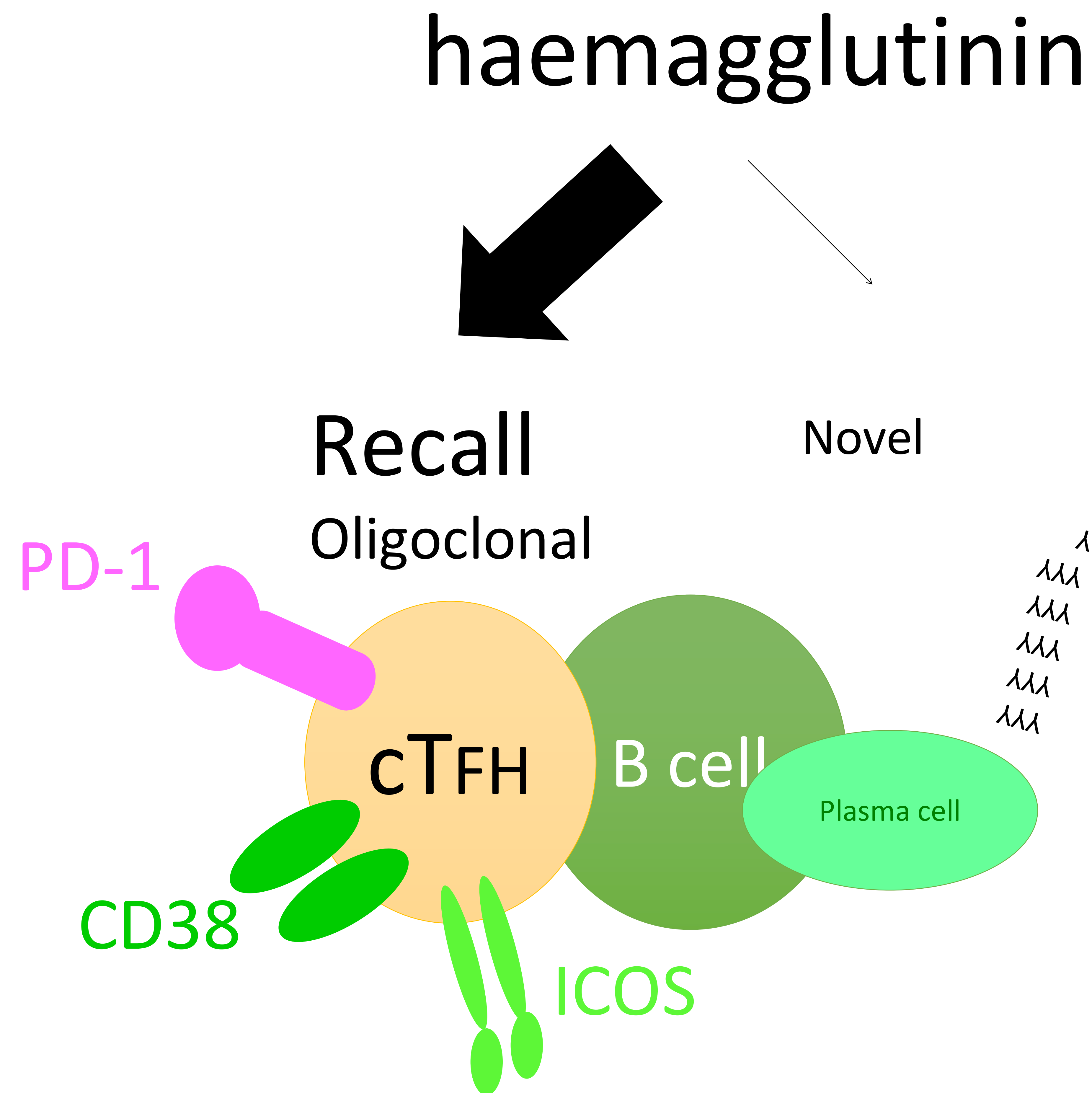


Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles

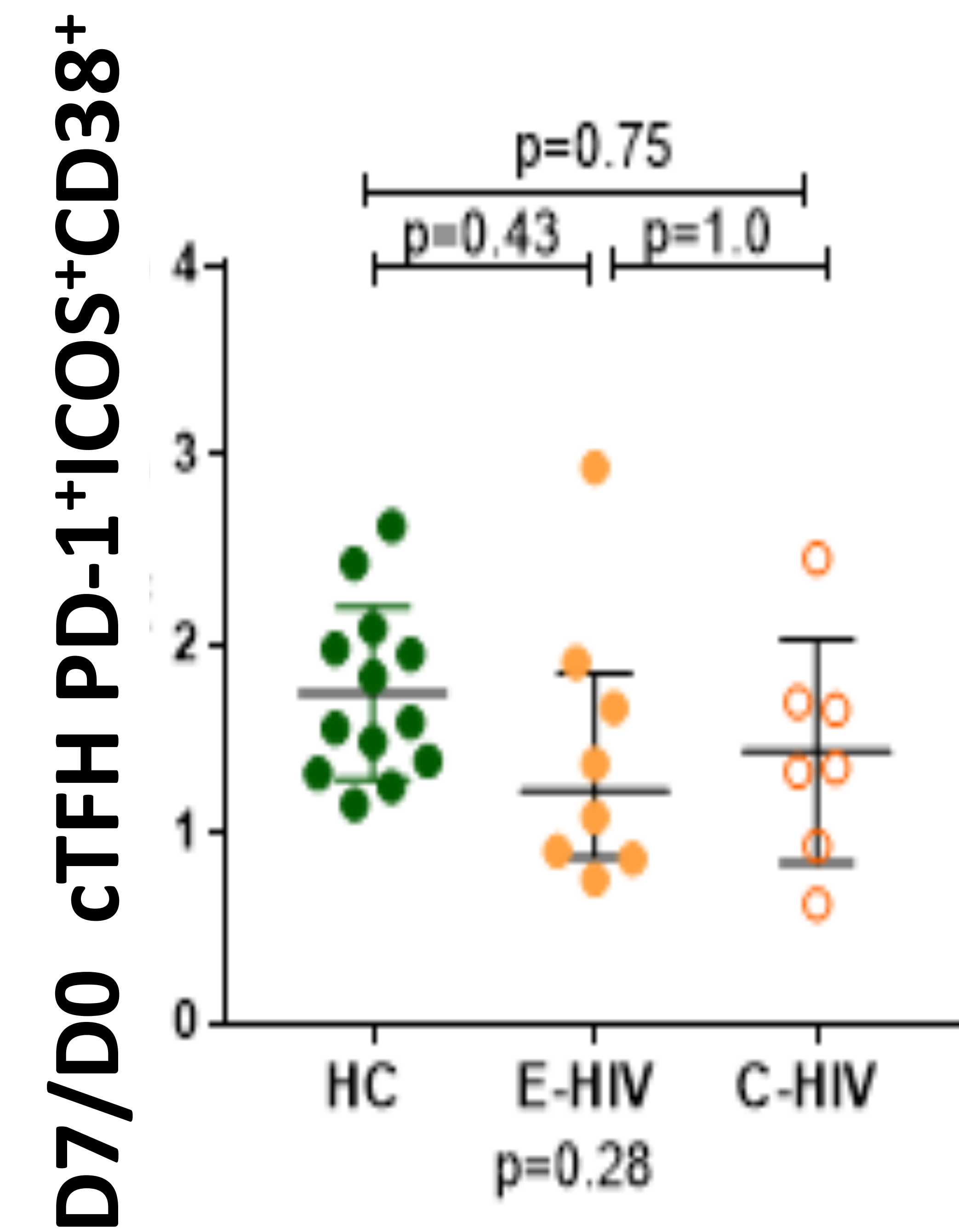
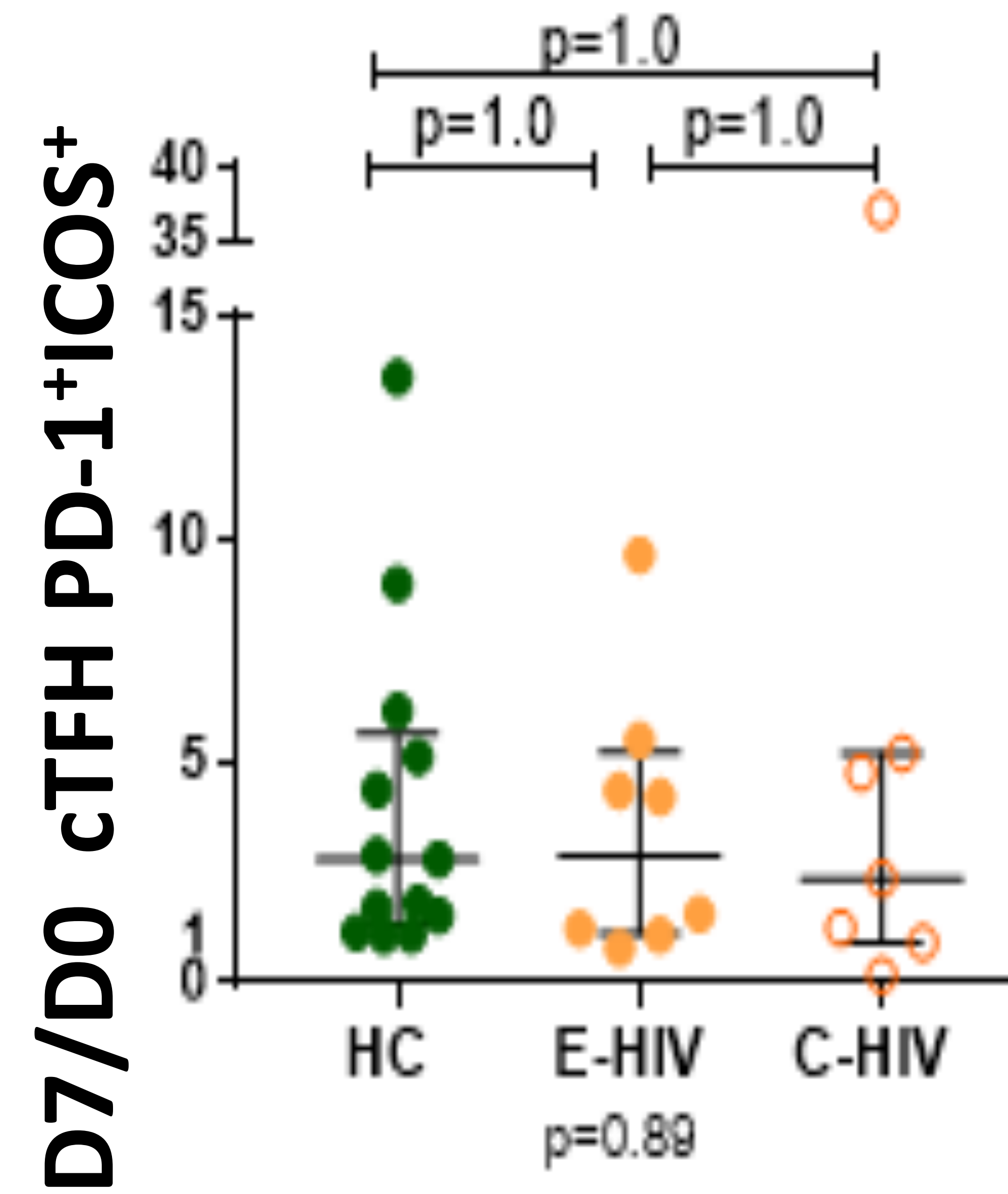
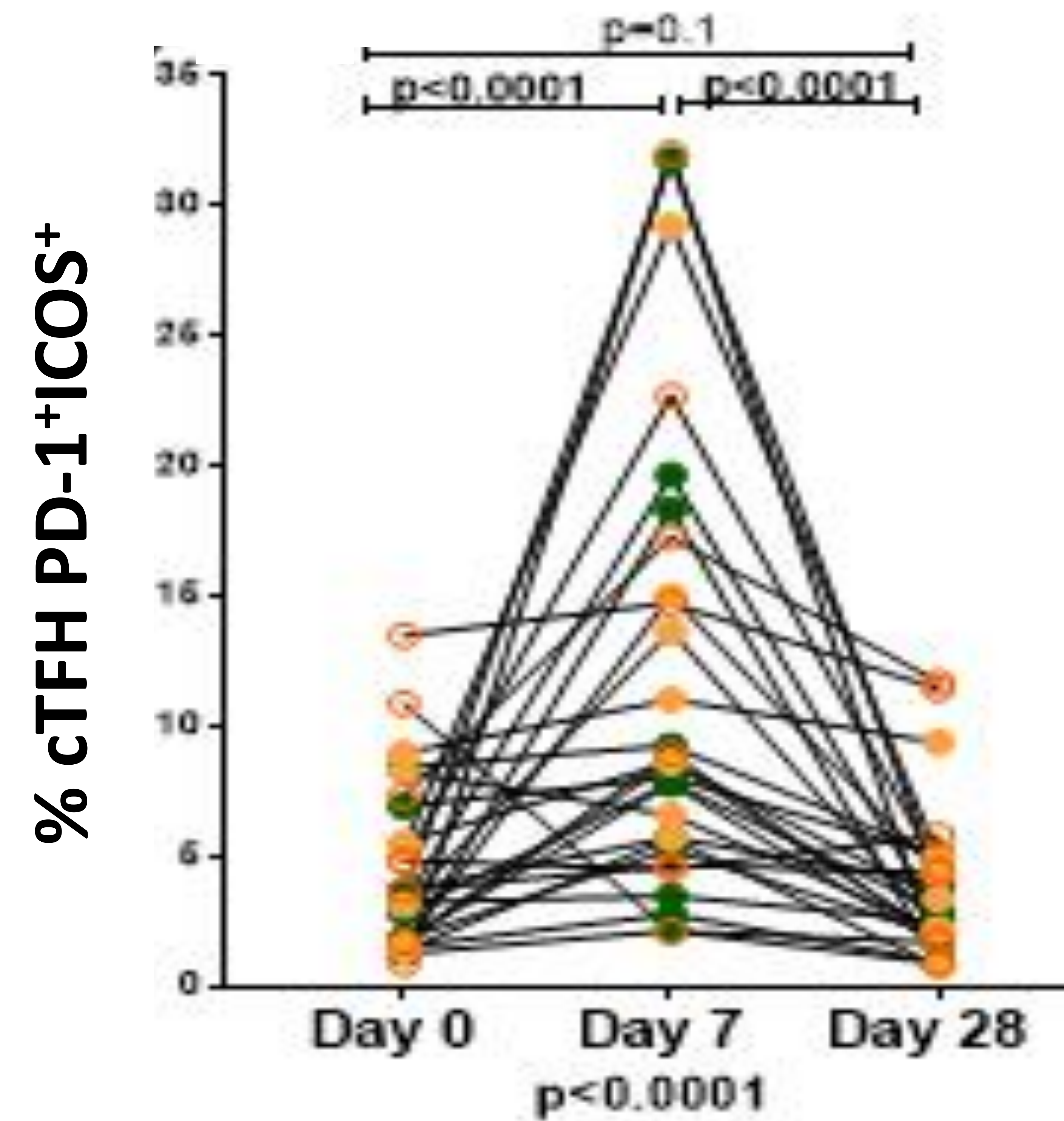
# Activation of circulating CD4+ T-follicular helper cells (cTFH) by quadrivalent influenza vaccination



