Impact of Influenza A(H3N2) virus infection on the antibody landscapes of hemagglutinin and neuraminidase protein in older adults.

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Background

Older adults have **complex immune history** because of lifetime exposure to different influenza viruses, which can shape the antibody dynamics after infection[1]. We studied the **hemagglutinin** (HA) and **neuraminidase** (NA) **antibody landscapes** to **A(H3N2) viruses** in a cohort of unvaccinated **older adults** (60-89 years old) in southeastern China.

Objectives

Examining the change in antibody repertoire of older adults to influenza viruses upon infections will help us understand the **potential of an NA-based influenza vaccine**, and the **robustness** of antibody responses to influenza in older adults. This will translate into **better protection** to older adults against influenza and alleviate the public health burden.

Methods

We studied the **China Aging REspiratory Study (CARES)** cohort to characterize the change in antibody landscapes after influenza infections (Table 1)[2]. We used **Hemagglutination Inhibition (HAI)** and **Neuraminidase Inhibition (NAI)** assays to characterize the antibody landscape of the serum samples.

Table 1. Characteristic of the China Ageing Respiratory Studies (CARES) cohort

Type	Prospective and longitudinal
Duration	2015 - 2017
Location	Southeastern China
Size and characteristic of participants	1532 community-dwelling older adults
Sample collection	Serum samples collected every six month

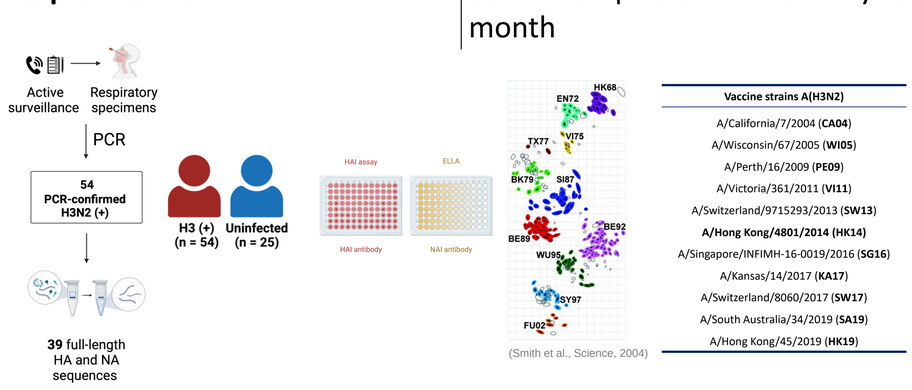


Fig 1. Overflow of the study design. Active surveillance were performed weekly to screen for acute respiratory illnesses (ARIs). Respiratory specimens were collected to identify 54 Polymerase Chain Reaction (PCR)-confirmed A(H3N2) infections. Twenty-five matched individuals who have not reported any ARIs were selected for comparison. Hemagglutination Inhibition (HAI) and Neuraminidase Inhibition (NAI) assays were used to study the antibody landscapes of their serum samples against 22 strains[3].

Results

1. All HA sequences belong to the **clade 3c.2a**, so **A/Hong Kong/4801/2014 (HK14)** was selected as the reference infection strain.

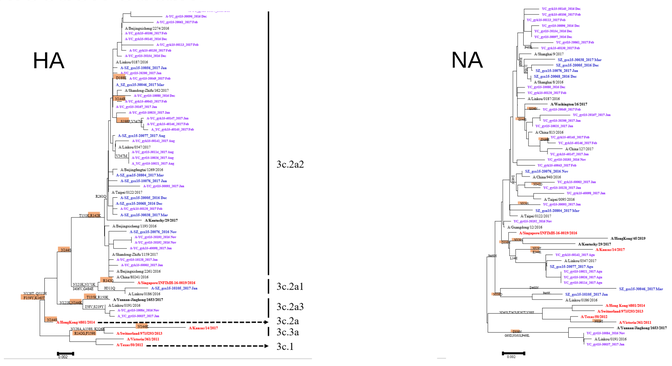


Fig. 2 Phylogenetic trees constructed from HA and NA sequences isolated from infected cases

2. The uninfected subcohort has **significantly higher HAI titres** to recent strains, and both subcohorts have **higher NAI titres** to **early** circulating strains

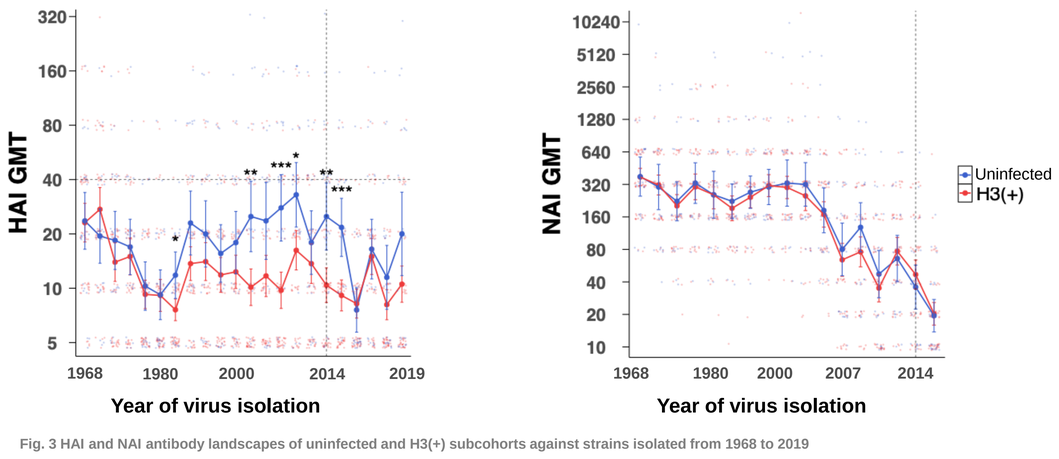


Fig. 3 HAI and NAI antibody landscapes of uninfected and H3(+) subcohorts against strains isolated from 1968 to 2019