# Activation of circulating CD4+ T-follicular helper cells (cTFH) by quadrivalent influenza vaccination



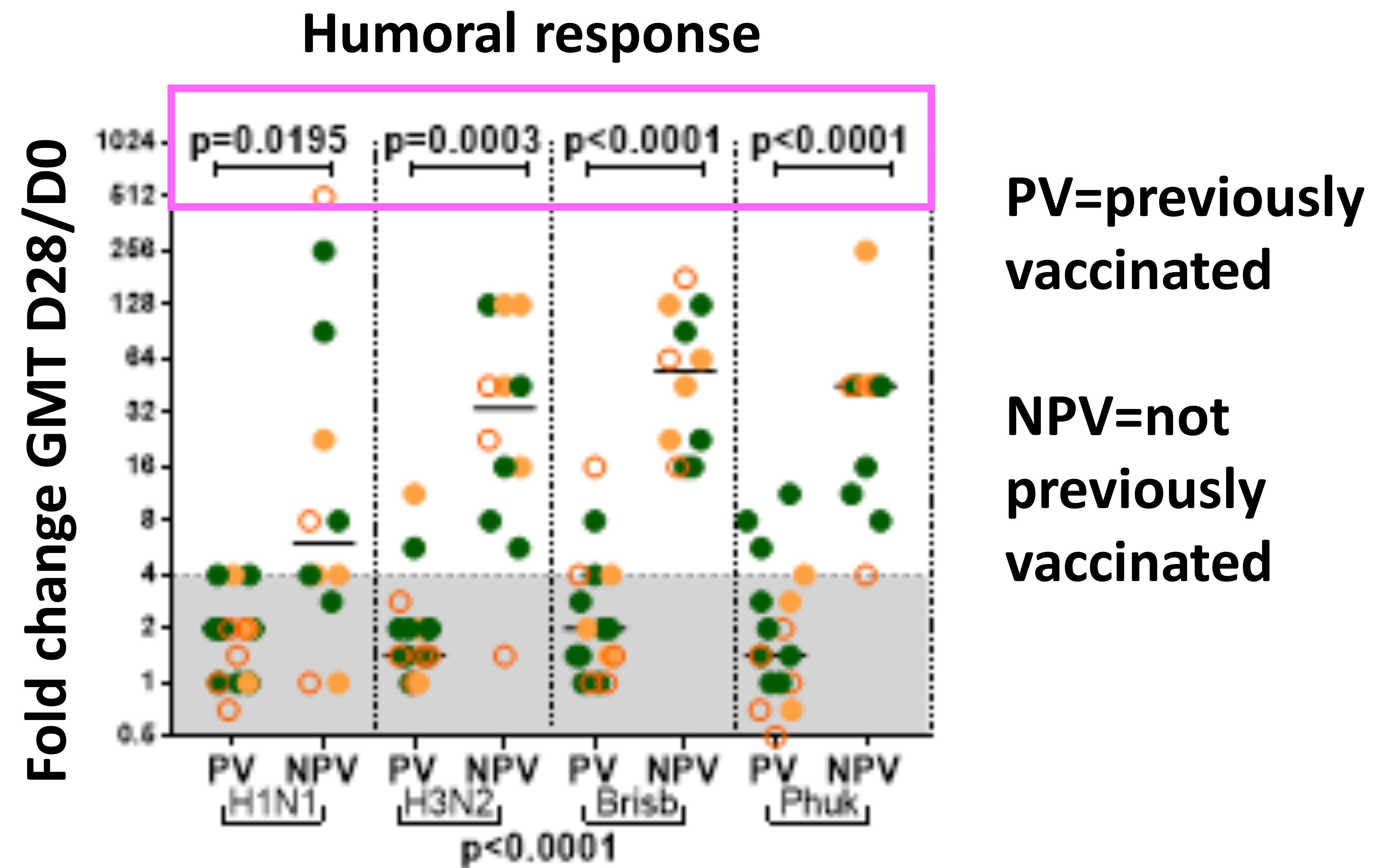
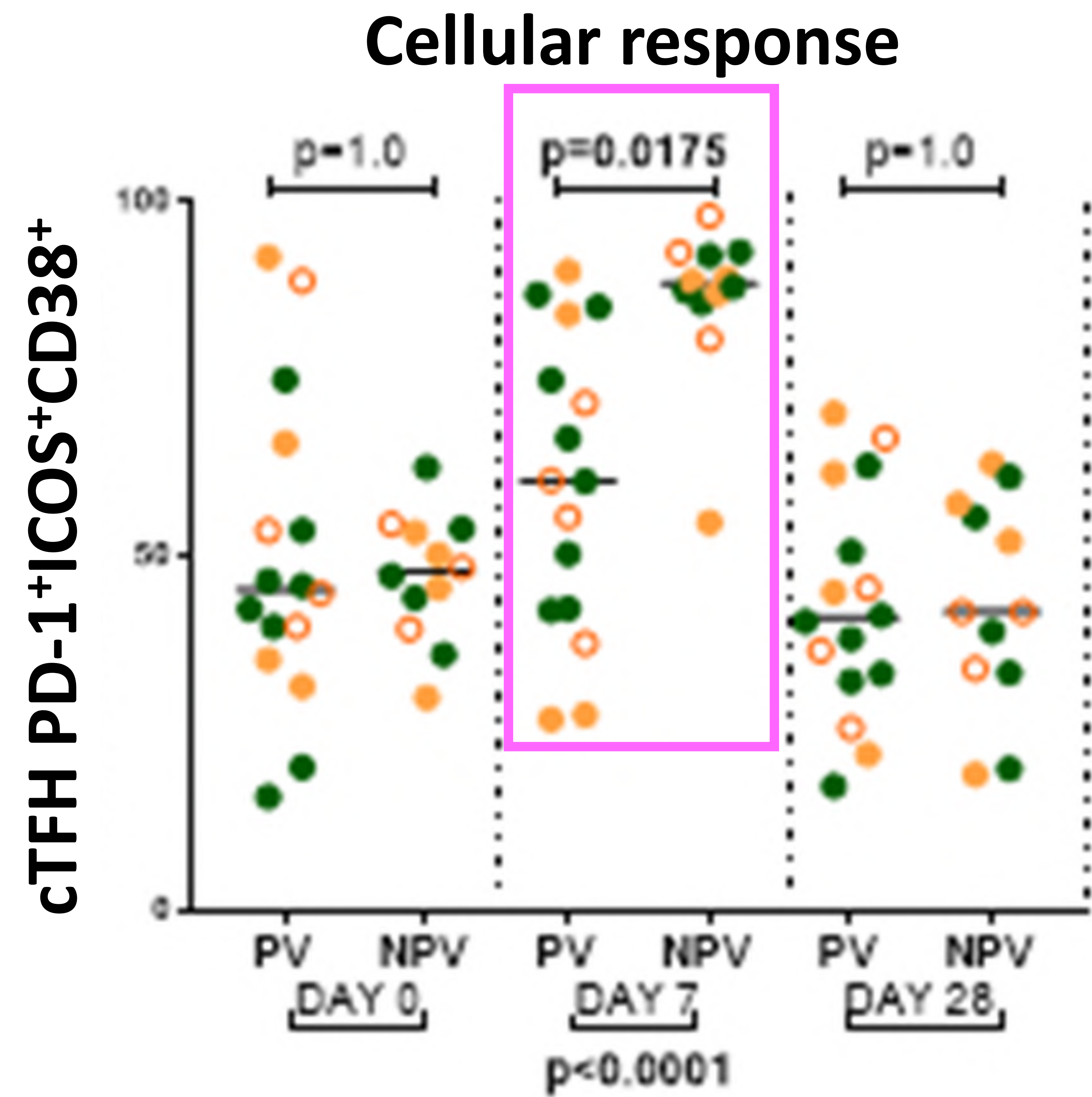
# Equivalent CD4+ T-helper cell (cTFH) response in PLWH and healthcare workers