3. There was a significant increase in **NAI titres** against **all strains**, while HAI responses were **restricted within clusters.**

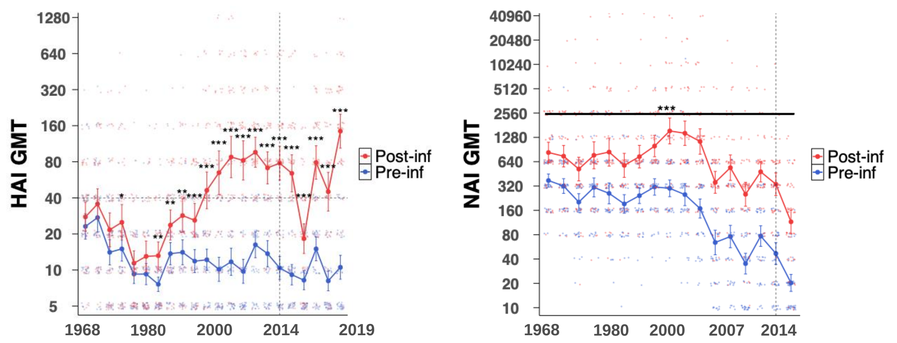


Fig. 5 Pre and post-infection HAI and NAI antibody landscapes of H3(+) subcohorts against strains isolated from 1968 to 2019

4. The **oldest** age group 80-89 years old **did not** show **impaired** antibody responses compared to the two younger age groups.

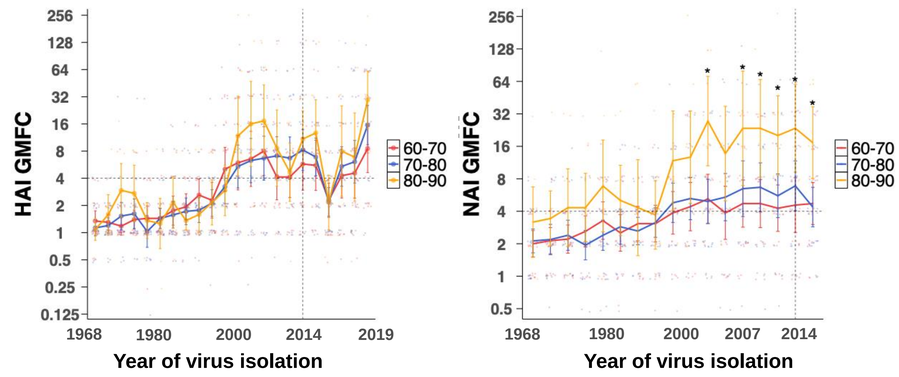
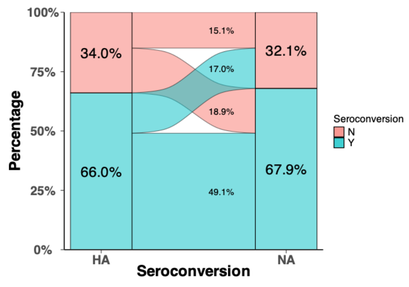


Fig. 6 Pre- and post-infection HAI and NAI antibody landscapes of H3(+) subcohorts against strains isolated from 1968 to 2019

5. **Absolute non-responders** were rare in this cohort. Conventional 'non-responders' show broad and back-boosted antibody responses to other targets.



Seroconversion rates to HK14

Fig. 7 Percentage of seroconversion to HA and NA of HK14. Seroconversion was defined as a four-fold increase in antibody titre.

Table 2. Seroconversion status of individuals who did not seroconvert to the HA of HK14

ID	Baseline HAI titre to HK14	HA of past and 'future' strains	NA of HK14	NA of past and 'future' strains
S1	80	Y	Y	Y
S4	80	Y	Y	Y
S45	80	N	N	N
S3	40	N	N	Y
S8	40	Y	Y	Y
S9	40	Y	N	N
S16	20	Y	N	N
S54	20	Y	Y	Y
S6	10	Y	N	Y
S14	10	N	Y	Y
S34	10	Y	Y	Y
S15	5	Y	Y	Y
S11	5	N	Y	Y
S12	5	Y	Y	Y
S13	5	Y	Y	Y
S24	5	Y	N	Y
S23	5	Y	Y	Y
S39	5	Y	N	Y
TOTAL	/	13	10	15

Conclusion

1. **HAI antibodies** were more **strongly associated** against infection than NAI antibodies.
2. A(H3N2) infections boosted **NAI titres a** **t HAI.**
3. The oldest age group was able to **mount robust antibo** **responses.**
4. **Absolute non-responders** were **rare** when examining the antibody repertoire.

Reference

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