**Fold change equivalent in all groups studied  $p = 0.89$**

Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles

# Vaccination history in preceding three years



Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles

# Conclusions

- First UK study of PLWH receiving the inactivated quadrivalent influenza vaccine
- High seroprotection rates, equivalent to those of healthcare workers, in men with suppressed HIV infection and immune recovery
- Findings support QIV in the seasonal influenza vaccination programme for PLWH
- Measurement of influenza-specific antibody in the mouth is a potential alternative to serum sampling

Under review *Scientific Reports* SREP-19-03442-T

E-Poster #319 Conference on Retroviruses and Opportunistic Infections, USA, 2019

Poster #025 Cole M *et al.* Responses to quadrivalent influenza vaccine reveal the landscape of CD32 expression on circulating T-follicular helper cells in men living with HIV infection.

# Thank you



Graham Taylor  
Sarah Fidler  
Alan Winston  
Graham Cooke  
Yanping Guo  
Jonathan Weber  
Charles Bangham



Katja Hoschler

HEATHER: HIV Reservoir targeting with  
Early Antiretroviral Therapy

POPPY: A Prospective, Observational Study to Examine the  
Effects of Ageing on the 'Pharmacokinetic and Clinical  
Observations in People Over Fifty'

Staff and patients of the Jefferiss Wing  
and the HIV Clinical Trials Centre

